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This page should only include the title of the manuscript, which should be carefully chosen to better reflect the contents of the study. No anusual abbreviations should be used in the title of the manuscript. A short title as running heading not exceeding 40 characters should be given which is desired to appear on top part of continuing pages when journal is published.

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Announcement

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Fetal Intracardiac Echogenic Focus in Pregnants Underwent Amniocentesis

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Abstract

Objective: It was aimed to define the frequency of intracardiac echogenic focuses in the fetuses with normal karyotype and with Down syndrome in our study population.

Methods: The intracardiac echogenic focuses obtained from second line USG are tested in the fetuses whom made amniocentesis and karyotyping because of the reasons like old maternal age, increased risks with in scanning tests, structural anomalies in the USG and family history.

Results: The 1,350 fetuses whom made karyotype analysis; 1,293 of the fetuses obtained with normal karyotype. Thirty-two of the fetuses diagnosed with Down syndrome, 10 of fetuses with trisomy 18, 6 of them with trisomy 13, 5 of them with Turner syndrome and 4 of fetuses are obtained with other aneuploidies. The frequency of fetal intracardiac echogenic focuses was found 2.4% with in normal fetuses,12.5% fetuses with in Down syndrome, 0% of fetuses with trisomy 18, 16.6% of fetuses with trisomy 13, 0% of fetuses with Turner syndrome and 4 fetuses having other karyotypes. The frequency of echogenic focuses was found higher significantly in fetuses with Down syndrome than the fetuses who have normal karyotype ($p<0.05$).

Conclusion: Although the frequency of fetal intracardiac echogenic focuses are seen to be higher in fetuses with Down syndrome by comparison with the fetuses which have normal karyotype, more studies must be performed to accept it as a marker.

Keywords: Fetal intracardiac echogenic focus, Down syndrome, karyotype analysis.

Amniosentez yapılan gebelerde fetal intrakardiak ekojenik odak

Amaç: Normal karyotipli ve Down sendromlu fetüslerde saptanan intrakardiak ekojenik odakların görülme sıklığını araştırmak.

Yöntem: lleri maternal yaş, tarama testlerinde risk artışı, ultrasonografide yapısal anomaliler, aile öyküsü gibi nedenler ile amniosentez ve karyotiplemesi yapılan fetüslerde 2. düzey ultrasonografide saptanan intrakardiak ekojenik odaklar değerlendirildi.

Bulgular: Karyotip analizi yapılan 1,350 fetüsun 1,293'ü normal, 32'si Down sendromu, 10'u trizomi 18, 6'sı trizomi 13, 5'i Turner sendromu, 4'ü de değişik anöploidi tanısı aldı. Fetal intrakardiak ekojenik odak normal karyotipli fetüslerde %2.4, Down sendromlularda %12.5, trizomi 18'de %0, trizomi 13'de %16.6, Turner sendromu ve 4 değişik anöploidili fetüste %0 oranında saptandı. Down sendromlu olgulardaki görülme oranı normal karyotipli fetüslerden anlamlı olarak yüksek bulundu ($p<0.05$).

Sonuç: Fetal intrakardiak ekojenik odak Down sendromlu olgularda normal karyotipli olgulara göre daha sık izlense de bir belirteç olarak kabul edilmesi için daha fazla çalışma yapılmalıdır.

Anahtar Sözcükler: Fetal intrakardiak ekojenik odak, Down sendromu, karyotip analizi.

Introduction

Frequency of chromosomal aberrations in newborn children is approximately 1 in 165.[1] Chromosomal aberrations increase as the mother's age increases. However, because only pregnant women over 35 are checked with screening tests, 80% of the fetal aneuploidies may be overlooked.[1,2] The evaluation of obstetric ultrasound findings in aneuploid diagnosis is used to detect risky pregnancies. The most common findings

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known as aneuploidy markers are echogenic intracardiac focus, echogenic bowel, shortness of long bones and renal pyelectasis. The detection of these soft markers increases the risk of trisomy.[21]

In this study, echogenic intracardiac focuses that were detected in normal fetuses and those with Down syndrome after carrying out amniocentesis and karyotyping for different reasons, have been examined and discussed.

Methods

It has been evaluated the cases which had invasive tests with the indications of advanced maternal age, increasing risk in screening tests, childbirth that has chromosomal aberrations before, family history and ultrasonographic indications such as structural anomalies and cases that were performed amniocentesis in the last 1.5 years in our hospital. Before the amniocentesis, level 2 ultrasound scan was performed to all pregnant women in their 16th to 20th week of pregnancy by the specialist physicians of our hospital. Echogenic intracardiac focuses and other pathologies that were detected by ultrasonographic examination were added into the computer records. The cases, whose karyotyping analysis was fully obtained after carrying out amniosynthesis, were taken into the scope of the study. The frequency rate of the fetal echogenic intracardiac focuses which are detected in fetuses with mainly Down syndrome and other chromosomal aberrations are compared with the fetuses with normal karyotype. The cases that karyotype analysis is not reached was excluded.

Chi-Square test was used in statistical evaluations.

Results

Normal chromosome structure was detected in 1,293 cases out of 1,350 after karyotyping analysis in our working group. Trisomy 21 was diagnosed in 32 cases (2.4 %). Echogenic intracardiac focus was detected in 39 out of 1,293 cases with normal karyotype by ultrasonographic scan. Echogenic intracardiac focus was detected in 4 % of the 32 cases with Down syndrome (12.5%). When the echogenic focus rates in fetuses with normal karyotype and Down syndrome are compared, a statistically significant difference was reported ($p<0.05$). Trisomy 18 was diagnosed in 10 cases. Echogenic intracardiac focus was not monitored in these cases. Trisomy 13 was diagnosed in 6 cases. Echogenic intracardiac focus was monitored in one of these cases (16.6%). Echogenic focus was not monitored in 5 Turner syndrome, 1 Klinefelter syndrome and 3 aneuploidy cases (Table 1).

Chromosomal aberration rate in total 44 fetuses, whose echogenic focuses are monitored, are calculated as 11.4 % (5 fetuses).

Discussion

In general, echogenic intracardiac focus is monitored in 2-5% of the fetuses.[3–5] Focus is usually monitored in the left ventricular, but it may occur in the right ventricular or in both. The focuses may be solitary or more and 95% of them vanish in the third trimester.[6]

Table 1. Karyotype and echogenic intracardiac focus results of 1,350 cases .

Karyotype analysis	n	Echogenic intracardiac focus	
		n	%
Normal karyotype	1,293	39	2.4
Down syndrome	32	4	12.5
Trisomy 18	10	0	0
Trisomy 13	6	1	16.6
Turner syndrome	5	0	0
Klinifelter syndrome	1	0	0
Pseudomosaicism of Y chromosome	1	0	0
47XI idic	1	0	0
46X(14) 46XY(56)	1	0	0

While some authors claim that echogenic focus is the marker of Down syndrome.[3,7,8] the others haven't found a relationship between the focus and Down syndrome.[4,7,9]

Brown et al. showed that the finding of an echogenic intracardiac focus at ultrasosonagrafy correlates with mineralization within a papillary muscle of the fetal heart.[10] Bromley et al. in 1995 reported a 4.9% incidence of EIF (echogenic intracardiac focus) among 1,334 fetuses studied. They also found that extremly high rate of 18% of fetuses with trisomy 21 had an EIF and that sonographic identification of an EIF had a fourfold increase risk of trisomy 21.[3] Petriskovsky et al. reported a 3.6% incidence of EIF in 1,139 patients, all of whom had a normal karyotype. The authors reported that they didn't detect any correlation between echogenic focus and adverse perinatal outcome.[6,11] EIF rate in our study was 2.4% among 1,293 fetuses with a normal karyotype at a similar rate in these studies.

Bromley et al. reported a 4.8% incidence of aneuploidy in 290 fetuses that had an EIF.[12] Chromosomal aberration rate in our study was 11.4% among 44 fetuses with EIF.

A meta-analysis conducted in 2001 by Smith-Bindman and friends determined that, (a total of 56 studies describing 1,930 fetuses with Down syndrome and 130,365 unaffected fetuses were included) when ultrasonographic markers were observed with structural malformations to detect Down syndrome, sensitivity for each one was 16% and when structural malformations were not observed, this rate was only 1%. Of the 5 studies in the meta-analysis that specifically looked at EIF, there were a total of 5,948 patients, 7.3% of whom had EIF. Authors suggested that in existance of intracardiac echogenic focus,if amniocentesis is offered in order to final exact diagnose of Down syndrome fetus,it is come up with that 2 in low risk group patient and 1 in high risk group of patient is going to be lost connection with amniocentesis complications.[13] In our study, there were a total of 32 Down syndrome cases, 12.5 % of whom had EIF, which was significantly higher than fetuses with a normal karyotype (2.4%). In trisomy 13 cases, this rate was extremly high rate of 16.6 % , but this marker was not observed in 10 cases with Trisomy 18. Roberts et al. reported a 16% incidence of EIF among Down syndrome cases and %2 incidence of EIF in the normal population.[5] Similarly, Bromley et al. detected a 18% incidence of EIF among Down syndrome cases and a 5% incidence of EIF among normal fetuses.[3]

Winter et al. evaluated 3,303 fetuses with an ultrasonograpic scan and karyotype analysis and determined that EIF was found in 4.6% of normal fetuses and 30% of fetuses with trisomy 21. The authors concluded that, an isolated echogenic intracardiac focus was associated with a 4.8 fold increase in relative risk for trisomy 21.[14]

Nyberg et al. evaluated the ultrasound findings in 186 fetuses with Down syndrome and 8.728 controls and they reported that EIF was the most common marker found among affected fetuses after exclusion of major anomalies (7.1%).[15] Rebarber et al. reported a 14.8% incidence of intracardiac fetus among 148 Japanese patients, whose maternal age was 30.7 on the average, but they didn't find any abnormal karyotypes.[16] These data are contradicted with idea of Bromley and Winter which says intracardiak focus trizomi 21 increases. This contradiction bring question mind; can we reach different result in ultrasonographic analysis in different societies or not.

Coco et al. evaluated 12,672 patients and detected 479 cases of echogenic focus; 90.4% of which were isolated. Eleven patients had fetuses with Down syndrome (%0.09), but only 3 of these had an echogenic focus. Up to statistical analysis; although the fetuses with an echogenic intracardiac focus have an increased risk of aneuploidy, amniocentesis need not be offered to patients who are otherwise at low risk and have an isolated echogenic intracardiac focus.[17] In another study that evaluated 62,111 patients and and found 2,223 echogenic intracardiac focus, Down syndrome was detected in 218 fetuses (0.4%). It is emphasized that the detection of isolated echogenic focus doesn't increase the risk of trisomy 21 for patients whose maternal age is younger than 35 years old.[18] In a study where intracardiac echogenic focus and multple echogenic focus are compared in terms of aneuploid risk, 6 (8.5%) patients with Down syndrome is found in 71 fetuses with multipl echogenic focus and 1 (0.6%) patient with Down syndrome is found in 171 fetuses with single echogenic focus.[19]

Conclusion

Echogenic intracardiac focus is monitored in Down syndrome cases more than normal karyotype cases, however more research should be done in order to detect EIF as the marker of Down syndrome.

References

1. Drugan A, Johnson MP, Evans MI. Ultrasound screening for fetal chromosome anomalies. *Am J Med Genet* 2000;90:98-107.
2. Hook EB. Cromosome abnormalities in older women by maternal age-evaluation of regression derived rates in chorionic villus biops specimens. *Am J Med Genet* 1990;35:184-7.
3. Bromley B, Lieberman E, Laboda L, Benaceraff BR. Echogenic intracardiac focus: a sonogrophic sing for fetal Down syndrome. *Obstet Gynecol* 1995;86:998-1001.
4. Merati R, Lovotti M, Norchi S, et al. Prevalence of fetal left ventricular hyperechogenic foci in a low risk population. *Br J Obstet Gynecol* 1996;103:1102-4.
5. Roberts DJ, Genest D. Cardiac histologic pathology choracteristic of trisomies 13 and 21. *Hum Pathol* 1992;23:1130-40.
6. Petrikovski BM, Challenger M, Wyse LJ. Natural history of echogenic foci within ventricles of the fetal heart. *Ultrasound Obstet Gynecol* 1995;5:92-4.
7. Simpson JM, Cook AC, Sharland GK. The significance of echogenic foci in the fetal heart: a prespective study of 228 cases. *Ultrasound Obstet Gynecol* 1996;8:225-8.
8. Sepulveda W, Cullen S, Nicolaidis P, et al. Echogenic foci in the fetal heart: a marker of chromosomal abnormality. *Br J Obstet Gynecol* 1995;102:490-2.
9. How HY, Villafane J, Parihus RR, Spinnato JA 2nd. Small hyperechoic foci of the fetal cardiac ventricle: a benign sonographic finding? *Ultrasound Obstet Gynecol* 1994;4:205-7.
10. Brawn DL, Roberts DJ, Miller WA. Left ventricular echogenic focus in the fetal heart: Pathologic correlation. *J Ultrasound Med* 1994;13:613-6.
11. Petrikovsky B, Challenger M, Gross B. Unusual appearances of echogenic foci within the fetal heart: are they benign? *Ultrasound Obstet Gynecol* 1996;8:229-31.
12. Bromley B, Lieberman E, Benacerraf BR. The incorporation of maternal age into the sonographic scaning index fort he detection at 14-20 weeks of fetuses with Down's syndrome. *Ultrasound Obstet Gynecol* 1997; 10:321-4.
13. Smith-Bindman R, Hosmer W, Feldstein VA, Deeks JJ, Goldbery JD. Second trimester ultrasound to detect fetuses with Down syndrome: a meta-analysis. *JAMA* 2001;285: 1044-55.
14. Winter TC, Anderson AM, Cheng EY, Komarniski CA, Souter VL, Uhnich SB, Nyberg DA. Echogenic intracardiac focus in second trimester fetuses with trisomy 21: usefulness as a US marker. *Radiology* 2000;216:450-6.
15. Nyberg DA, Souter VL, El Bastawissi A, Young S, Luthhardt F, Luthy DA. Isolated sonographic markers for detection of fetal Down syndrome in the second trimester of pregnancy. *Ultrasound Med* 2001;20: 1053-63.
16. Rebarber A, Levey KA, Funai E, Monda S, Paidas M. An ethnic predilection for fetal echogenic intracardiac focus identified during targeted midtrimester ultrasound examination: a retrospective review. *BMC Pregnancy Childbirth* 2004;4:12-6.
17. Coco C, Jeanty P, Jeanty C. An isolated echogenic heart focus is not an indication for amniocentesis in 12672 unselected patients. *J Ultrasound Med* 2004;23:489-96.
18. Shanks AL, Odibo AO, Gray DL. Echogenic intracardiac foci: associated with increased risk for fetal trisomy 21 or not? *J Ultrasound Med* 2009;28:1639-43.
19. Towner D, Gerscovich EO, Chiong BB, Morris LR, Mc Gahan JP. Comparison of single versus multiple echogenic foci in the fetal heart regarding risk of aneuploidy. *J Ultrasound Med* 2010;29:1061-7.

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Lamellar Body Count in Diabetic Pregnancies with Good Glycemic Control

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Abstract

Objective: To evaluate the influence of diabetes with strict glycemic control on fetal lung maturity in pregnancies by using lamellar body counts (LBC).

Methods: Twenty-two diabetic and 53 non-diabetic pregnant women were conducted to the study. The glucose levels were strictly controlled and kept within normal ranges in all the diabetic women. The mean LBC, the rate of low LBC, the rate of neonatal intensive care unit stay (ICU), the rate of respiratory need and the pregnancy outcome were compared between the diabetic and non-diabetic groups. LBC was accepted as low when it was fewer than 50,000/microl. The relation of low LBC with gestational age, presence of diabetes, administration of antenatal steroid, cord blood PH, base deficit, neonatal intensive care unit stay and need of respiratory support were analyzed.

Results: The mean age of women, characteristics of pregnancy and pregnancy outcome, antenatal corticosteroid administration rate, rate of neonatal intensive care unit stay and respiratory need were similar in the groups. The mean LBC and the rate of low LBC were also similar in the groups. There was no statistically significant relation between the risk of low LBC and the presence of diabetes, antenatal corticosteroid administration, cord blood PH, base deficit and need of respiratory support. The independent predictor of low LBC was found as the low gestational age (OR=0.693, 95% CI: 0.49-0.98, P=0.038). The relation of low LBC with the increased stay in neonatal intensive care unit became insignificant when its effect was analyzed together with the gestational age (OR=9.2; 95% CI: 0.947-88.95, p=0.056).

Conclusion: Lamellar body count, thus fetal lung maturity and the neonatal outcome was not altered in diabetic pregnancies with good glycemic control. The only independent predictor of low LBC was low gestational age.

Keywords: Lamellar body count, diabetes, lung maturity.

İyi glisemik kontrollü diyabetik gebelerde lamellar cisim sayımı

Amaç: Diyabetik gebelerde iyi glisemik kontrollün fetal akciğer matüritesi üzerine etkisini değerlendirmek.

Yöntem: Yirmi iki diyabetik ve 53 non-diyabetik gebe kadın prospektif olarak çalışmaya alındı. Tüm diyabetik olgularda sıkı glisemik kontrol yapıldı ve kapiller kan glikoz düzeyleri normal aralıklarda tutuldu. Ortalama lamellar cisim sayısı, düşük lamellar cisim sayısı oranları, yenidoğan yoğun bakım ihtiyacı oranları, ventilatör desteği ihtiyacı oranları ve gebelik ve neonatal sonuçlar diyabetik ve non-diyabetik gebeler arasında karşılaştırıldı. Lamellar cisim sayısı 50,000/microl'nin altında olan değerler "düşük lamellar cisim sayısı" olarak kabul edildi. Düşük lamellar cisim sayısı ile gebelik haftası, diyabet varlığı, antenatal kortikosteroid uygulanması, kord kanı pH, kord kanı baz açığı, yenidoğan yoğun bakım ihtiyacı ve ventilatör ihtiyacı arasındaki ilişki incelendi.

Bulgular: Olguların yaş ortalamaları, gebelik özellikleri ve gebelik sonuçları, antenatal kortikosteroid uygulanma oranları, yenidoğan yoğun bakım ihtiyacı oranları ve ventilatör desteği ihtiyacı oranları iki grupta benzerdi. Düşük lamellar cisim sayısı ile diyabet varlığı, antenatal kortikosteroid uygulanması, kord kanı pH ve kord kanı baz açığı ve solunum desteği arasında istatistiksel olarak anlamlı bir ilişki bulunmadı. Düşük lamellar cisim sayısı ile gebelik haftası arasında anlamlı bağımsız bir ilişki izlendi (OR=0.693, %95 CI: 0.49-0.98, P=0.038). Artmış düşük lamellar cisim sayısı riski ile artmış yenidoğan yoğun bakım ihtiyacı arasında anlamlı bir ilişki tespit edildi, ancak bu ilişkinin gebelik haftası ile birlikte incelendiğinde önemsizleştiği izlendi (OR=9.2; %95 CI: 0.947-88.95, p=0.056).

Sonuç: Bu çalışmada iyi glisemik kontrol yapılan gebelerde lamellar cisim sayısının, dolayısıyla fetal akciğer matüritesi ve neonatal sonuçların değişmediği bulundu. Bu olgularda düşük lamellar cisim sayısınınn sadece gebelik haftası ile ilişkili olduğu saptandı.

Anahtar Sözcükler: Lamellar cisim sayısı, diyabet, akciğer maturasyonu.

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Introduction

Diabetes mellitus with unfavorable maternal and fetal outcomes, is the most important endocrinology-metabolic disorder that can complicate pregnancy. The most important complications of diabetes in pregnancy are macrosomia (27%), prematurity (21%) and perinatal mortality (2.7%).[1] In a study of high risk pregnancies the rate of Respiratory Distress Syndrome (RDS) was found as 44.2% of which 17.4% belonged to diabetic pregnancies.[2] After Gluck and Kulovich showed that the diabetes delayed fetal lung maturation, the timing of delivery became an important problem in the management of pregnant women with diabetes.[3,4] Therefore in diabetic pregnancies, to determine the timing of delivery, biochemical evaluation of the fetal lung maturity became the main clinical management, especially when the gestational age cannot be determined.

To determine the fetal lung maturity several biochemical tests like lecithin/sphingomyelin ratio,[3] phosphatidyl glycerol,[4] foam stability test,[5] OD650[7] and lamellar body count (LBC)[8] can be used. The accuracy of lecithin/sphingomyelin or phosphatidyl glycerol in determining fetal lung maturity is high.[9,10] However these tests are technically complex and costly tests and therefore cannot be performed in most of the centers. LBC has cost advantage and technically simple that can be performed by all the centers that can do the cell counting.[11] In addition LBC was shown as accurate as the commercial phospholipid analysis in predicting the fetal lung maturity.

The aim of the current study is to determine the impact of diabetes on fetal lung maturity in diabetic pregnancies with good glycemic control compared to non-diabetic pregnancies, via lamellar body count in amniotic fluid.

Methods

Between the dates January 2010 and September 2010, diabetic pregnant women treated and followed-up in the Obstetrics and Gynecology and Endocrinology clinics of Inonu University School of Medicine were conducted prospectively to our case control cohort study without randomization. Healthy pregnant women with no medical condition who were followed-up for antenatal care by the obstetrics policlinic were conducted to the study as the control group. A power analysis was performed by using the data reported in the publications and necessary sample size in each group was found as 22 when the desired significance level was set at .05 (α) and power was set at 0.8 (1-β). Therefore 22 and 53 cases were enrolled to diabetic and non-diabetic groups, respectively.

Blood glucose levels of diabetic pregnant women were measured via a capillary blood glucose monitorization system (glycometer). To meet the desired glycemic goals, cases were treated with either case specific diabetic diet or insulin when the diabetic diet was not sufficient. The treatment goal were to meet the capillary blood glucose levels of ≤95 mg/dl on fasting, ≤120 mg/dl on 2nd hour postprandial and >60 mg/dl (3.3 mmol/l) on all occasions.[13] Therefore a good glycemic control was accomplished with keeping the glucose levels within the objective ranges.

From each case a 2 ml of amniotic fluid and 1 ml of cord blood was collected to EDTA containing test tube and heparin washed syringe, respectively. Amniotic fluid was collected with a syringe before amniotic membrane was ruptured to prevent blood contamination. Amniotic fluid samples were analyzed without centrifugation with a cell counter (Coulter LH 780 Hematolgoy Analyzer, Beckman, CA-USA) for platelet number and therefore for the LBC. Cord blood was analyzed with a blood gas analyzer ((Rapidlab 348, Siemens, Deerfield-USA) for pH and base deficit. All of the newborns were examined by a pediatrician and were hospitalized to neonatal intensive care unit if needed. The cut off value of LBC in predicting fetal lung maturity was found as ≥50,000 /microl in recent studies.[1] Therefore we accepted the LBC values under 50,000 /microl as "low LBC".

The mean maternal age, gestational age, gravidity (G), parity (P), abortus (A), live (L), rate of corticosteroid administration, mean LBC, rate of low LBC, mean birth weight, need for neonatal intensive care unit stay, need for ventilator support, mean cord blood pH and mean base deficit were compared between the diabetic and non-diabetic groups. In all cases the relation of the low LBC with gestational age, presence of gestational diabetes mellitus, administration of antenatal steroid, cord blood PH, base deficit, neonatal

intensive care unit stay, need of respiratory support were analyzed.

Statistical Analysis

The data was analyzed using the Statistical Package for Social Sciences soft-ware 15.0 (SPSS, Inc., Chicago, IL, USA). The mean values were compared with the Mann Whitney-U test and the rates were compared with the Pearson chi-square test. Binomial regression analysis was conducted to find out the relation of low lamellar body count with gestational age, presence of gestational diabetes mellitus, administration of antenatal steroid, cord blood PH, base deficit, neonatal intensive care unit stay, need of respiratory support. The related factors were re-analyzed in multinomial regression analyses to find out the independently related factor.

Results

The mean age of women, characteristics of pregnancy and pregnancy outcome other than birth weight, antenatal corticosteroid administration rate, rate of neonatal intensive care unit stay and respiratory need were similar in the diabetic and non-diabetic groups. The mean birth weight was significantly greater in diabetic group compared to non-diabetic group (3005.9±589.1 gr and 2625.3±720.9 gr, P=0.023). The mean LBC and the rate of low LBC were similar in the diabetic and non-diabetic groups (Table 1). We did not find a significant relation between the risk of low LBC and the presence of diabetes, antenatal corticosteroid administration, cord blood pH, base deficit and need of respiratory support. The risk of low LBC decreased with increasing gestational week (OR=0.597; 95% CI: 0.443-0.806, p=0.001). The low LBC was also related with the increased stay in neonatal intensive care unit (OR=30.2; 95% CI: 3.7-246.8, P=0.001). However the relation of the latter became insignificant when its effect was analyzed together with the gestational age, in the multinomial regression analysis (OR=9.2; 95% CI: 0.947-88.95, p=0.056). The independent predictor of low LBC was found as the low gestational age (OR=0.693, 95% CI: 0.49-0.98, P=0.038).

Discussion

In our study, we found that LBC, low LBC ratio and neonatal results were similar in diabetic patients with good glycemic control and normal control subjects. Although the mean gestational age was similar to non-diabetic group and the fasting and postprandial blood glucose levels were kept below the cut off levels, the mean birth weight was significantly greater in diabetic group compared to non-diabetic group. However none of the cases had birth weight greater than 90th percentile according to the gestational age. In our

Table 1. Characteristics of pregnancy and pregnancy outcome.

	Diabetics (n=22)	Non-diabetics (n=53)	P
Age (year)	32.6±6.1	30.3±6.2	0.148
G	3.1±2.4	2.8±1.8	0.881
P	1.7±1.9	1.4±1.4	1
A	0.5±0.9	0.3±0.7	0.388
Live	1.3±1.6	1.4±1.4	0.389
Gestational age (week)	37.0±2.2	36.2±3.4	0.431
Corticosteroid administration rate (%)	13.6	17	0.719
LBC microl.	67,140±54,412	67,720±58,384	0.705
Low LBC rate (%)	59.1	54.7	0.728
Birth weight (gr)	3005.9±589.1	2625.3±720.9	0.023
Cord blood PH	7.28±0.08	7.32±0.07	0.067
Cord bloodbase deficit	-4.7±5.2	-5.2±3	0.518
Neonatal intensive care unit stay (%)	27.3	17	0.310
Respiratory need (%)	4.6	7.6	0.635

Data is given in mean±standard deviation or percentage.

clinic fasting blood glucose levels are kept at or below 95 mg/dl and postprandial 2nd hour blood glucose level are kept at or below 120 mg/dl. However HAPO study found the fetal weight and macrosomia risk increased with increasing blood glucose levels even for the levels below the cut off values.[14] Therefore the finding of us and HAPO study support the need of a re-evaluation of cut off values for blood glucose levels in diabetic pregnancies with further studies.

It is known that diabetes mellitus can worsen neonatal results, delay fetal lung maturation and increase RDS risk.[3 4,15,16] However it was previously shown that the increase in risk was due to high maternal glucose level and in diabetic pregnant women with good glycemic control the perinatal and neonatal risks were similar to non-diabetic pregnant women.[17] High RDS incidence in diabetic pregnancies was shown to be decreased with advanced neonatal care, accurate calculation of fetal age with early fetal ultrasonography and good glycemic control.[18] It was found that, especially good glycemic control in diabetic patients equalized the RDS frequency with normal pregnancies.[19] However fetal lung maturation can delay in diabetic pregnancies with bad glycemic control.[20]

Lamellar body count became popular because of its technical ease, low cost, fast result, and accurate prediction of fetal lung maturity.[11] However in different studies different cut-off values were used to determine fetal lung maturity. Although in Dubin et al.'s study it was shown that the fetal lung was mature for LBC >26,000/microl, Lewis et al. found that LBC >32,000/microl predicted a mature L/S ratio and PG levels in 99% of cases.[8,11] The reason of different cut-off values may be different cell counting devices used in these studies. Askwod et al. documented in 1993 that in a series of 247 cases whose LBC were higher than 48,000/microl none of infants developed RDS.[21] Also in recent studies the fetal lung was assumed as mature, in pregnancies with amniotic fluid LBC more than 50,000/microl.[1] Because of these recent literatures we took 50,000/microl as cut-off value for our study.

In our study we found that low LBC ratio was found similar both in diabetic and non-diabetic pregnant women. We found the low LBC risk increased with the decreasing gestational week and was related to increased neonatal intensive care unit stay. However when the data was controlled for the gestational age, the relation between the low LBC and the neonatal intensive care unit stay disappeared. Also no relationship was found between low LBC risk and the presence or absence of diabetes in both diabetic patients with good glycemic control and non diabetic patients. This finding proved that the need for neonatal intensive care unit was related to the deceasing gestational age and showed that the fetal lung maturity in diabetics with good glycemic control was similar to non-diabetics. Gluck et al. also showed that the fetal lung maturity occurred in similar gestational ages in diabetic pregnants with good glycemic control and non-diabetic pregnants.[3]

Conclusion

In the current study lamellar body count, thus fetal lung maturity and the neonatal outcome was found not altered in diabetic pregnancies with good glycemic control. The only independent predictor of low LBC was low gestational age. With concordance to prior literature adequate glucose control seems to lower the risk of fetal pulmonary immaturity to that seen in the non-diabetic population. With the current data, in euglycemic, metabolically controlled diabetic patients fetal lung maturation is not delayed and therefore routine fetal lung maturation testing might be abandoned in term pregnancies of diabetic mothers.

References

1. Piazze JJ, Anceschi MM, Maranghi L, Brancato V, Marchiani E, Cosmi EV. Fetal lung maturity in pregnancies complicated by insulin-dependent and gestational diabetes: a matched cohort study. *Eur J Obstet Gynecol Reprod Biol* 1999;83:145-50.
2. Abd El Aal DE, Elkhirshy AA, Atwa S, El-Kabsh MY. Lamellar body count as a predictor of neonatal lung maturity in high-risk pregnancies. *Int J Gynaecol Obstet* 2005;89:19-25.
3. Gluck L, Kulovich MV, Borer RC Jr, Brenner PH, Anderson GG, Spellacy WN. Diagnosis of the respiratory distress syndrome by amniocentesis. *Am J Obstet Gynecol* 1971;109:440-5.
4. Kulovich MV, Gluck L. The lung profile: II. Complicated pregnancy. *Am J Obstet Gynecol* 1979;135:64-70.
5. Sher G, Statland BE. Assessment of fetal pulmonary maturity by the Lumadex Foam Stability Index Test. *Obstet Gynecol* 1983;61:444-9.

6. Tait JF, Foerder CA, Ashwood ER, Benedetti TJ. Prospective clinical evaluation of improved fluorescence polarization assay for predicting fetal lung maturity. *Clin Chem* 1987;33:554-8.
7. Turner RJ, Read JA. Practical use and efficiency of amniotic fluid OD 650 as a predictor of fetal pulmonary maturity. *Obstet Gynecol* 1983;61:551-5.
8. Dubin SB. Characterization of amniotic fluid lamellar bodies by resistive-pulse counting: relationship to measures of fetal lung meturity. *Clin Chem* 1989;35:612-616.
9. Higuchi M, Hirano H, Gotoh K, Otomo K, Maki M. Comparison of amniotic fluid disaturated phosphatidylcholine, phosphatidylglycerol and lecithin/sphingomyelin ratio in predicting the risk of developing neonatal respiratory distress syndrome. *Gynecol Obstet Invest* 1990;29:92-6.
10. Tsao FH, Zachman RD. Use of quantitative amniotic fluid phosphatidylglycerol as a criterion for fetal lung maturation. *Am J Perinatol* 1992;9:34-7.
11. Lewis PS, Lauria MR, Dzieczkowski J, Utter GO, Dombrowski MP. Amniotic fluid lamellar body count: cost-effective screening for fetal lung maturity. *Obstet Gynecol* 1999;93:387-91.
12. Neerhof MG, Haney EI, Silver RK, Dohnal JC, Ashwood ER, Lee IS. Lamellar body counts are preferable to traditional phospholipid analysis as a primary assay for fetal lung maturity. *Am J Obstet Gynecol* 2000;182:S60.
13. Gabbe SG, Graves CR. Management of diabetes mellitus complicating pregnancy. *Obstet Gynecol* 2003;102: 857–68.
14. HAPO Study Cooperative Research Group. Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med* 2008;358:1991-2002.
15. Piper JM, Langer O. Does maternal diabetes delay fetal pulmonary maturity. *Am J Obstet Gynecol* 1993;168:783-6.
16. Ferroni KM, Gross TL, Sokol RJ, Chik L. What affects fetal pulmonary maturation during diabetic pregnancy. *Am J Obstet Gynecol* 1984;150:270-4.
17. Piper JM. Lung maturation in diabetes in pregnancy: if and when to test. *Semin Perinatol* 2002;26:206-9.
18. Livingston EG, Herbert WN, Hage ML, Chapman JF, Stubbs TM. Use of the TDx-FLM assay in evaluating fetal lung maturity in an insulin-dependent diabetic population. The Diabetes and Fetal Maturity Study Group. *Obstet Gynecol* 1995;86:826-9.
19. Mimouni F, Miodovnik M, Whitsett JA, Holroyde JC, Siddiqi TA, Tsang RC. Respiratory distress syndrome in infants of diabetic mothers in the 1980s: no direct adverse effect of maternal diabetes with modern management. *Obstet Gynecol* 1987;69:191-5.
20. Ylinen K. High maternal levels of hemoglobin A1c associated with delayed fetal lung maturation in insulin-dependent diabetic pregnancies. *Acta Obstet Gynecol Scand* 1987;66:263-6.
21. Ashwood ER, Palmer SE, Taylor JS, Pingree SS. Lamellar body counts for rapid fetal lung maturity testing. *Obstet Gynecol* 1993;81:619-624.

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Retinal Findings in Cases of Preeclampsia

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Abstract

Objective: In this study, we aimed to investigate the ophthalmological findings in the patients hospitalized and treated for a diagnosis of preeclampsia during last 5 years in Department of Obstetrics and Gynecology, Faculty of Medicine, Yuzuncu Yil University.

Methods: Records of 193 patients hospitalized due to preeclampsia and consulted Ophthalmology Department between September 2005 and 2010 were searched retrospectively. We could find 148 of those.

Results: The most common complaints were headache, epigastric pain, blurred vision. The ophthalmological findings of 98 patients were assessed as normal while 50 of those were pathologic. Hypertensive retinopathy, bilateral, right and left retinal detachment were detected in 24, 4, 3, 1 of 50 patients who had pathological ophtalmologic findings, respectively.

Conclusion: Findings of retinal detachment, hypertensive retinopathy and hemorrhage may be detected in patients independent of severity of preeclampsia while maculopathy and macular edema might be found more often in the patients with severe preeclampsia.

Keywords: Preeclampsia, ophtalmological findings, retinal detachment.

Kliniğimizdeki preeklampsi olgularına ait göz dibi bulgularının araştırılması

Amaç: Bu çalışmada, Yüzüncü Yıl Üniversitesi Tıp Fakültesi Kadın Hastalıkları ve Doğum Kliniği'nde son 5 yılda preeklampsi tanısıyla takip ve tedavileri yapılmış hastaların göz dibi bulgularının incelenmesi amaçlanmıştır.

Yöntem: Eylül 2005 ile Eylül 2010 tarihleri arasında, Yüzüncü Yıl Üniversitesi Tıp Fakültesi Hastanesi Kadın Hastalıkları ve Doğum Kliniği'nde preeklampsi tanısıyla hospitalize olan ve göz konsültasyonu istenen 193 hastanın kayıtları retrospektif olarak incelenmiş ve 148' inin göz dibi muayene bulgularına ulaşılabilmiştir.

Bulgular: Göz dibi muayenesi yapılan hastalarda en sık baş ağrısı, epigastrik ağrı, bulanık görme ve gözlerde sinek uçuşması şikayetlerine rastlanılmıştır. Doksan sekiz hastanın göz dibi muayenesi normal olarak değerlendirilirken 50 hastanınkinde patolojik bulgular saptanmıştır. Patolojik göz dibi muayenesi olan 50 hastanın 24'ünde hipertansif retinopati, 4'ünde bilateral retina dekolmanı, 3'ünde sağ retina dekolmanı ve 1'inde sol retina dekolmanı görülmüştür.

Sonuç: Retina dekolmanı, hipertansif retinopati ve hemoraji bulguları preeklampsi şiddetinden bağımsız olarak hastalarda tespit edilebilmekle birlikte makülopati ve makülada ödeme, şiddetli preeklamptik hastalarda daha fazla rastlanılabilir.

Anahtar Sözcükler: Preeklampsi, göz dibi bulguları, retina dekolmanı.

Introduction

Preeclampsia is characterized by hypertension (140/90 mmHg and above) and proteinuria (300 mg/day) which appear after 20th gestational week. It can be seen about 5-10% of all pregnancies, especially frequent in primipare.[1,2]

Preeclampsia affects all organs and systems including eyes.[3] Visual symptoms are photopsia, hemianopsia, unexpected focusing deficiency, blurred vision, decrease in vision, and complete blindness in severe cases.[4,5] Although visual defects develop in 25% of severe preeclamptic

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women, complete blindness is rare in these patients and the incidence is between 1% and 3%[4,5,6] However, Cunningham et al. reported that blindness is more prevalent and the incidence is about 15%[5,7,8] This blindness may be caused by occipital cortex or retina involvement.[9] There are retinal vascular changes in 30-100% of preeclampsia cases. The most frequent ocular change is the vasoconstriction of retinal arterioles. Exudative retinal detachment caused by the involvement of choroidal vascularization is a rare reason for vision loss in preeclampsia syndrome[3]. It affects 1-2% of patients with preeclampsia and it is frequently bilateral and serous. Full recovery after delivery by clinical management is observed within a few weeks in patients who have serous detachment during pregnancy, and any surgical intervention is not required.[10]

In this study, we aimed to investigate the ophthalmological findings in the patients hospitalized and treated for a diagnosis of preeclampsia during last 5 years in Department of Obstetrics and Gynecology, Faculty of Medicine, Yüzüncü Yıl University.

Methods

Records of 193 patients hospitalized in Department of Obstetrics and Gynecology, Faculty of Medicine, Yüzüncü Yıl University due to preeclampsia and asked eye consultation between September 2005 and 2010 were reviewed retrospectively and retinal findings of 148 patients could be reached. Statistical evaluation was performed by Fisher's exact test and p value lower than 0.05 was statistically accepted as significant.

Results

The youngest patient was 18 years old while the oldest one was 47 years old. Mean age was 30 and mean gestational week was 32. Average systolic and diastolic blood pressures of patients were measured as 174/107 mmHg. Proteinuria amount in 24 hours of urine was found as 3,809.14 mg/l/day. While 111 patients were delivered by cesarean and 62 patients were delivered by normal spontaneous vaginal method, 20 patients were dispatched or taken to another center during follow-up.

The most common complaints of patients were headache, epigastric pain, and blurred vision and floating specks in vision. Retinal findings of only 148 of 193 patients could be reached. While retinal examinations of 98 patients were evaluated as normal, pathological findings were detected in 50 patients. The most pathological retinal finding was found as hypertensive retinopathy and the relation between pathological retinal finding and preeclampsia severity was summarized in Table 1. Establishing retinal detachment, hypertensive retinopathy and hemorrhage as retinal finding was found as independent from preeclampsia severity ($p>0.05$). Edema and maculopathy in macula or papilla was found more in patients diagnosed severe preeclampsia than those with mild preeclampsia ($p=0.01$).

Discussion

Vision system of 30-100% of preeclamptic patients may be affected.[10] Symptoms related with vision in preeclampsia include decrease in vision, photophobia and hemianopsia. The most prevalent 3 vision complications seen in preeclampsia

Table 1. The distribution of preeclamptic patients diagnosed pathological retinal finding.

Retinal finding	Severe preeclampsia (n)	Mild preeclampsia (n)	Total (n)	p
Hypertensive retinopathy	13	11	24	0.56
Edema in macula or papilla	5	0	5	0.01*
Hypertensive hemorrhage	4	1	5	0.21
Retinal detachment	5	3	8	0.62
Pigment epithelium detachment	1	0	1	-
Maculopathy	5	0	5	0.01
Degenerative fundus + myopic crescent	0	1	1	-
Left abducent paralysis	1	0	1	-
Nulliparity	46.8%	29.3%	0.0019	

are hypertensive retinopathy, exudative retinal detachment and cortical blindness. Possible reasons of these complications are coexisting or existing systemic vascular disease, hormonal changes, endothelium damage, abnormal autoregulation, hypoperfusion ischemia and hypoperfusion edema.[5]

In our study, it was found that visual systems of 33.7% of preeclamptic patients were affected. While the most frequent complaint in these patients are floating specks in vision, blurred vision and decrease in vision, the most frequent complications are hypertensive retinopathy and retinal detachment.

Hypertensive retinopathy is seen in 60% of patients and it is the most frequent ocular complication of preeclampsia and eclampsia.[11] It may be related with secondary changes such as focal arteriolar spasm and diffuse retinal edema, hemorrhage, exudate and infarcts in nerve fiber.[12] Arteriolar constriction is reversible in most of the patients.[13] In our study, hypertensive retinopathy was detected in 48% of patients with pathological retinal finding.

Another complication seen in preeclamptic patients is retinal detachment and its incidence is 1-2%. It was observed that 10% of patients with retinal detachment were eclamptic. It may occur before or after delivery and it is frequently bilateral, bullous, and serous and generally vascular changes of preeclampsia are not observed. Intensive arteriolar vasospasm secondary choroidal ischemia is held responsible for the development of retinal detachment. Choroidal vascular failure may cause lesions in retinal pigment epithelium, fluid transudation, and crescendo focal retinal detachment. Full recovery after delivery by clinical management is observed within a few weeks in patients who have serous retinal detachment during pregnancy, and any surgical intervention is not required. However, some macular sequelas in pigment epithelium may persist.[10]

In our study, we detected retinal detachment in 16% of patients together with hypertensive retinopathy, edema and hemorrhage. The most frequent complaint in these patients was vision loss and 5 of them were diagnosed as preeclamptic. Mean blood pressure value of severe preeclamptic patients was 174/110 mmHg and mean proteinuria amount in 24 hours of urine was 5.5 g/day. It was seen that all patients detected as having retinal detachment did not have antenatal follow-up and they applied to the hospital with a severe clinical situation. As a result of eye examination, bilateral retinal detachment was found in 4 patients, right retinal detachment was found in 3 patients, and left retinal detachment was found in one patient. In the fundus examinations of these patients, severe hypertensive retinopathy diagnoses were not observed in retinal arterial structures and generally all of them were told that their tensions should be taken under control. Systemic steroid treatment in 1 mg/kg dose was initiated only in one case. It was seen in these patients that retinal detachment underwent resolution by the recovery of preeclampsia after delivery. All of the patients were dispatched by reducing their visual problems and no surgical intervention was needed for averagely 6 months of follow-up period in the Eye Polyclinic.

Visual loss caused by cortex part of optic tracts may rarely appear in preeclampsia cases. Therefore, fundus examination and pupil reflex seem normal in these patients. The reasons of cortical visual loss are petechial bleeding, ischemia or focal edema and they are generally irreversible. It regresses by anti-hypertensive and anti-edema treatments in most of the patients. In this study, we did not observe any acute cortical blindness in our cases.[14].

Conclusion

In the case of visual complaints in preeclamptic patients, other retinal findings may also be observed other than hypertensive retinopathy. Retinal detachment, hypertensive retinopathy and hemorrhage findings can be observed in patients independent of preeclampsia severity, but maculopathy and edema in macula can be seen in severe preeclamptic patients more frequently. More study series reviewing preeclampsia severity and pathological retinal findings are required.

References

1. Fodor A, Gyorffy A, Orosz L, Major T. Hemorheological changesand their clinical revelance in in preeclampsia. *Orv Hetil* 2011;152:205-11.

2. Yılmaz A, Pata Ö, Öz Ö, Yıldırım Ö, Dilek S. Preeklampside iki taraflı seröz retina dekolmanı. *Retina-Vitreus* 2005;13:307-10.
3. Mihu D, Mihu CM, Talu S, Costin N, Ciuchina S, Malutan A. Ocular changes in preeclampsia. *Ophthalmologia* 2008;52:16-22.
4. Jyotsana, Sharma AK, Bhatt S. Reversible blindness in severe preeclampsia and eclampsia. *JK Science* 2004;6:43-5.
5. Bona M, Wong A. The eyes in pregnancy. *Ophthalmology Rounds* 2007;5(3). http://www. ophthalmologyrounds.ca (baskıda).
6. Swende TZ, Abwa T. Reversible blindness in fulminating preeclampsia. *Annals of African Medicine* 2009;8:189-91.
7. Tung CF, Peng YC, Chen GH, Chow WK, Yang DY, Hu WH. Hemolysis, elevated liver enzymes and low platelet count (HELLP) syndrome with acute cortical blindness. *Chin Med J (Taipei)* 2001;64:482-5.
8. Cunningham FG, Fernandez CO, Hernandez C. Blindness associated with preeclampsia and eclampsia. *Am J Obstet Gynecol* 1995;172:1291-8.
9. Llovera I, Roit Z, Johnson A, Sherman L. Cortical blindness, a rare complication of pre-eclampsia. *J Emerg Med* 2005;29:295-7.
10. Prado RS, Figueiredo EL, Magalhaes TV. Retinal detachment in preeclampsia. *Arq Bras Cardiol* 2002;79:183-6.
11. Schultz K, Birnbaum A, Goldstein D. Oculer disease in pregnancy. *Curr Opin Ophthalmol* 2006;16:308-14.
12. Tadin I, Bojic L, Mimca M, Karelovic D, Dogas Z. Hypertensive retinopathy and pre-eclampsia. *Coll Antropol* 2001;25:77-81.
13. Sunness J. The pregnant woman's eye. *Surv Ophthalmol* 1988;32:219-38.
14. Köken G, Yaman M, Yılmazer M, Oruç S. Ağır preeklampside akut görme kaybı. *Tıp Araştırmaları Dergisi* 2007:5:36-8.

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The Relationship Between Elevated Maternal Uric Acid Level and Bilateral Early Diastolic Notching at Uterine Arteries at Second Trimester and Pregnancy Complications

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Abstract

Objective: The aim of this study was to evaluate the relationship between maternal uric acid level, abnormal uterine artery waveform at second trimester and adverse pregnancy outcome.

Methods: We evaluated 319 women with Doppler sonography at 20-26 weeks of gestation. The presence of early diastolic notching at uterine arteries and maternal serum uric acid levels were determinated. Pregnancy induced hypertension was defined as new-onset elevated blood pressure ≥140 mmHg systolic or ≥90 mm/Hg diastolic after 20 weeks of gestation. Small for gestational age was defined as birth weight <10th centile. Delivery <37 weeks was termed as preterm.

Results: The number of cases with PIH, SGA and preterm delivery were significantly higher in the group of bilateral notching (n: 145). In cases with bilateral notching mean uric acid level was significantly higher (3.08±0.88 versus 2.58±0.76 mg/dl). The number of the cases which developed PIH (P=0.016), small for gestational age- birth weight (P=0.0013) and fetal demise (P=0.02) were higher in the highest quartile of uric acid level (>3.4- 6.2 mg/dl). Maternal serum level of uric acid showed significant negative correlation with birth weight (r:-0.24; 95% confidence interval for r: -0.34 to-0.14, P<0.0001). Using >3.4mg/dl as a cut off value for uric acid level we could detect the cases with pregnancy induced hypertension with a sensitivity of 40.4%, specificity 79.8%, and small for gestational age birth weight with a sensitivity of 44.2%, specificity 80.45%.

Conclusion: The presence of bilateral notching at uterine arteries at second trimester is related with pregnancy induced hypertension, small for gestational age, preterm delivery and elevated maternal uric acid level. Maternal serum uric acid level at second trimester may be used in the prediction pregnancy induced hypertension and small for gestational age birth weight.

Keywords: Uric acid, Doppler ultrasonography, pregnancy induced hypertension, Small for gestational age, fetal demise.

İkinci trimester yüksek maternal ürik asit değerlerinin uterin arterlerde bilateral erken diyastolik çentiklenme mevcudiyeti ve gebelik komplikasyonları ile ilişkisi

Amaç: Bu çalışmanın amacı ikinci trimester maternal ürik asit değeri ile anormal uterin arter dalga formunun kötü gebelik sonucu ile ilişkisini araştırmaktır.

Yöntem: Doppler ultrasonografi ile 319 gebeyi 20-26. gebelik haftaları arasında değerlendirdik. Uterin arterlerde erken diyastolik çentiklenme mevcudiyeti ve maternal serum ürik asit değerleri belirlendi. Gebeliğe bağlı hipertansiyon, 20. gebelik haftasından sonra yeni ortaya çıkan, sistolik ≥140 mmHg ve diyastolik ≥90 mmHg kan basıncı olarak tanımlandı. Doğum kilosu <10. persatilde olanlar gebelik haftasına göre küçük kabul edildi. Doğumda <37. Gebelik haftasında olanlar preterm olarak tanımlandı.

Bulgular: Bilateral çentiklenme bulunan (n:145) grupta gebeliğe bağlı hipertansiyon, gebelik haftasına göre küçük ve erken doğum olgularının sayısı anlamlı olarak yüksekti. Bilateral çentiklenme bulunan olgularda ortalama ürik asit değeri anlamlı olarak yüksekti (3.08±0.88'e karşılık 2.58±0.76 mg/dl). Ürik asit değerleri en yüksek olan dörtte birlik grupta (>3.4-6.2 mg/dl) PIH (P=0.016), SGA doğum kilosu (P=0.0013) ve fetal kayıp (P=0.02) gelişen olguların sayısı anlamlı olarak yüksekti. Maternal serum ürik asit değeri doğum kilosu ile anlamlı negatif korelasyon göstermekte idi (r:-0.24; %95 güven aralığı (-0.34-0.14), P<0.0001). Ürik asit değeri >3.4

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mg/dl sınır olarak alındığında gebeliğe bağlı hipertansiyon olguları %40.4 duyarlılık, %79.8 özgüllük ve SGA doğum kilosu %44.2 duyarlılık, %80.45 özgüllük ile tespit edilebildi.

Sonuç: Uterin arterde ikinci trimesterde bilateral çentiklenme mevcudiyeti gebeliğe bağlı hipertansiyon, gebelik haftasına göre küçük, preterm doğum ve yüksek ürik asit değerleri ile ilişkilidir. İkinci trimester maternal serum ürik değerleri gebeliğe bağlı hipertansiyon, gebelik haftasına göre küçük yenidoğanların öngörüsünde değerli olabilir.

Anahtar Sözcükler: Ürik asit, Doppler ultrasonografi, PIH, SGA, fetal kayıp.

Introduction

Pre-eclampsia and intrauterine growth restriction are important obstetrical complications which are suggested to be caused by impaired placentation. The failure to undergo physiological vascular changes is reflected by the high impedance to the blood flow at uterine arteires. Uterine artery Doppler screening identifies women at high risk for developing complications.[1] Combinations of biochemical and ultrasonographic markers might improve the predictive performance of single markers.[1-4]

Increased uric acid levels generally precedes the onset of hypertension and proteinuria in preeclampsia.[5] Hyperuricemia in pregnant women without proteinuria is at least as good a predictor of fetal morbidity as hypertension and proteinuria.[6] Postpartum normalization of blood pressure in preeclamptics has also been shown to be directly related to uric acid levels.[7] It has been speculated that uric acid may play direct roles in the pathological processes of preeclampsia at both the level of the placenta and maternal vasculature.[8]

The aim of this study was to evaluate the relationship between maternal uric acid level, abnormal uterine artery waveform at second trimester and pregnancy induced hypertension (PIH), small for gestational age (SGA) birth weight, preterm delivery and fetal demise.

Methods

Study Design and Population

Between January 2009 and February 2010, women attending for second trimester anomaly screening at 20-26 weeks of gestation were enrolled in the study. Baseline demographic information and medical history were collected. A total of 360 cases with a singleton pregnancy without preexisting diabetes, hypertension, renal disease or major fetal anomalies were examined with transabdominal Doppler ultrasonography (Logic 400). The presence or absence of early diastolic notching at uterine arteries was noted for both sides.

All of the women were asked to provide blood samples for the investigation of serum uric acid levels at the day of examination. Uric acid was measured using an uricase based colorimetric assay (Architect C16000) with a lower detection limit of 1mg/dl.

Pregnancy induced hypertension (PIH) was defined as new-onset elevated blood pressure ≥140 mmHg systolic or ≥90 mm/Hg diastolic after 20 weeks of gestation. Normotensive women were those without gestational blood pressure elevations. Neonatal outcomes assessed included birth weight and birth weight centile. Small for gestational age (SGA) was defined as birth weight <10th centile. Gestational age was determined by obstetrical assessment, using early ultrasound data where available. Delivery <37 weeks was termed as preterm and <28 weeks severe preterm.

Statistical Analysis

The collected data were analysed with use of the MedCalc for Windows, version 8.1.00 (MedCalc Software, Mariakerke, Belgium). Data were presented as means ± standard deviations or numbers of subjects and percents. Student's t-test was used for continuous variables and Chi-square test or Fisher exact test for categorical variables , while one-way ANOVA was used to compare the variables of four groups. Correlation between maternal uric acid level and birth weight was assessed by Pearson's correlation coefficient. The efficiency of serum uric acid levels in predicting PIH and SGA was examined with the analysis of the area under the receiver operator characteristic (ROC) curves. A P value of <0.05 was regarded as significant.

Results

A total of 319 cases were available for analysis with a mean gestational age at sampling of 22.3±1.3 weeks and uric acid concentration of 2.81 ± 0.85 mg/dl. Bilateral early diastolic notching (BLN+) was detected in 145 of the cases and 174 of the cases were found to have bilateral or unilateral absent early diastolic notching (BLN- or ULN-). Mean maternal age and the percentage of cases after 30 years was significantly higher in the group of BLN+, significantly higher percent of the cases were nullipares (Table 1).

The number of cases with PIH, SGA and preterm delivery were significantly higher in the group of BLN+. Mean birth weight and gestational age at delivery were significantly higher in the group with normal Doppler finding. Mean uric acid level was significantly higher in the group of BLN+ (Table 2).

We evaluated uric acid concentration by quartile for the entire study population, comparing the highest quartile to the lower three quartiles. The number of the cases in the highest quartile was significantly higher for the group with BLN+ (Table 3).

The number of the cases which developed PIH, SGA birth weight and fetal demise were higher in the highest quartile of uric acid level. In this group mean birth weight was lower than the other quar-

Table 1. Demografic findings of the groups with or without bilateral notching.

	BLN+ (n=145)	BLN- or ULN- (n=174)	P value
Maternal age (years) (mean±SD)	27.3±5.55	28.8±5.86	0.02
Age≥30	29.6%	45.9%	0.0042
Gestational age (weeks) (mean±SD)	22.3±1.39	22.3±1.29	1
Parity (mean±SD)	0.74±0.9	1.15±1.16	0.0006
Nulliparity	46.8%	29.3%	0.0019

BLN: Bilaretal notch, **ULN:** Unilateral notch

Table 2. Prognosis, neonatal characteristics and mean uric acid level of the cases according to the Doppler findings.

	BLN+ (n=145)	BLN- or ULN- (n=174)	P value
PIH (n)	44	8	<0.0001
SGA (n)	35	17	0.0009
Preterm (<37w) (n)	33	14	0.0004
Severe preterm (<28w) (n)	5	1	0.09
Fetal demise (n)	7	1	0.025
Birth weight (gram) (mean±SD)	2888±786	3215±496	<0.0001
GA at delivery (weeks) (mean±SD)	37.9±3.15	38.8±1.77	0.0015
Uric acid (mg/dl) (mean±SD)	3.08±0.88	2.58±0.76	<0.0001

PIH: Pregnancy induced hypertension, **SGA:** Small for gestational age, **BLN:** Bilaretal notch, **ULN:** Unilateral notch

Table 3. Evaluation of the cases for the presence of notching in groups according to the uric acid concentration by quartiles (Chi-square test).

Group	Uric acid (mg/dl)	BLN+	BLN- or ULN-	P value
1 (<25. percentile)	0.9-2.17	21	59	
2 (25-50. percentile)	>2.17-2.81	42	52	
3 (>50-75. percentile)	>2.81-3.4	33	36	
4 (>75. percentile)	>3.4-6.2	49	27	
Total		145	174	<0.0001

(BLN: Bilaretal notch, **ULN:** Unilateral notch)

Table 4. Doppler findings, maternal and neonatal prognosis according to the quartiles of uric acid.

	Group1 (n=80)	Group 2 (n=94)	Group 3 (n=69)	Group 4 (n=76)	P value
BLN+ (n)	21	42	33	49	<0.0001
PIH (n)	10	10	11	21	0.016
SGA (n)	7	11	11	23	0.0013
Preterm (<37h) (n)	10	14	10	13	0.88
Ciddi preterm (<28h) (n)	0	1	1	4	0.083
Fetal kayıp (n)	1	2	0	6	0.02
Doğum kilosu (gram) (ort.±SD)	3193	3135	3116	2803	0.001
Doğumdaki gestasyonel yaş (hafta) (ort.±SD)	38.65	38.68	38.62	37.72	0.051

BLN: Bilaretal notch, **PIH:** Pregnancy induced hypertension, **SGA:** Small for gestational age

tiles. The number of preterm deliveries did not show any significant difference (Table 4).

Maternal serum level of uric acid showed significant negative correlation with birth weight (r:-0.24; 95% confidence interval for r: -0.34 to -0.14, P<0.0001). Scatter diagram for uric acid levels, birth weight the presence of PIH is presented in Figure 1.

We analyzed the predictive value of second trimester maternal uric acid level for PIH (AUC:0.622, P=0.006) and SGA birth weight (AUC: 0.65, P=0.0003)with Roc curve. Using 3.4 mg/dl as a cut off value we could detect the cases with PIH with a sensitivity of 40.4% and specificity 79.8%, SGA with a sensitivity of 44.2% and specificity 80.45% (Figures 2 and 3).

Discussion

In this study we evaluated the relationship between second trimester maternal uric acid levels and the presence of bilateral early diastolic notching at uterine arteries. In our study population mean uric acid level and the number of cases with various pregnancy complications were higher in the group of BLN+. In the group of women with

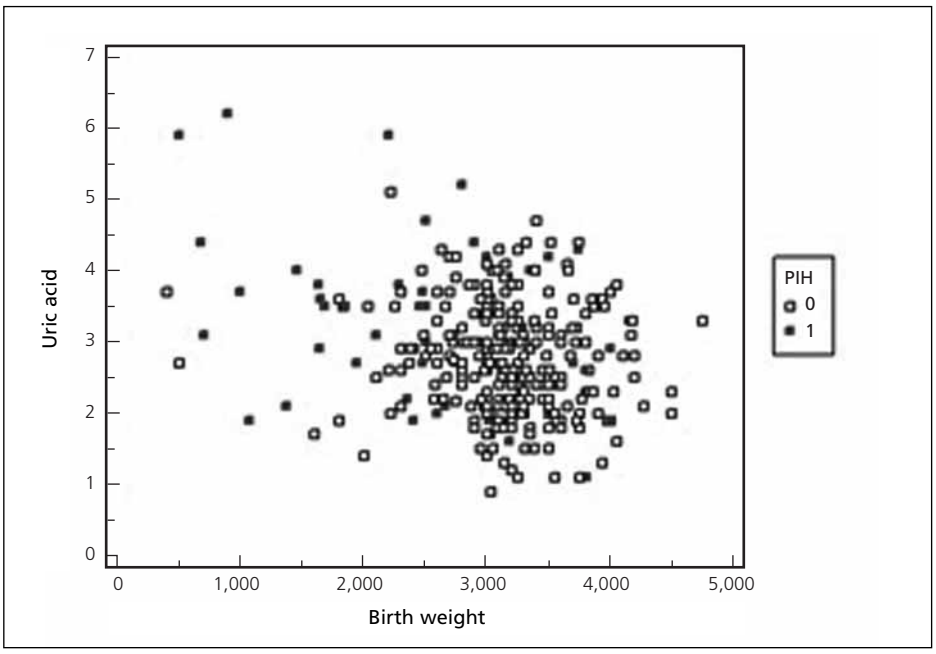

Figure 1. Scatter diagram of the cases showing the correlation of uric acid and birth weight (colored points indicate the cases with PIH).

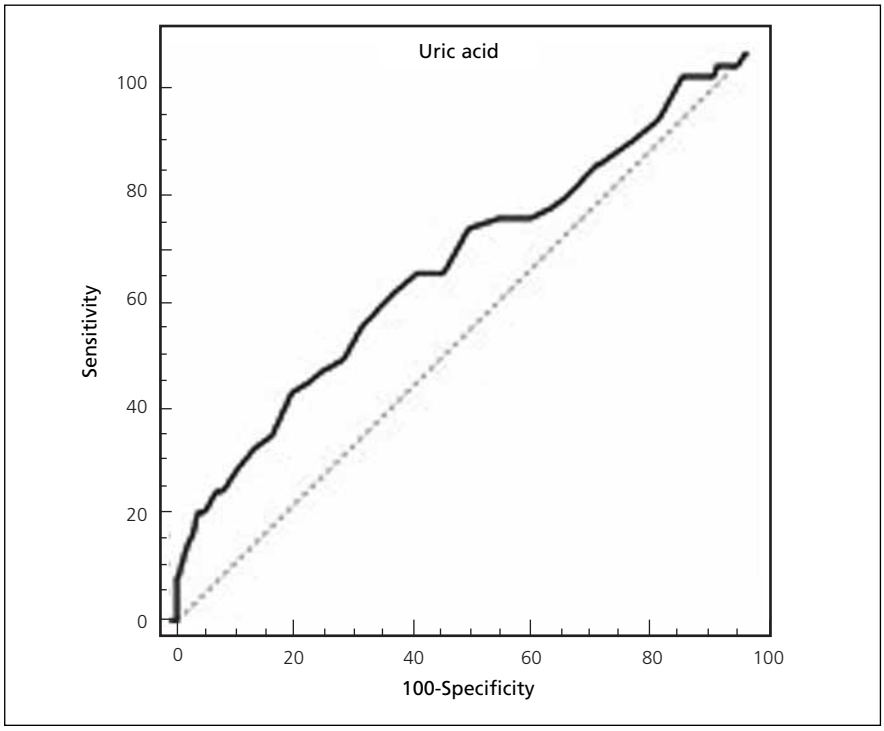

Figure 2. ROC curve analysis of uric acid levels for the prediction of PIH (AUC:0.622, P=0.006).

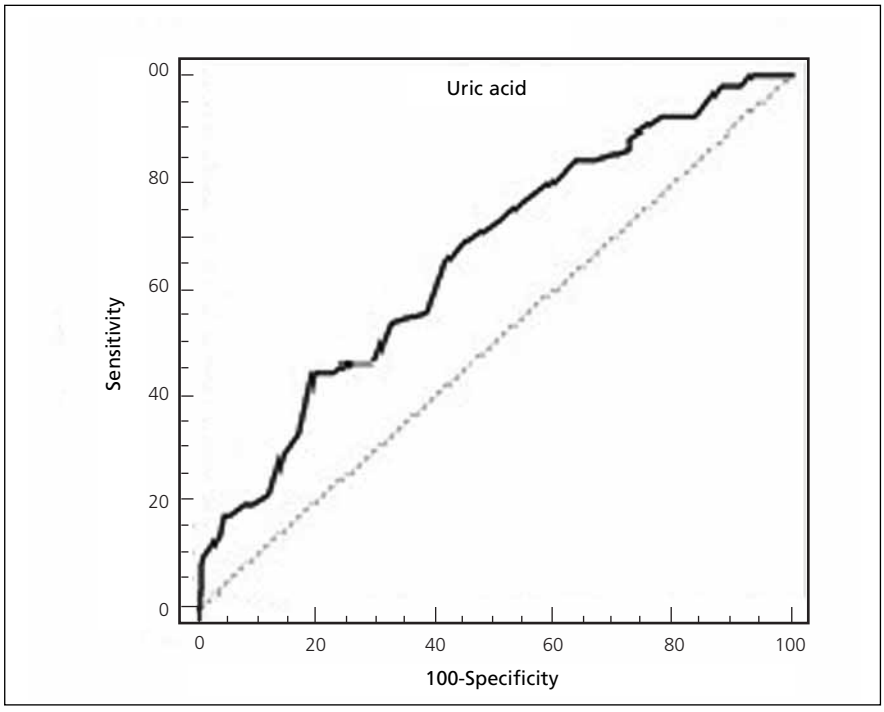

Figure 3. ROC curve analysis of uric acid levels for the prediction of SGA (AUC:0.65, P=0.0003).

an uric acid level at the highest quartile the percentage of cases with PIH, SGA birth weight and fetal demise were significantly higher.

Abnormal uterine artery waveforms were reported to be a better predictor of pre-eclampsia than of intrauterine growth restriction. Pulsatility index alone or combined with notching was advised to be used in clinical practice.[9] Bilateral uterine notching between 23 and 25 weeks' gestation was reported to be an independent risk factor for the development of early-onset preeclampsia and gestational hypertension and suggested to be considered in the assessment of risk for the development of these pregnancy complications.[10] The addition of uterine Doppler waveform analysis to the monitoring profile of women at risk of preeclampsia, small for gestational age, intrauterine death and preterm delivery was reported further define those in a higher risk group.[11] In this study we found that bilateral notching at uterine arteries at second trimester was related with PIH, SGA, preterm delivery and fetal demise. Therefore we also suggest that the presence of bilateral notching should be considered as a risk factor.

As previously reported the increase in uric acid antedates the reduction of glomerular filtration and hypovolemia in PIH.[12] An elevation in serum uric acid has been associated with an increased risk for the development of hypertension. Even mild hyperuricemia causes hypertension and renal injury with stimulation of the renin-angiotensin system and inhibition of neuronal NO synthase.[13] It was suggested that women who develop preeclampsia come into pregnancy with elevated uric acid as part of the metabolic syndrome or that uric acid production is increased in early pregnancy. Elevated concentration of uric acid in preeclamptic women is not simply a marker of disease severity but rather contributes directly to the pathogenesis of the disorder.[14]

Uric acid could contribute to failed placental bed vascular remodeling by impeding trophoblast invasion with resultant reduced placental perfusion, setting the stage for ischemia reperfusion injury to the placenta.[8] In this study we found that the number of cases with bilateral notching was significantly higher in the group of women with an uric acid in the highest quartile at second trimester. This result indicates the possible relationship between impaired placentation and high maternal uric level before the clinical appearance of pregnancy complications.

Myers et al. evaluated maternal uric acid levels at 22 and 26 weeks and concluded that these time points were remote from the diagnosis of preeclampsia and this might contribute to the lack of differences.[15] In our study population at the same time point we could predict PIH by using an uric acid level of 3.4 mg/dl with a sensitivity of 40.4% and specificity 79.8%.

A striking increase in the odds for small gestational age infants in preeclamptic women with increasing serum uric acid concentration has been reported.[6,16] Lower birth weight of children born to mothers found to have hyperuricemia (>58.3 mg/l) for more than 2 weeks was reported as a consequence of hyperuricemia.[17] In our study population serum level of maternal uric acid showed a significant negative correlation with birth weight and the number of the cases with SGA birth weight was significantly higher in the group of highest quartile of uric acid. Elevated uric acid was also recognized many years ago as a better predictor for fetal risk than blood pressure in preeclampsia.[18,19] In our study the risk of fetal demise was higher either in the group with elevated maternal uric acid level at second trimester.

Conclusion

The presence of bilateral notching at uterine arteries at second trimester is related with PIH, SGA and preterm delivery and elevated maternal uric acid level. Maternal serum uric acid level at second trimester may be used in the prediction PIH and SGA birth weight.

References

1. Papageorghiou AT, Leslie K. Uterine artery Doppler in the prediction of adverse pregnancy outcome. *Curr Opin Obstet Gynecol* 2007;19:103-9.
2. Groom KM, North RA, Stone PR, Chan EH, Taylor RS, Dekker GA, et al. Patterns of change in uterine artery Doppler studies between 20 and 24 weeks of gestation and pregnancy outcomes. *Obstet Gynecol* 2009;113: 332-8.
3. Palma Dias RS, Fonseca MM, Brietzke E, Fritsch A, Schlatter D, Maurmann CB, et al. Screening for placental insufficiency by transvaginal uterine artery Doppler at 22-24 weeks of gestation. *Fetal Diagn Ther* 2008;24:462-9.

4. Giguere Y, Charland M, Bujold E, Bernard N, Grenier S, Rousseau F, et al. Combining biochemical and ultrasonographic markers in predicting preeclampsia: a systematic review. *Clin Chem* 2010; 56:361-75.
5. Redman CWG, Williams GF, Jones DD, Wilkinson RH. Plasma urate and serum deoxycytidylate deaminase measurements for the early diagnosis of preeclampsia. *Br J Obstet Gynaecol* 1977;84:904–8.
6. Roberts JM, Bodnar LM, Lain KY, Hubel CA, Markovic N, Ness RB, et al. Uric acid is as important as proteinuria in identifying fetal risk in women with gestational hypertension. *Hypertension* 2005;46:1263-9.
7. Ferrazzani S, De Carolis S, Pomini F, Testa AC, Mastromarino C, Caruso A. The duration of hypertension in the pueperium of preeclamptic women: relationship with renal impairment and week of delivery. *Am J Obstet Gynecol* 1994;171:506–12.
8. Bainbridge SA, Roberts JM. Uric acid as a pathogenic factor in preeclampsia. *Placenta* 2008;22:67-72.
9. Cnossen JS, Morris RK, ter Riet G, Mol BW, van der Post JA, Coomarasamy A, et al. Use of uterine artery Doppler ultrasonography to predict pre-eclampsia and intrauterine growth restriction: a systematic review and bivariate meta-analysis. *CMAJ* 2008;178:701-11.
10. Espinoza J, Kusanovic JP, Bahado-Singh R, Gervasi CMAJ MT, Romero R, Lee W, et al. Should bilateral uterine artery notching be used in the risk assesment for preeclampsia, small-for-gestational-age, and gestational hypertension? *J Ultrasound Med* 2010;29:1103-15.
11. El-Hamedi A, Shillito J, Simpson NA, Walker JJ. A prospective analysis of the role of uterine artery doppler waveform notching in the assessment of at-risk pregnancies. *Hypertens Pregnancy* 2005;24:137-45.
12. Powers RW, Bodnar LM, Ness RB, Cooper KM, Gallaher MJ, Frank MP, et al. Uric acid concentrations in early pregnancy among preeclamptic women with gestational hyperuricemia at delivery. *Am J Obstet Gynecol* 2006;194: 160.e1–160.e8.
13. Mazzali M, Hughes J, Kim YG, Jefferson JA, Kang DH, Gordon KL, et al. Elevated uric acid increases blood pressure in the rat by a novel crystal-independent mechanism. *Hypertension* 2001;38:1101-6.
14. Kang DH, Finch J, Nakagawa T, Karumanchi SA, Kanellis J, Granger J, et al. Uric acid, endothelial dysfunction and preeclampsia: searching for a pathogenetic link. *J Hypertens* 2004;22:229-35.
15. Myers JE, Jewsbury S, Sheikh N, Crocker I, Baker PN. Plasma uric acid levels do not correlate to plasma-evoked changes in endothelial function in women with preeclampsia. *Eur J Obstet Gynecol Reprod Biol* 2008;137:118-27.
16. Merviel P, Ba R, Beaufils M, Breart G, Salat-Baroux J, Uzan S. Lone hyperuricemia during pregnancy: maternal and fetal outcomes. *Eur J Obstet Gynecol Reprod Biol* 1998; 77:145-50.
17. Bainbridge SA, von Versen-Höynck F, Roberts JM. Uric acid inhibits placental system a amino acid uptake. *Placenta* 2009;30:195-200.
18. Redman CW, Beilin LJ, Bonnar J, Wilkinson RH. Plasma-urate measurements in predicting fetal death in hypertensive pregnancy. *Lancet* 1976;1:1370-3.
19. Varma TR. Serum uric acid levels as an index of fetal prognosis in pregnancies complicated by pre-existing hypertension and preeclampsia of pregnancy. *Int J Gynaecol Obstet* 1982;20:401-8.

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The Incidence of HBSAg, Anti-HBS and Anti-HCV in Pregnant Women

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Abstract

Objective: The proportion of infection in babies born from hepatitis B early antigen positive mothers is 60-90% and if they are not treated more than 90% of them will be chronic hepatitis B carriers and this brings the risk for chronic hepatitis and hepatocellular cancer. We tried to find out the proportion of the pregnant women with HbsAg (surface antigen of hepatitis B), anti-HBs (antibody against hepatitis B surface antigen) and anti-HCV (antibody of hepatitis C).

Methods: In this study, 795 pregnant women are evaluated retrospectively for HbsAg, anti-HBs and anti-HCV in Taksim Training and Research Hospital, Clinics of Obstetrics and Gynecology between October and December 2010. The percentages are determined.

Results: None of the parameters like age, week of gestation and social or economical status were criteria for the pregnants taken into the study. 29 of the 795 pregnants (3.65%) were HbsAg positive, 69 of them (8.68%) were anti-HBs positive and 6 of them (0.75%) were anti-HCV positive. These findings of our study is correlated the results of other studies in our country.

Conclusion: It has been necessary to make serological tests for hepatitis B routinely for the protection and treatment of the newborn. All of the pregnant women should be informed. Also after the screening tests for hepatitis B, vaccination before the conception should be done. Our country is involved by the vaccination program in 1998. Although low percentage of spread, the screening of hepatitis C infection in risk groups is important for community and newborn health. The results of our study is correlated with the statistics of these study of our country.

Keywords: Pregnancy, hepatitis B, hepatitis C.

Gebelerde HBSAg, anti-HBS ve antiİ-HCV sıklığı

Amaç: Hepatit B virüsü ile enfekte annelerden doğan bebeklerin enfeksiyon oranı annenin hepatit B early antijen (HbeAg) pozitif olması durumunda %60-90'a çıkmaktadır ve tedavi edilmedikleri taktirde %90'ından fazlası kronik HBV (hepatit B virüsü) taşıyıcısı olmaktadır ki bu da hayatlarının ilerleyen dönemlerinde kronik hepatit ve hepatosellüler karsinom riskini beraberinde getirir. Biz bu çalışmada hastanemize başvuran gebelerde HBsAg (hepatit B yüzey antijeni), anti-HBs (hepatit B yüzey antijenine karşı antikor) ve anti-HCV (hepatit C virüs antikoru) pozitiflik oranını saptamayı amaçladık.

Yöntem: Bu çalışmaya 01 Ekim-31 Aralık 2010 tarihleri arasında Taksim Eğitim ve Araştırma Hastanesi Gebe Polikliniği'ne başvuran 795 gebe alındı. Gebelerin HBsAg, anti HBs ve anti-HCV değerleri retrospektif olarak incelendi. Hastalarda bulunan pozitif değerler olgu sayısı ve yüzdelik değerler olarak hesaplandı.

Bulgular: Yaş, gebelik haftası ve sosyoekonomik durumlara bakılmaksızın çalışmaya alınan 795 gebenin 29'u (%3.65) HBsAg pozitif, 69'u (%8.68) anti HBs pozitif ve 6'sı (%0.75) anti-HCV pozitif idi. Bu araştırmada bulduğumuz değerler, ülkemizde gebelerde tespit edilmiş olan pozitiflik oranları ile benzerdir.

Sonuç: Gebe takibinde rutin olarak hepatit B için serolojik tarama yapılması yenidoğanların enfeksiyondan korunma ve tedavi edilmesi için gereklidir. Gebeler bu konuda bilgilendirilmelidir. Hepatit B için gerekli taramalar yapıldıktan sonra prekonsepsiyonel dönemde aşılama yapılmalıdır. Ülkemiz aşılama programına 1998 yılında dahil olmuştur. Hepatit C'nin bulaş oranı düşük olmasına karşın hastalık seyri ve sonuçları açısından özellikle riskli gruplarda taranması toplum ve yenidoğan sağlığı açısından önemlidir. Hastanemizde yaptığımız bu çalışmanın sonuçlarına göre hastanemize başvuran gebelerin seropozitiflik oranları ülkemiz istatistikleri ile örtüşmektedir.

Anahtar Sözcükler: Gebelik, hepatit B, hepatit C.

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Introduction

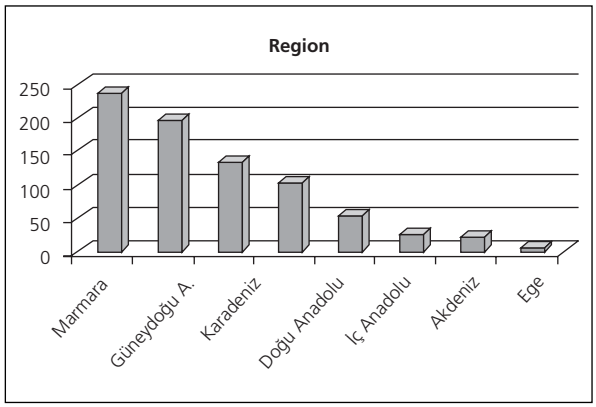
The infections with the virus of Hepatitis B (HBV) and C (HCV) take place among the most important health issues both in our country and in the world and they are the most common cause of the cirrhosis and the hepatocellular carcinoma.[1] There are lots of ways for contamination, one of them is the vertical transmission from mother to newborn. The transmission from infected mother to her baby is actualizes in labor, after labor or rarely in pregnancy. The 70-90% of babies born from infected mothers positive for HbeAg are infected and 90% of them have chronic infection. The 10-40% of babies born from mothers negative for HbeAg are infected and 40-70% of them have chronic infection.[2] Over the 90% of babies born from mothers infected with HBV can be protected by immunization.[3] However the risk for perinatal transmission of HCV is lower than 5% and there is not any special suggestion for protection.[4] According to all these information it is clearly important to determine the immunization for Hepatitis B in all pregnant women and hepatitis C infection in risky pregnants. HBV carrier pregnants should be determined and the newborn should have prophilaxy. Hepatitis B vaccine and Hepatitis B hiperimmuneglobuline (HBIG) should be applied to the newborns of Hepatitis B infected mothers. If the mother is negative for HbeAg, in the case of absence of HBIG, the vaccine only itself is highly protective enough.[5] The transmission of HBV, from mother to baby, becomes usually in the third trimester. If the acute infection occurs in first or second trimester the studies report that the transmission does not exist.[6] In this study we tried to find out the proportion of the pregnant women with HbsAg, anti-HBs and anti-HCV (antibody of Hepatitis C).

Method

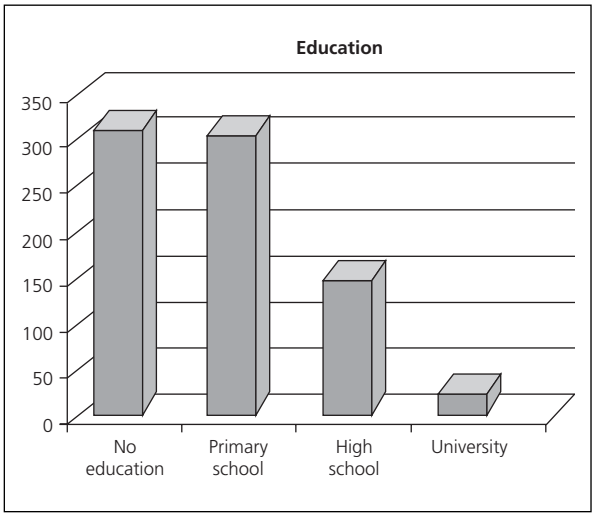
In this study, 795 pregnant women are evaluated retrospectively for HbsAg, anti-HBs and anti-HCV in Taksim Training and Research Hospital, Clinics of Obstetrics and Gynecology between October and December 2010. The samples are tested with Tritrus system microparticule enzyme immunassay in our hospital and GBC kit is used for HBsAg and AntiHBs, Murex kit is used for Anti-HCV. The positivity edge of HBsAg and anti-HCV was taken as 1 IU/ml, 10 IU/ml is taken for AntiHBs. The number of the cases and percentages of them are determined. Also age, education, occupation, living area and gestational age are recorded.

Results

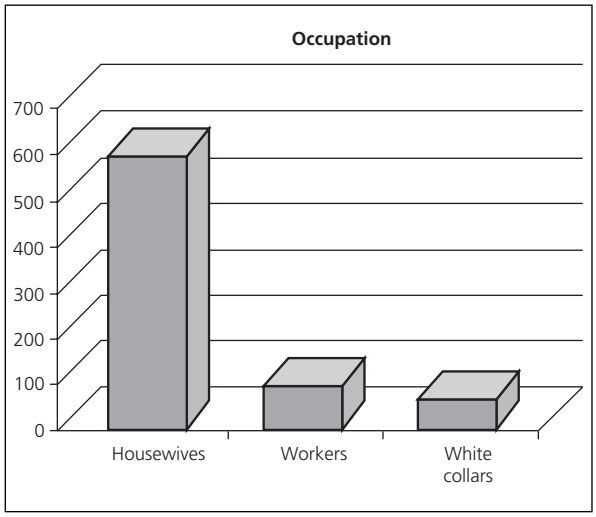
The mean age is found as 28.35±6.18 and gestational age is found as 30.84±2.3. The living regions are as following; 29.7% (236 pregnant) Marmara, 25% (199 pregnant) Southeast Anatolia, 16.9% (135 pregnant) Black Sea, 14% (111 pregnant) Eastern Anatolia, 7.4% (59 pregnant) Central Anatolia, 3.4% (27 pregnant) Mediterranean, 2.8% (22 pregnant) Aegean and %0.8 (6 pregnant) were foreigner. The distribution acording to the regions is shown in the Graphic 1. The educational distribution is as following; 39.25% (312) primary school, 18.11 % (144) high school, 3.14% (25) university and 39.5% (314) do not have any educa-



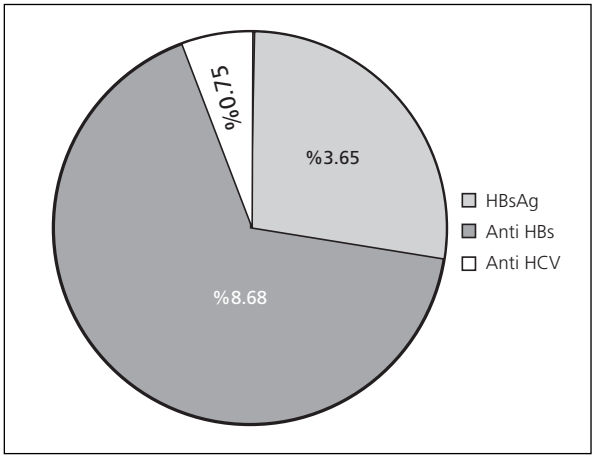
Graphic 1. Distribution according to regions.



Graphic 2. Pregnants according to education.



Graphic 3. Distribution of pregnants according to occupation.



Graphic 4. Distribution of HBsAg, Anti HBs and Anti HCV positivity.

tion. It is shown in Graphic 2. 76.98% (612) of the pregnants are housewives, 13.46% (107) are workers, 9.56% (76) are white-collars. It is shown in Graphic 3. In the study group, 29 of the pregnants (3.65%) are HBsAg positive, 69 of them (8.68%) are anti HBs positive and 6 of them (0.75%) are found to be anti-HCV positive. The distribution of seropositivity is shown in Graphic 4.

Discussion

The infections caused by HBV and HCV causes acute and chronic hepatitis, cirrhossis and hepatocellular carcinoma. Also these infections are the important causes of morbidity and mortality and also seen more common both in our country and in the world. Both of the viruses have many ways of transmission and one of these is the vertical transmission from mother to newborn. The transmission from the infected mother to baby is rarely during the pregnancy or during and after the delivery. Along the vaginal discharge swalloving the mother's blood, contact during the cesarean section and the transmission of the maternal blood to fetal circulation because of placental damage can result with transmission of the infection. The 70-90 % of babies born from infected mothers positive for HbeAg are infected and 90% of them have chronic infection. The 10-40% of babies born from mothers negative for HbeAg are infected and 40-70% of them have chronic infection.[2] Over the 90% of babies born from mothers infected with Hepatitis B virus are protected by immunization.[3] HBV vaccination is done in many countries of the world since 1991 with the suggestion of World Health Organization (WHO). In our country the vaccination is done routinely since 1998. It should be established how to follow up the pregnants infected with hepatitis according to the prevalance of the disease.

The percentages of the hepatitis carriage differ in countries; it is 11.6% in Nigeria, 10% in Hong Kong, 0.44% in Holland and 1.4% in Germany.[7,8] In our country HBV carriage differs among regions and our country is accepted as one of the middle endemic countries in the world. In the studies, the

percentage of the HBsAg positivity is reported between 2.1% - 16.6%.[9,10] Aslan and colleagues reported 4.66% positivity among 450 pregnants, Anti-HBs percentage was 21.1%; Madendağ and colleagues found the HBsAg positivity as 2.11%.[11,12] In the study that is made by Gül and colleagues, HBsAg positivity is 4.08%, Anti-HBs positivity is 18.6%.[6] In our study, we found HBsAg positivity as 3.65% and Anti-HBs positivity as 8.68%. HBsAg positivity of our study is concordant with the literature but Anti-HBS percentage is lower than theother studies. In our country that places in the mean endemic countries, the most effective way to break down the transmission chain is to screen the pregnants for HBsAg and to apply Hepatitis vaccine and HBIG to all newborns of the mothers carry HBsAg. One of the importance of the establishment of carriage is to determine all of the members of the family under risk and immunize them if necessary.

The percentage of HCV positivity is reported as 0.44% and 2.04%. A study made in Van reports this as 2.04% and a study in Ankara reports as 0.17%. This is 0.75% in our study. Our result is like the medium of our country. Hepatitis C has also a vertical transition but infection rate is much lower than hepatitis B. Maternal antibodies passes from mothers to babies passively and disappear in six months. Because of this reason the positive HCV-RNA is more meaningful than Anti-HCV in diagnosis of vertical transmission. It is recommended to detect HCV-RNA in maternal serum for vertical passing and it is not recommended detecting Anti-HCV routinely. It should be investigated for under risk of HCV infection in settings of blood transfusion, positivity of HIV infection and chronic hemodialysis. HCV and HIV co-infection increases the perinatal transmission rate. In Australia 125 of 131 drug addicted pregnanats have been reported as anti-HCV positive.[13] In United Kingdom this is found as 0.19% and 1.9% in Italy.[14,15] HCV is commonly positive especially with the risk factors like as drug addiction, blood transfusion and HIV positivity.[16]

Conclusion

The screening of hepatitis B is needed routinely for protection and diagnosis of newborn. The pregnants should be informed for this situation. The vaccination programme which our country was indepraded in 1998 should be done in preconceptional period after screening of hepatitis B infection. Although low risk of spread, the screening of HCV infection in risk groups is very important for community and newborn health. According to results of our study, the percentage of seropositivity pregnancy admitted to our hospital are correlated with statistical results of our country. As a result for protection of newborns, we suggest that it is necessary to scrren all pregnants for hepetitis B and the pregnants for hepatitis C who have risk factors.

References

1. Karaca Ç, Karaca N, Usta T, Demir K, Kaymakoğlu S, Beşışık F ve ark. Gebe populasyonunda hepatit B,C,D virüs infeksiyonu sıklığı ve hepatit C virusunun perinatal yolla geçiş oranı. *Akademik Gastroenteroloji Dergisi* 2003;2:122-4.
2. Özdemir D, Kurt H. Hepatit B virüsü enfeksiyonlarının epidemiyolojisi. *Viral Hepatitle Savaşım Derneği Yayını* 2005;108-17.
3. Washmuth JC. Hepatitis-B Epidemiology, transmission and natural history. Almanya-Flying Publisher 2009;25-39.
4. Pembrey L, Newell ML, Tovo PA. The management of HCV infected pregnant women and their children European paediatric HCV network. *J Hepatol* 2005;43:515-519.
5. Reesink HW, Reerink Brongers EE, Lafaber –Schut BJ, Kalshoven-Benschop J, Brummelhius HG. Prevention of chronic HBsAg carrier state in infants of HBsAg positive mothers by hepatitis B immunoglobulin. *Lancet* 1979;2:436-8.
6. Gül A, Türkdoğan M, Zeteroğlu Ş. Bir grup gebede hepatit B ve hepatit C prevalansı. *Perinatoloji Dergisi* 1998:6.
7. Kwan LC, Ho YY, Lee SS. The declining HBsAg carriage rate in pregnant women in Hong Kong. *Epidemiol Infect* 1997;119:281-3.
8. Niesert S, Messner U, Tillmann HL, Gunther HH, Schneidr J, Manns MP. Prevalance of hepatitis B in pregnancy and selective screening. *Geburtshilfe Frauenilkd* 1996; 56:283-6.
9. Tekeli E, Kandilci S, Balık İ, Kurt H. Sağlıklı gebelerde HBV markerlerinin prevalansı. *Ankara Tıp Bülteni* 1988;10:255-60.
10. Kuru Ü, Tosun Ö, Ceylan Y. Gebelerde HBsAg taşıyıcılığı sıklığı. *Klimik Dergisi* 1992;5:19.
11. Aslan G, Ulukanlıgil M, Harma M, Seyrek A, Taşçı S. Şanlıurfa'da gebelerde HBV seroprevalansı. *Viral Hepatit Dergisi* 2001;7:324-26.
12. Madendağ Y, Çöl Madendağ İ, Çelen Ş, Ünlü S, Danşman N. Hastanemize başvuran tüm obstetrik ve jinekolojik hastalarda hepatit B, hepatit C ve HIV seroprevalansı. *Türkiye Klinikleri J Gynecol Obst* 2007;17:442-6.
13. Latt NC, Spencer JD, Beeby PJ. Hepatitis C in injecting drug-using women during and after pregnancy. *J Gastroenterol Hepatol* 2000;15:175-81.

14. Ades AE, Parker S, Walker J, Cubitt WD, Jones R. HCV prevalance in pregnant women in the UK. *Epidemiol Infect* 2000;125:399-405.

15. Baldo V, Floreani A, Menegon T, Grella P, Paternoster DM, Trivello R. Hepatitis C virus, hepatitis B virus and human immunodeficiancy virus infection in pregnant women in North-East Italy: a seroepidemiological study. *Eur J Epidemiol* 2000;16:87-91.

16. Burns DN, Minkoff H. Hepatitis C: screening in pregnancy. *Obstet Gynecol* 1999; 94:1044-8.

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Evaluation of The Emergency Peripartum Hysterectomy Cases: Experience of 5 years

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Abstract

Objective: The purpose of this study is to evaluate the emergency peripartum hysterectomies performed due to obstetric complications.

Methods: We analyzed retrospectively 18 cases of emergency peripartum hysterectomy that were performed at Cerrahpaşa School of Medicine, Department of Obstetrics and Gynecology from January 2006 to December 2010. The incidence, demographic characteristics, associated risk factors, indications of hysterectomy, peripartum complications, maternal morbidity and mortality of the cases were analyzed retrospectively.

Results: Emergency peripartum hysyerectomy performed in 18 cases. The overall incidence of emergency peripartum hysterectomy was 2.9 per 1,000 deliveries. The indications of hysterectomy were identified as 6 cases (33.6%) placenta insertion anomalies, 5 cases (27.7%) placenta previa, 4 cases (22.2%) uterine atonia, 2 cases (11.1%) uterine rupture, and 1 case (5.6%) with an adnexial mass respectively. The emergency peripartum hysterectomy was done in 4 of the cases (22.2%) after vaginal delivery and 14 of the cases (77.7%) during cesarean section. 14 cases (77.7%) were underwent total, 4 cases (22.2%) were underwent subtotal hysterectomy. During the operation, urinary complications occurred in 5 cases (27.7%). In 3 cases (16.6%) relaparatomy was performed. Maternal and fetal mortality occured in 1 case (5.5%).

Conclusion: In our study, the most common indication for emergency peripartum hysterectomy was placental insertion abnormalities. Together with a significant increase in cesarean rates, significant increases in the frequency of plasenta inserton abnormalities is noteworthy. Cases of pregnant women who had placenta previa and prior cesarean section, the placenta should be carefully evaluated in terms of placenta insertion abnormalities. Entering the risk group of pregnant women, the centers which have adequate staff and equipment to be recommended for delivery. As a result; emergency peripartum histerectomy is a procedure with high mortality and morbidity but is life-saving when performed at suitable time.

Keywords: Emergency peripartum hysterectomy, incidance, endication, placenta insertion abnormalities, mortality.

Acil peripartum histerektomi olgularının değerlendirilmesi: 5 yıllık deneyim

Amaç: Hastanemizde obstetrik nedenlerle gerçekleştirilen acil peripartum histerektomi olgularının, değerlendirmesini yapmak.

Yöntem: Cerrahpaşa Tıp Fakültesi Kadın Hastalıkları ve Doğum Kliniğinde Ocak 2006 ile Aralık 2010 tarihleri arasında obstetrik nedenlerle acil peripartum histerektomi yapılan 18 olgunun demografik özellikleri, insidansı, risk faktörleri, histerektomi endikasyonları, gelişen komplikasyonları, maternal mortalite ve morbiditesi retrospektif olarak incelendi.

Bulgular: 18 olguya acil peripartum histerektomi yapıldı. Acil peripartum histerektomi insidansı binde 2.9 olarak belirlendi. Histerektomi endikasyonları; plasenta yapışma anomalisi 6 olgu (%33.6), plasenta previa 5 olgu (%27.7), uterin atoni 4 olgu (%22.2), uterin rüptür 2 olgu (%11.1) ve adneksiyal kitle 1 olgu (%5.6) olarak kaydedildi. Histerektomilerin 14'ü (%77.7) sezaryen sonrası, 4'ü (%22.2) normal doğum sonrası uygulandı. Olguların 14'üne (%77.7) total, 4'üne (%22.2) subtotal histerektomi yapıldı. Operasyon sırasında 5 olguda (%27.7) üriner komplikasyon gelişti. 3 olguya (%16.6) relaparatomi yapıldı. 1 olguda (%5.5) maternal ve fetal mortalite gelişti.

Sonuç: Çalışmamızda acil peripartum histerektominin en sık endikasyonu plasenta yapışma anomalileri olarak bulundu. Sezaryen oranlarındaki belirgin artış ile birlikte plasenta yapışma anomalilerinin sıklığında da ciddi artışlar dikkati çekmektedir. Plasenta previa olguları ve daha önce sezaryen operasyonu geçirmiş gebeler, plasenta yapışma anomalisi açısından dikkatlice değerlendirilmelidir. Riskli gruba giren gebelere, yeterli ekip ve ekipmanın bulunduğu merkezlerde doğumun gerçekleştirilmesi önerilmelidir. Sonuç olarak APH; yüksek maternal mortalite ve morbidite ile seyretmekle birlikte, zamanlaması doğru ve yerinde yapıldığında hayat kurtarıcı bir işlemdir.

Anahtar Sözcükler: Acil peripartum histerektomi, insidans, endikasyon, plasenta yapışma anomalisi, mortalite.

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Introduction

Peripartum bleedings are one of the most important reasons of maternal mortality and morbidity in developing countries[1] Serious bleedings that may cause hemorrhagic shock due to pregnancy may appear due to placenta detachment, placenta praevia, placenta attachment anomalies, uterus rupture, uterus atonia, inversion of uterus, delivery laceration and placenta retention. Plasma volume in a normal pregnancy increases approximately 1500 ml. This hypervolemia plays a protective role for peripartum bleedings. In addition to fix hypervolemia and coagulopathy, effective treatment of underlying reason of bleeding is essential by surgical methods. Emergency peripartum hysterectomy (EPH) is applied due to life-threatening uterine bleedings after normal vaginal delivery, during cesarean or after cesarean.[2] Though EPH operations display high mortality, it can be life-saving when it is applied in emergency cases and on proper indication. EPH has shown decrease in recent years thanks you efficient antibiotherapy, uterotonic agents and blood transfusion techniques.

Uterine rupture, uterine atonia, and placenta attachment anomalies are frequent EPH indications. While uterine rupture and uterine atonia were deemed as the most frequent reasons of EPH in previous years, it is seen in developed countries that placenta attachment anomalies are the most frequent reason due to the increase of cesarean rates, development of surgical treatment of uterine atonia as well as medical and hysterectomy developments. Placenta attachment anomaly is often associated with uterine scar, cesarean history and advanced maternal age.[3, 4]

Our purpose in this study is to determine the incidence, indications, risk factors of EPHs, and their effects on maternal and fetal mortality and morbidity in last 5 years.

Methods

We analyzed 18 EPH cases applied to Cerrahpaşa School of Medicine, Department of Obstetrics and Gynecology due to various obstetric reasons from January 2006 to December 2010. Also delivery number in our clinic was determined. EPH incidence was calculated. Patient information was obtained from hospital records and patient files.

Demographical aspects of the patients were recorded (age, gravida, parity, gestational week, delivery types). Hysterectomy indications, applied hysterectomy type, required blood transfusion amount, complications developed intraoperatively and postoperatively were determined.

Uterine massage and uterotonic medical treatment were applied before hysterectomy (especially in atonia cases). Hypogastric artery ligation was tried on cases that did not response. EPH was performed on postpartum bleeding cases that continued despite all these precautions.

Cases which developed intraoperative or postoperative disseminated intravascular coagulation (DIC) were evaluated with the results of prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen and fibrinogen degradation products.

Results

Totally 6043 deliveries performed in our clinic between January 2006 and December 2010.

In the same period, emergency hysterectomy was performed to 18 (0.29%) patients for various reasons. Mean age of the patients was calculated as 34.2, gravida as 4.0 and mean parity as 1.7. All cases were multigravida. Mean gestational week was found as 32.4. Blood transfusion was performed to all patients.

13 of EPHs were total (72.2%) while 4 (22.2%) of them were subtotal. EPH indications were shown in Table 1. According to this, it was found that the most frequently detected EPH indication was placenta attachment anomaly (placenta accreta, placenta increta, placenta percreta) (33.3%). By confirming with pathology reports, 3 patients with placenta attachment anomaly were diagnosed as placenta percreta, 2 patients as placenta increta and 1 patient as placenta accreta. Two of 3 cases with placenta percreta previously had two cesarean sections and 1 case had only one normal delivery.

Two cases with placenta increta had two cesarean sections undergone. One case with placenta accreta had three cesarean sections undergone.

In EPH cases, most frequently detected second indication was found as placenta praevia (27.7%).

Table 1. Demographical aspects of cases.

	Average values	Minimum – Maximum
Average age	34.2	30-43
Gravida	4.0	2-7
Parity	1.7	1-5
Gestational week	32.4	17-38
Given blood product (unit)	7.3	4-10

Table 2. Emergency peripartum hysterectomy indications.

	Patient number
Uterine atonia	4 (22.2%)
Placenta praevia	5 (27.7%)
Uterine rupture	2 (11.1%)
Placenta attachment anomaly (P. percreta, P. increta, P. accreta)	6 (33.3%)
Adneksiyal kitle	1(%5.5)

Table 3. Peripartum hysterectomy complications.

	Patient number
Bladder injury	3 (16.6%)
Ureteral injury	2 (11.1%)
Disseminated intravascular coagulation	6 (33.3%)
Relaparatomy	3 (16.6%)
Maternal mortality	1 (5.5%)
Fetal mortality	1 (5.5%)

Three cases were diagnosed as placenta praevia totalis and 2 cases were diagnosed as placenta praevia marginalis. All placenta praevia cases had cesarean section history undergone.

Most frequently detected third indication in EPH cases was uterine atonia (22.2%). Uterine atonia was developed in 2 cases after normal delivery and in 2 cases after cesarean. Subtotal hysterectomy was performed to all these cases.

EPH was applied to 2 cases due to uterus rupture indication. Uterus rupture spontaneously existed in the first case (G 2, P 1) after a long labor at 39th gestational week and in the second case (with one cesarean section history) at 17th gestational week.

Other EPH indication was adnexal mass detected at 10th gestational week. It was decided to follow up the mass during pregnancy. It was concluded to perform the labor at 34th gestational week due to compression symptoms of the mass which filled whole pelvis and abdomen and caused general condition disorder. As frozen response of the biopsy taken from the mass during cesarean section came from mucinous cystadenocarcinoma, Total Abdominal Hysterectomy, Bilateral Salpingo-oophorectomy + Omentectomy + Pelvic Lymphadenectomy+Paraortic Lymphadenectomy + Appendectomy were performed.

Bilateral hypogastric artery ligation was performed to 5 cases who were applied EPH. Averagely 7.3 (4-10) units of blood products (blood, fresh frozen plasma, erythrocyte and thrombocyte suspension) were transfused to all cases.

Bladder injury occurred in 3 cases and ureteral injury occurred in 2 cases as intraoperative complications. Bladder was primarily repaired during operation in our cases that had bladder injury. Ureteroneocystostomy was done by relaparatomy to our 2 cases that had ureteral injury. Relaparatomy was done to our one case due to hemorrhage developed during postoperative period.

DIC developed totally in 6 cases. Our only case which was resulted maternal and fetal mortality was the patient who had maternal aorta stenosis. Uterine atonia and DIC developed during operation in the patient who was taken to cesarean due to fetal distress at her 34th gestational week. Fetus who had 1st minute APGAR score as 2 and 5th minute APGAR score as 2 was delivered. During operation, cardiac arrest developed in the patient who had EPH. Mother and fetus did not response to the resuscitation and maternal and fetus exitus occurred.

Discussion

Cesarean hysterectomy was first performed by Dr. Eduardo Porro in 1876 in order to protect maternal and fetus health. Performing hysterectomy as a final treatment step in bleedings due to obstetric reasons is quite essential surgical treatment method for saving mother's life.[5] In our clinic, EPH incidence was determined as 2.9/1,000 different than the literature. This rate was reported as 0.33/1,000 in Holland, 0.5/1,000 in Israel, 1.43/1000 in the USA, 2.3/1,000 in Southern Korea,

and 4.34/1,000 in Nigeria.[3,6-8] Rates reported in the studies performed in Turkey are 0.25/1,000 by Özden et al., 0.26/1,000 by Zeteroğlu et al. and Akar et al., and 4/1,000 by Yalınkaya et al.[9-13] Wide incidence range given in these studies can be associated with different geographical and socio-economic structures, difference of antenatal and peripartum care conditions and patient density of hospitals.

Advanced maternal age and multiparity are prominent risk factors for peripartum hysterectomy.[15-17] In our study, mean maternal age was 34.2 and mean gravida was 4.0. These findings were consistent with the literature.

When compared in terms of delivery type, it was reported that the rate of performing hysterectomy after cesarean was 10 times higher than performing after normal delivery.[3] In our study, consistent with the literature, EPH was performed to 4 (28.6%) cases after normal delivery and to 14 (71.4%) cases after cesarean section.

Yamani et al. reported in their study that the most frequent indication of EPH was uterine atonia.[17] However, it was reported in the studies of Kwe et al., Kastner et al., and Kayabaşoğlu et al. that the most frequent indication was placenta attachment anomalies.[3,6,18] In our study, placenta attachment anomalies were the first frequent indication of EPH with the rate of 33.3%, uterine atonia was the third frequent indication of EPH with the rate of 22.2%. In the studies performed, it was shown that cesarean delivery was a risk factor for placenta attachment[15] In 5 of 6 cases detected as having placenta attachment anomaly had the history of cesarean undergone. Placenta percreta developed only in one case after previous normal delivery. Yet, this case had the history of 2 curettages. Within the lights of literature, placenta attachment anomaly as the most frequent indication of EPH in our study may be associated with increased cesarean rates.

In our study, placenta praevia (27.7%) is seen as the most frequent second indication. Placenta attachment anomalies are seen approximately 25% of cases who have placenta praevia and the history of cesarean undergone.[19] EPH possibility of cases that undergone two or more cesarean sections previously and detected placenta praevia varies between 30% and 50%.[15,20]

Peripartum hysterectomy can be done as subtotal (supracervical) or total depending on clinical conditions. While total hysterectomy is performed in planned conditions, subtotal hysterectomy may be preferred in emergency cases where there is life-threatening hemorrhage or difficult cervix dissection. Compared to total hysterectomy, subtotal hysterectomy is a more rapid process and recommended for non-stable patients though it is not associated with less blood loss or less morbidity.[21] The possibility of performing subtotal hysterectomy in atonia cases is higher. Total hysterectomy was performed to 14 (77.8%) cases and subtotal hysterectomy was applied to 4 (22.2%) cases in our study. All of those who were applied subtotal hysterectomy were atonia cases.

Cesarean hysterectomy technique includes some surgical principles as non-pregnants. If possible, it should be paid attention to push bladder downward before hysterectomy as it may be difficult to push bladder after uterine incision and delivery of fetus.

As frozen response of the biopsy taken from the mass during cesarean section came from mucinous cystadenocarcinoma +

In our study, we performed total abdominal hysterectomy + bilateral salpingo-oophorectomy + pelvic lymphadenectomy + paraortic lymphadenectomy + appendectomy (frozen response: mucinous cystadenocarcinoma) to one case due to adnexal mass diagnosis during pregnancy.

First of all, bilateral hypogastric artery ligation was performed in our 5 cases. EPH process was performed in these cases when bleeding could not be controlled. Hypogastric artery ligation can be done before or together with the hysterectomy in order to get under control bleeding.

Main complications of EPH are urological injuries and bleeding. Transfusion frequency was reported as 75%.[22] Blood and blood products were transfused to all cases in our study. Average transfused blood product was determined as 7.3 (4-10) units. There were 5 (27.7%) cases who had ureteral injury as 3 of them were bladder injury (16.6%) and 2 of them were ureteral injury (11.1%). DIC developed in our 6 cases (33.3%). Relaparatomy was applied to our 3 cases. 2 of them were done due to ureteral repair (neocystostomy) and one of them was done due to hemorrhage developed postoperatively.

In the literature, maternal mortality together with EPH is reported between 0% and 17%. [9,23] In our study, maternal and fetal mortality occurred in the same case. The case with maternal aortic stenosis was taken to cesarean section due to fetal distress at her 34th gestational week. Maternal and fetal mortality could not be prevented in the patient who developed DIC and atonia during the operation. In our study, maternal and fetal mortality incidence in EPH cases was reported as 5.5%.

In developing countries, uterine atonia has still been the most frequent indication for postpartum hemorrhage and EPH. However, together with the certain increase in cesarean rates, it stands out that there are serious increases in the incidence of placenta attachment anomalies. In our study, we see that placenta attachment anomalies are the most frequent indication of emergency peripartum hysterectomy. Placenta praevia cases and pregnants who previously had cesarean operations should be evaluated carefully in terms of placenta attachment anomaly. Delivering in the centers which have adequate staff and equipment should be recommended for pregnants who are in risk group.

Conclusion

EPH is with high mortality and morbidity but also a life-saving procedure if it is performed properly and well-timed.

References

1. Henrich W, Surbek D, Kainer F, Grottke O, Hopp H, Kiesewetter. Diagnosis and treatment of peripartum bleeding. *J Perinat Med* 2008;36:467-78.
2. Forna F, Miles AM, Jamieson DJ. Emergency peripartum hysterectomy: A comparison of cesarean and postpartum. *Am J Obstet Gynecol* 2004;190:1440-4.
3. Kwee A, Bots ML, Visser GH, Bruinse HW. Emergency peripartum hysterectomy: a prospective study in The Netherlands. *Eur J Obstet Gynecol Reprod Biol* 2006; 124:187-92.
4. Yucel O, Ozdemir I, Yucel N, Somunkiran A. Emergency peripartum hysterectomy: a 9-year review. *Arch Gynecol Obstet* 2006;274:84-7.
5. Drife J. Management of primary postpartum haemorrhage. *Br J Obstet Gynaecol* 1997;104:275-7.
6. Kastner ES, Figueroa R, Garry D, Maulik D. Emergency peripartum hysterectomy: experience at a community teaching hospital. *Obstet Gynecol* 2002;99:971- 5.
7. Habek D, Becareviç R. Emergency peripartum hysterectomy in a tertiary obstetric center: 8 year evaluation. *Fetal Diagn Ther* 2006;22:139-42.
8. Bai SW, Lee HJ, Cho JS, Park YW, Kim SK, Park KH. Peripartum hysterectomy and associated factors. *J Reprod Med* 2003;48:148-52.
9. Zeteroglu S, Ustun Y, Engin-Ustun Y, Sahin G, Kamaci M. Peripartum hysterectomy in a teaching hospital in the eastern region of Turkey. *Eur J Obstet Gynecol Reprod Biol* 2005;120:57-62.
10. Ozden S, Yildirim G, Basaran T, Gurbuz B, Dayicioglu V. Analysis of 59 cases of emergent peripartum hysterectomies during a 13-year period. *Arch Gynecol Obstet* 2005;271:363-7.
11. Maral I, Sözen U, Balık E. Peripartum hysterectomy: analysis of 64 cases. *Anatolian J Gynecol Obst* 1993;3: 43-7.
12. Akar ME, Yilmaz ES, Yuksel B, Yilmaz Z. Emergency peripartum hysterectomy. *Eur J Obstet Gynecol Reprod Biol* 2004;113:178-81.
13. Yalınkaya A, Hakverdi AU, Ölmez G. Acil peripartum histerektomi. *Perinatoloji Dergisi* 2004;12:155-9.
14. Williams MA, Mittendorf R. Increasing maternal age as a determinant of plasenta previa. More important than increasing parity? *J Reprod Med* 1993;38:425- 8.
15. Clark SL, Yeh SY, Phelan Jp, Bruce S, Paul RH. Emergency hysterectomy for obstetric hemorrhage. *Obstet Gynecol* 1984;64:376- 80.
16. Selo-Ojeme DO, Bhattacharjee P, Izuwa-Njoku NF, Kadir RA. Emergency peripartum hysterectomy in a tertiary London hospital. *Arch Gynecol Obstet* 2005;271:154-9.
17. Yamani Zamzami TY. Indication of emergency peripartum hysterectomy: review of 17 cases. *Arch Gynecol Obstet* 2003;268:131-5.
18. Kayabasoglu F, Guzin K, Aydogdu S, Sezginsoy S Turkgeldi L, Gunduz G. Emergency peripartum hysterectomy in a tertiary Istanbul hospital. *Arch Gynecol Obstet* 2008;278:251-6.
19. Stanco LM, Schrimmer DB, Paul RH, Mischell DR Jr. Emergency peripartumhysterctomy and associated risk factors. *Am J Obstet Gynecol* 1993;168:879-83.
20. Silver RM, Landon MB, Rouse DJ, et al. Maternal morbidity associated with multiple repeat cesarean deliveries. *Obstet Gynecol* 2006; 107:1226-32.
21. Van Horn MA, Van Dongen PW, Mulder J. Maternal consequencesof cesarean section. A retrospective study of intraoperative and postoperative maternal complications of cesarean section during a 10- year period. *Eur J Obstet Gynecol* 1997;74:1-6.
22. Shellhaas C. The MFMU cesarean registry: hysterectomy-its indications, morbidities and mortalities. *Am J Obstet Gynecol* 2002;185:123.
23. Zelop CM, Harlow BL, Frigoletto FD Jr, Safon LE, Saltzman DH. Emergency peripartum hysterectomy. *Am J Obstet Gynecol* 1993;168:1443-8.

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First Trimester Diagnosis of Pentalogy of Cantrell: A Case Report

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Abstract

Objective: Pentalogy of Cantrell is a very rare congenital malformation complex, in which the intrathoracic and intraabdominal organs are completely or partially located outside the body secondary to the thoracoabdominal body wall defects.

Case: In this report, a 23-year-old primigravid woman who admitted to our perinatology clinic in the 12th week of her pregnancy was presented. Following the first trimester scanning, the fetus was diagnosed as having a large abdominal defect, an ectopia cordis and club foot. Informed consent was obtained and termination of pregnancy was performed.

Conclusion: Neonatal prognosis of the fetuses with pentalogy of Cantrell is generally poor and termination of pregnancy should be offered in cases prenatally diagnosed at early weeks.

Keywords: Pentalogy of Cantrell, ectopia cordis, first trimester.

İlk trimesterde tanısı koyulan Cantrell pentalojisi: Olgu sunumu

Amaç: Cantrell pentalojisi torakal ve abdominal defektlere eşlik eden, intratorasik-intraabdominal organ evisserasyonları ile karakterize, son derece nadir görülen bir anomali kompleksidir.

Olgu: Bu vaka sunumunda 23 yaşında primigravid, 12. gebelik haftasında ultrasonografi aracılığıyla Cantrell pentalojisi tanısı konulan bir olgu tanımlanmaktadır. Obstetrik ultrasonografisinde fetusta geniş omfalosel, ektopia kordis ve pes ekinovarus anomalileri saptanmıştır. Ailenin onayı ile gebelik terminasyonu uygulanmıştır.

Sonuç: Neonatal cerrahi sonuçları genelde kötüdür ve erken gebelik haftalarında tanı alan olgulara gebelik sonlandırması önerilmektedir.

Anahtar Sözcükler: Cantrell pentalojisi, ektopia kordis, ilk trimester.

Introduction

Pentology of Cantrell or thoracoabdominal ectopia cordis defined by Cantrell in 1958 for the first time is an anomaly complex characterized by sternal, anterior, diaphragmatical, pericardial or supraumbilical abdominal defects together with heart located out of thorax.[1] Its incidence is 100,000 and it is 0.5-0.7 in pregnancy, but its certain etiology is not known.[2]

Though prenatal diagnosis is easy, most of the cases can be diagnosed at second trimester. Cardiac anomalies such as atrial septal defect, ventricular septal defect and Fallot tetralogy frequently accompany to the syndrome and the most important factor determining the prognosis is the severity of intracardiac anomalies.[3] Rare cases which live by corrective surgery performed in neonatal period are reported in the literature.[4, 5]

In this case report, a case diagnosed as pentalogy of Cantrell by ultrasonography at 12th gestational week and the management are discussed in company with current literature information.

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Case Report

Twenty-two years old patient with Gravida 1 and Parity 0 applied to our clinic at her 12th gestational week for routine follow up. There was no prominent diagnosis in the obstetric history or family history of the patient. In the obstetric ultrasonography, single, living fetus with 58 mm crown-rump length and compatible with 12 weeks was detected. In the ultrasonographical examination of fetus, sternal defect, ectopia cordis and abdominal anterior wall defect were detected (Figure 1).

It was seen that liver and intestinal structures were herniated due to abdominal anterior wall defect. Flow in ductus venosus was evaluated as normal in the colored Doppler sonography. In the light of current findings, nuchal translucency (NT) value of the fetus diagnosed as pentalogy of Cantrell was measured as 2.7 mm (bigger than 95. percentile). Though any major anomaly was not detected fetal extremities, pes equinovarus deformity was detected in both lower extremities. Examination by 3D ultrasonography could not be performed. Current findings and the prognosis of the disease were told to the family. After their informed consent was taken, pregnancy was terminated within 9 hours by totally 800 microgram vaginal misoprostol. In the macroscopic examination of 34 gram female fetus, a wide median defect including abdominal anterior wall and thorax, and intraabdominal organs herniated by this defect and ectopic located heart were observed (Figure 2).

Skin biopsy was taken from the fetus for genetic examination. As a result of the genetic examination, it was found as 46, XX normal karyotype. In the pathological examination, thoracic ectopia cordis together with sternum defect, abdominal anterior wall defect and herniation of intraabdominal organs were observed in the fetus.

Discussion

Pentalogy of Cantrell is a quite rare anomaly in eviscerations of intrathoracic-intraabdominal organs accompanying thoracic and abdominal defects. All components of the syndrome rarely coexist. In the series of Toyoma et al.[6] including 61 cases, it is categorized into three groups according to the existence of components forming pentalogy. In type 1, all five defects exist diagnostically. In type 2, four or five defects are together with an estimated diagnosis. In type 3, only incomplete expression of defects exists in various degrees.[6]

Pathogenesis of the syndrome is not known exactly. Thoracic and abdominal wall develop-

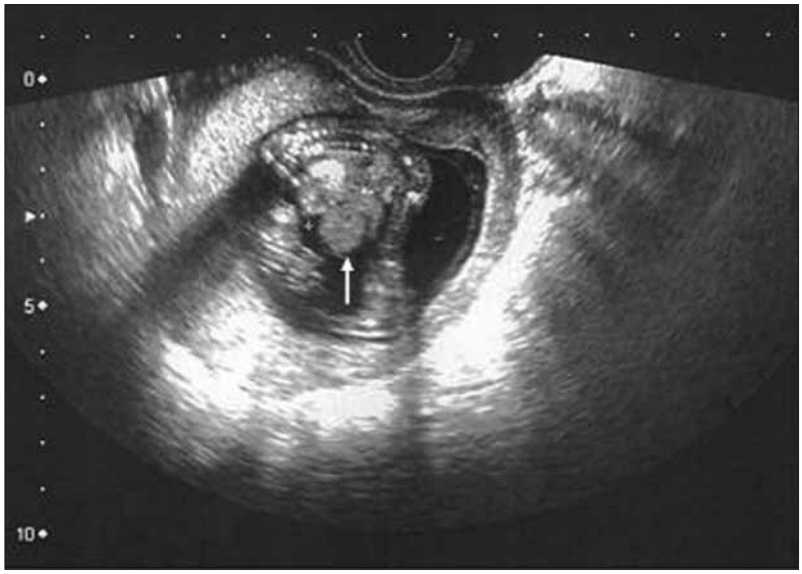

Figure 1. Appearance of abdominal anterior wall defect (white arrow) including liver tissue in first trimester and ectopic located heart (+ sign).

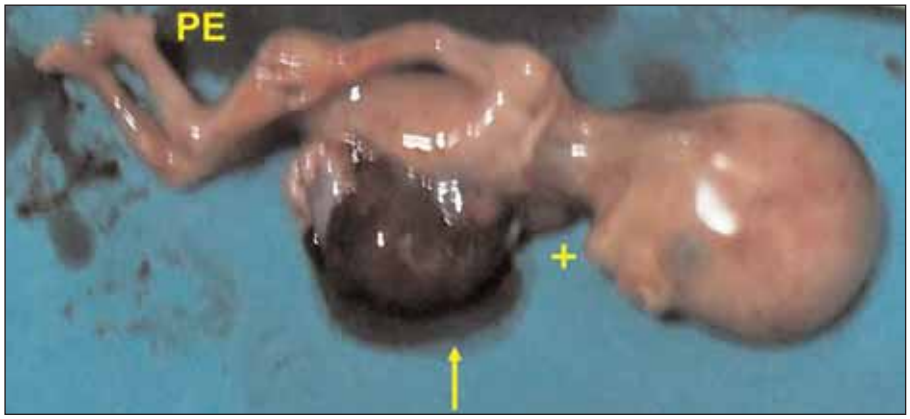

Figure 2. The appearance of ectopic cordis (+ sign), herniated liver and intestinal segments (white arrow) and 12 week fetus having pentalogy of Cantrell with pes equinovarus (PE).

ments are completed at 9th week of embryo. It is reported that if any defect appears on the midline fusion of embryonic lateral mesoderms due to genetic or external reasons at this period, clinical situations may appears varying from isolated ectopia cordis to complete ventral evisceration according to the location and severity of defect.[6,7]. Some researchers reported that pentalogy of Cantrell may occur by the effect of "mechanical teratogenity" caused by chorionic or yolk sac rupture.[8]

In complete cases, the diagnosis of the syndrome can be established easily beginning from 10th gestational week; however, especially as in our case, the diagnosis can be established on second trimester in 60% of cases with incomplete defects or isolated ectopia cordis .[9] Our case is an example in terms of establishing early diagnosis. Heart out of thorax together with the existence of liver and intestine segments eviscerated by abdominal anterior wall defect in ultrasonographic examination is diagnostic[7,10] In first trimester cases where it is suspicious to diagnose, 3D ultrasonography or fetal magnetic resonance examination may provide more detailed information about disease.[10]

Pentalogy of Cantrell is accepted as a sporadic malformation group, but also hydrocephaly, encephalocele, cloacal exstrophy and intrinsic cardiac defects may accompany to the syndrome.[4-6] In our case, bilateral club foot deformity was detected in addition to the pentalogy. Most frequently defined chromosomal anomaly associated with pentalogy is Trisomy 18 which can be found in 5-10% of cases.[1-4] Chromosome examination result of our case was found as 46, XX normal karyotype. Before giving consultancy about prognosis, prenatal diagnosis should certainly be suggested to couples who do not want the option of dispatch by current diagnosis.

The prognosis in pentalogy of Cantrell varies according to other accompanying anomalies and intrinsic heart anomalies; however, syndrome generally is accepted as lethal.[6-9]. Gestational termination is reported as a proper approach in early gestational weeks.[2-5] An atraumatic cesarean delivery and then a corrective surgery are recommended in cases that have isolated ectopic heart anomaly and normal karyotype. It was reported that rarely positive results are obtained by corrective surgery applied to these cases at neonatal period.[4,5] It was accepted that it is the most significant factor causing low surgical success of major vessel bendings caused by the reduction of cavities of visceral organs such as heart and liver.

Conclusion

Consequently, as a rare congenital anomaly group, pentalogy of Cantrell requires a proper perinatal evaluation plan when it is detected at prenatal period. Fetus should be investigated in terms of other accompanying anomalies and intrinsic cardiac defects. According to the literature, termination is suitable when anomaly is detected at

early gestational weeks or in case of the existence of accompanying chromosomal anomalies. Atraumatic cesarean delivery can be applied by pediatric surgery under consultation in cases with isolated ectoia cordis and with diploid chromosome diagnosed after 2nd trimester.

References

1. Cantrell JR, Haller JA, Ravitch MM. A syndrome of congenital defects involving the abdominal wall, sternum, diaphragm, pericardium, and heart. *Surg Gynecol Obstet* 1958;107:602–14.
2. Desselle C, Herve P, Toutain A, Lardy H, Sembely C, Perrotin F. Pentalogy of Cantrell: sonographic assessment. *J Clin Ultrasound* 2007;35:216-20.
3. Hornberger LK, Colan SD, Lock JE, Wessel DL, Mayer JE. Outcome of patients with ectopia cordis and significant intracardiac defects. *Circulation* 1996;94:32-7.
4. Korver AM, Haas F, Freund MW, Strengers JL. Pentalogy of Cantrell: successful early correction. *Pediatr Cardiol* 2008;29:146-9.
5. Samir K, Ghez O, Metras D, Kreitmann B. Ectopia cordis, a successful single stage thoracoabdominal repair. *Interact Cardiovasc Thorac Surg* 2003;2:611-3.
6. Toyama WM. Combined congenital defects of the anterior abdominal wall, sternum, diaphragm, pericardium and heart: a case report and review of the syndrome. *Pediatrics* 1972;50:778–92.
7. Önderoğlu L, Baykal C, Tulunay G, Talim B, Kale G. Prenatal diagnosis of Cantrell's pentalogy: a case report. *Turk J Pediatr* 2003;45:357-8.
8. Groner JI, Ziegler MM, Azizkhan RG, Weber TR. Operative Pediatric Surgery. New York: McGraw-Hill Inc, 2003;279-93.
9. Repondek-Liberska M, Janiak K, Wloch A. Fetal echocardiography in ectopia cordis. *Pediatr Cardiol* 2000; 21:249-52.
10. Peixoto-Filho FM, Do Cima LC, Nakamura-Pereira M. Prenatal diagnosis of pentalogy of Cantrell in the first trimester: is 3-dimensional sonography needed? *J Clin Ultrasound* 2009;37:112-4.
11. McMahon CJ, Taylor MD, Cassady CI, Olutoye OO, Bezold LI. Diagnosis of pentalogy of Cantrell in the fetus using magnetic resonance imaging and ultrasound. *Pediatr Cardiol* 2007;28:172-5.
12. Murata S, Nakata M, Sumie M, Mastsuabra M, Sugino N. Prenatal diagnosis of pentalogy of Cantrell with craniorachischisis by three-dimensional ultrasonography in the first trimester. *Taiwan J Obstet Gynecol* 2009;48: 317-8.
13. Gün I, Kurdoğlu M, Müngen E, Muhcu M, Babacan A, Atay V. Prenatal diagnosis of vertebral deformities associated with pentalogy of cantrell: the role of threedimensional sonography? *J Clin Ultrasound* 2010;38:446-9.

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Fetal Cardiac Rhabdomyoma which Tuberous Sclerosis did not Attend: A Case Report

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Abstract

Amaç: Prenatal dönemde fetuslar intrakardiak kitle açısından mutlaka değerlendirilmeli, saptandığında da akla ilk rabdomyom gelmelidir. Ayrıca tuberoz skleroz birlikteliği açısından da dikkatli olunmalıdır.

Olgu: Prenatal 32. haftada yapılan ultrasonografide fetal kalpte, sağ ventrikül içinde bir adet hiperekojen kitle saptanan olgu sunulmuştur. Doğum sonrası çekilen ekokardiyografisinde de kalpte iki adet rabdomyom ile uyumlu kitle saptanan olgunun tuberz oskleroz açısından yapılan tetkiklerinde herhangi bir başka patolojiye rastlanmadı. Kitleler kalp çıkışında obstrüksiyona ya da aritmiye neden olmadığı için cerrahi ve antiaritmik tedavi düşünülmedi. Yapılan ekokardiyografi takiplerinde kitlelerin üçüncü ayda gerilediği görüldü.

Sonuç: Prenatal dönemde fetuslar intrakardiak kitle açısından mutlaka değerlendirilmeli, saptandığında da akla ilk rabdomyom gelmelidir. Ayrıca tuberz oskleroz birlikteliği açısından da dikkatli olunmalıdır.

Anahtar Sözcükler: Prenatal, rabdomyom, tuberoz skleroz.

Tuberoz sklerozun eşlik etmediği fetal kardiak rabdomyom: Olgu sunumu

Objective: Fetuses must be evaluated prenataly for intracardiac mass. Rhabdomyoma must be recurred to the mind firstly when intracardiac mass is determined and tuberous sclerosis is invastigated because of high synergy rate.

Case: A case was preferred that one mass was determined in fetal cardiac right ventricule at her prenataly 32nd week with ultrasonography. Also two massses which were competibled with rhabdomyoma were determined in heart at echocardiography which is performed postnatally. But pathologic finding was not determined at exeminations for thubero sclerosis. Surgical and antiarrhythmic treatment were not performed because of there was not obstruction due to the massses in heart or arrhythmia. The massses regressed spontanously at third mounth of follow up.

Conclusion: Fetuses must be evaluated prenataly for intracardiac mass. Rhabdomyoma must be recurred to the mind firstly when intracardiac mass is determined and tuberous sclerosis is invastigated because of high synergy rate.

Keywords: Prenatal, rhabdomyoma, tuberous sclerosis.

Introduction

Rhabdomyomas are the cardiac tumors most frequently met at childhood.[1] Prenatal diagnosis of rhabdomyomas can generally be established by ultrasonographical examinations after 32nd gestational week. Due to their frequent association, tuberous sclerosis should be considered in cases that were detected rhabdomyomas in heart.[2] Tuberous sclerosis is one of the neurocutaneous syndromes characterized with tumoral and non-tumoral proliferations and anomalies holding many systems especially central nervous system, skin, retina, kidney and heart. It is inherited as autosomal dominant. Cerebral cortical anomalies, subependymal tumors, seizures, mental retardation, renal angiomyolipomas and cardiac rhab-

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domyomas may be seen.[1,3] In the studies performed, cardiac rhabdomyoma is seen in 43-60% of cases with tuberous sclerosis.[2]

In this case report, a case that was diagnosed as having rhabdomyoma in prenatal period, where tuberous sclerosis was excluded in the postnatal period and rhabdomyoma regressed in the follow-up.

Case Report

A hyperechogenic mass was detected in the right ventricle of fetal heart in the ultrasonography performed in the 32nd gestational week of a 20-years-old mother whose gestational follow-up was performed regularly (Figure 1).

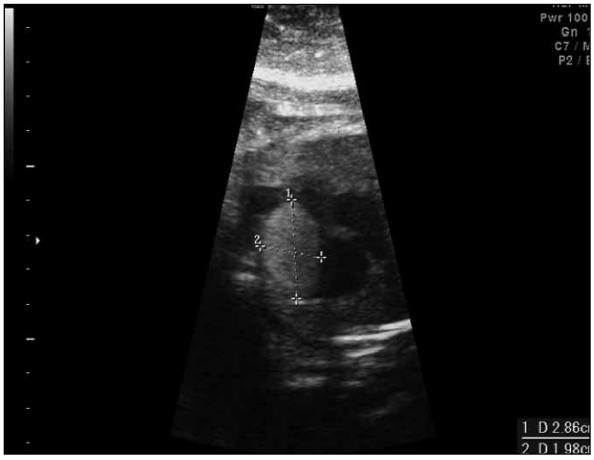

Figure 1. Intracardiac mass in prenatal ultrasonography.

The birth weight of a girl baby taken to newborn intense care unit after born by cesarean at 38th-39th week according to the last menstrual date of a twenty-years-old mother with G2P1 and the history of cesarean was 3200 gr (25-50p) while length was 49 cm (10-25p) and head circumference was 34 cm (10p). Arterial blood pressure was 72/43 mmHg and arterial oxygen saturation was 98%. No murmur and additional sound was detected in the cardiac auscultation of the cases and heart beats were rhythmic; and other system inspections were evaluated as ordinary.

In the laboratory examinations, hemoglobin was found as 17.1 g/dL, hematocrit as 47.6%, leucocyte count as 16,600/mm^3, and thrombocyte level as 334,000/mm^3. Urea, creatinine, blood electrolytes, blood glucose, AST, ALT and cardiac enzymes were at normal levels.

It was seen that the cardiac shadow of the case was normal in telecardiography, the case had sinus rhythm in electrocardiographic examination, axis was on right inferior and there were ST changes and left ventricle hypertrophy Figures 2 and 3.

In the echocardiography, two masses considered as rhabdomyomas and not causing stenosis on ventricle outlet were found as one of them was 18x11 mm in intraventricular septum within right ventricle and other one was 9 x 17 mm in lateral wall basal of right ventricle (Figure 4).

No pathology was found in the cranial tomography of the case that was planned to investigate in terms of tuberous sclerosis. Tuberous sclerosis

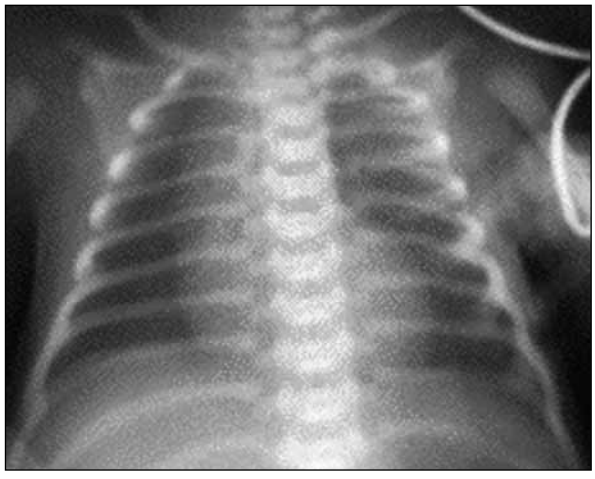

Figure 2. Telecardiography.

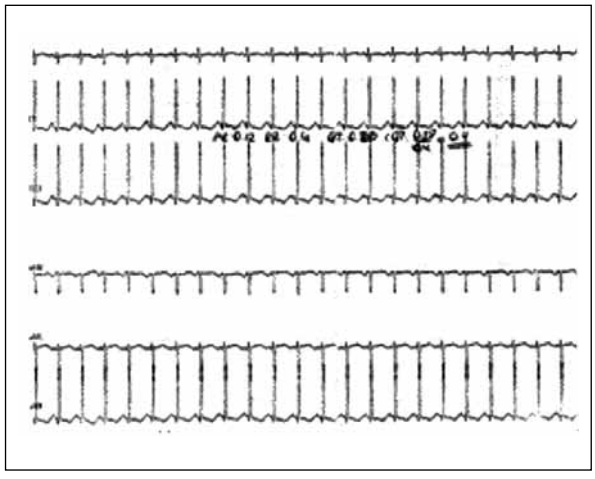

Figure 3. Electrocardiography.

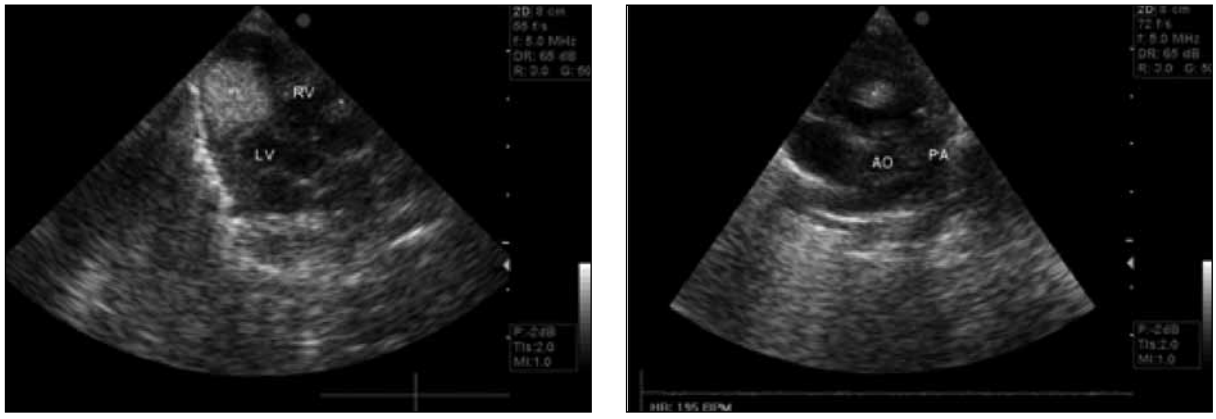

Figure 4. Two hyperechogenic masses on right ventricle in echocardiography.

was excluded in the evaluation of the case of which was found normal by urinary system ultrasonography and retinal examination performed in terms of kidney and eye involvements.

No arrhythmia occurred and heart beat rate was around 100-140/min. Since rhabdomyomas in the heart did not cause any obstruction and arrhythmia, surgical and anti- arrhythmic treatments were not considered. As cardiac rhabdomyomas could regress by themselves, the patient was followed up by echocardiography with two weeks of intervals. It was observed that masses regressed on the third month of the follow up.

Discussion

Tuberous sclerosis is a disease holding many systems by mental retardation, epilepsy, and adenoma sebaceum. It is inherited as autosomal dominant. Rhabdomyomas are the most frequent cardiac tumors of childhood; they are frequently seen together with tuberous sclerosis and are very significant for early diagnosis of tuberous sclerosis.[1,2,4]

While rhabdomyomas may settle on any part of the heart, they are generally seen in ventricles and areas close to septum.[5] They often stay as many masses together. Their clinical findings are quite variable. While they may not display any indication, they may also cause stenosis, heart failure, arrhythmia and even sudden baby deaths depending on their sizes and numbers.[5,6] In our case, masses located on right ventricle and did not display any clinical finding. The reason is that masses locate on septum and lateral wall, and are not so big.

In a multi-centered study, tuberous sclerosis was detected in 10 of 19 fetuses with cardiac tumor (52.6%), and it was seen that lesions were more than one in 9 of these 10 fetuses (90%).[7] In another study, tuberous sclerosis was detected later on in 51 of 85 fetuses with rhabdomyoma (59.3%).[8] In our case, masses more than one were detected, but there was no tuberous sclerosis.

As rhabdomyomas can regress in time, it is suggested to follow them by echocardiography. Surgical treatment is recommended when they cause mechanical stenosis in heart and life-threatening arrhythmias.[6] Surgical intervention was not considered since rhabdomyoma detected in our case did not cause hemodynamic disturbance and arrhythmia; therefore the case was followed up by echocardiography and it was observed that it regressed completely on third month.

Fetuses should certainly be investigated in prenatal period in terms of intracardiac mass and when detected, rhabdomyomas should be considered first. Patients should be evaluated by echocardiography in postnatal period and it should not be forgotten that it may cause mechanical stenosis in heart, obstruction and arrhythmia and may cause serious life-threatening results. It should also be paid attention for the association with tuberous sclerosis and other systems certainly should be checked.

Conclusion

Fetuses should certainly be investigated in prenatal period in terms of intracardiac mass and when detected, rhabdomyomas should be consid-

ered first. Patients should be evaluated by echocardiography in postnatal period and it should not be forgotten that it may cause mechanical stenosis in heart, obstruction and arrhythmia and may cause serious life-threatening results. It should also be paid attention for the association with tuberous sclerosis and other systems certainly should be checked.

References

1. Nadas AS, Ellison RC. Cardiac tumors in infancy. *Am J Cardiol* 1968;21:363-6.
2. Harding CO, Pagon RA. Incidence of tuberous sclerosis in patients with cardiac tumors in early infancy and childhood. *J Thoracic Cardiovasc Surg* 2005; 129:1358-63.
3. Gomez MR. Neurocutaneus disease. In: Bradley WC, Daroff RB, Fenichel GM, Marsden CD. Neurology in Clinical Practice. 2nd ed. Oxford: Butterworth Heinemann, 1996:1566-71.
4. Werner H, Mirlesse V, Jacquemard F, Sonigo P, Delezoide AL, Gonzales M, et al. Prenatal diagnosisi of tuberous sclerosis. Use of magnetic resonance imaging and its implications for prognosis. *Prena Diagn* 1994;14:1151-4.
5. Butany J, Nair V, Naseemuddin A, Nair GM, Catton C, Yau T. Cardiac tumors: diagnosis and management. *Lancet Oncol* 2005;6:219-28.
6. Bader RS, Chitayat D, Kelly E, et al. Fetal rhabdomyoma: prenatal diagnosis, clinical outcome, and incidence of associated tuberous sclerosis complex. *J Pediatr* 2003;143:620-4.
7. Holley DG, Martin GR, Brenner JI, et al. Diagnosis and management of fetal cardiac tumors: a multicenter experience and review of published reports. *J Am Coll Cardiol* 1995;26:516-20.
8. Söğüt A, Ömeroğlu RE, Özmen M, Aydın M, Yüksel A. Tuberosklerozlu bir olguda kardiyak rabdomyom. *İstanbul Tıp Fakültesi Mecmuası* 2001;64:102-4.

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Five Times of Cord around Neck in Cesarean Section: A Case Report

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Abstract

Objective: We discussed a rare case of spinal muscular atrophy (SMA) type 0, was followed with prenatal diagnosis of intrauterine growth restriction (IUGR), five times of cord around neck detected during cesarean section, in the highlights of the literature.

Case: A pregnant woman who was followed with the diagnosis of IUGR during 32. gestational week. In the 38. gestational week; cord around neck for five times and a real knot were detected in the cesarean section. Difficulty in swallowing and absorbing, also significant respiratory muscle weakness were found at the follow up of the baby. SMA was suspected according to these symphtoms. With the analyse of PCR RFLP (Polymerase chain reaction – restriction fragment length polymrphism) SMN 1 (Telomeric survival motor neuron gene) homozygot exon 7 and 8 deletions were found, SMA type 0 was diagnosed according to these findings.

Conclusion: During the 2. trimester of pregnacy, with a careful ultrasound examination, cord around neck can be succesfully determined. It should be considered that cord around neck risk rate can be increased in the 3. trimester. Hypotonia, severe respiratory muscle weakness involving the infants to be a good antenatal and postnatal history, examination and molecular study will identify the rare cases of SMA. Genetic counseling should be given to the parents.

Keywords: Pregnancy, umblical cord around neck, intrauterine growth retardation, spinal muscular atrophy.

Doğumda boyun çevresinde beş kez kordon dolanması: Olgu sunumu

Amaç: Prenatal dönemde intrauterin gelişme kısıtlılığı (IUGK) tanısı ile takip edilen ve miyadında yapılan sezaryen sırasında boyun çevresinde beş kez kordon dolanması saptanan spinal musküler atrofi (SMA) tip 0 olgusu nadir görülmesi sebebiyle, literatür bilgileri ışığında tartışılmıştır.

Olgu: 32. gebelik haftasından itibaren IUGK tanısı ile takip edilen hastanın, 38. gebelik haftasında yapılan sezaryeni esnasında boyun çevresinde beş kez kordon dolanması ve bir adet gerçek düğüm tespit edildi. Bebeğin izleminde; yutma ve emmede güçlük çekmesi, aynı zamanda solunum kaslarında belirgin güçsüzlük olması üzerine SMA'dan şüphelenildi. PCR RFLP (polymerase chain reaction restriction fragment length polymorphism) yöntemi ile yapılan analizde; SMN 1 (telomerik survival motor nöron geni) homozigot ekzon 7 ve 8 delesyonlarının gösterilmesi üzerine SMA tip 0 tanısı konuldu.

Sonuç: Gebeliğin 2. trimesterinden itibaren yapılan dikkatli bir ultrasonografik inceleme ile umbilikal kordonun fetus boynuna dolanmış olduğu saptanabilir. 3. trimestere yaklaşan haftalarda bu oranın arttığı akılda tutulmalıdır. Hipotoni ve solunum kaslarını da içine alan ağır güçsüzlüğü olan yenidoğanlarda iyi bir antenatal ve postnatal öykünün alınması, muayene bulguları ve moleküler çalışma ile birlikte nadir görülen SMA olgularının tanınmasını ve ailelere gerekli genetik danışmanlığın verilmesi olanağını sağlayacaktır.

Anahtar Sözcükler: Gebelik, boyunda kordon dolanması, intrauterin gelişme kısıtlılığı, spinal musküler atrofi.

Introduction

The coiling of umbilical cord around fetus neck is seen in 23-33% of all pregnancies and it is generally evaluated as benign.[1,2] It is reported that this situation can be seen at a rate of 6% on 21st gestational week.[3] It is less often to observe coiling or knotting of cord around fetus body and extremities.[4,5]

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One of the most frequently seen genetic diseases causing child death around the world is autosomal recessively inherited spinal muscular atrophy (SMA).[6] While SMA was grouped into three sub-groups according to their clinical aspects and beginning age in previous years, Dubowitz defined severe cases (previously classified as SMA Type 1) as SMA 0. SMA Type 0 is clinically characterized severe symmetrical muscle weakness and flaccidity seen much more in lower extremities than upper extremities after birth and affected much more in proximal extremity than distal. Patients frequently require resuscitation and ventilator support at delivery.[6-9]

SMA occurs as a result of SMN (survival of motor neuron) gene mutations on long side of 5th chromosome.[6-10] In this article, SMA Type 0 case which was followed up by IUGR diagnosis in prenatal period and found cord coiled 5 times around neck during cesarean was discussed within the light of literature since it is seen rarely.

Case Report

Thirty-four years old, G2 P1 pregnant applied to our clinic for routine pregnancy follow-up. Brother of the patient had cerebral palsy, but there was no kin marriage history of the pregnant. At her 1st trimester screening, free beta HCG was 28.3 ng/ mL (0.61 MoM) and PAPP- A was 0.83 mIU /mL (0.63 MoM). In the ultrasonographical examination of fetus at 11th-14th gestational week, it was found that nuchal translucency was 1.9 mm, a wave in ductus venosus blood flow was positive, there was no regurgitation on tricuspid valve, and nasal bone was 1.6 mm. Anatomy and development of fetus was normal. Notches were detected on bilateral uterine arteries. Fixed Down syndrome risk was calculated as 1/8136.

In the ultrasonographical examination of fetus at 22nd gestational week, biparietal diameter (BPD) was found as 54 mm, head circumference (HC) as 201 mm, abdominal circumference (AC) as 166 mm, femur length (FL) as 39 mm, fetal heart beat rate as 138 beat/min., and a cord existence located on placenta anterior wall and on neck. It was seen that a wave in ductus venosis was positive and there was no regurgitation on tricuspid valve. Notching was continuing on bilateral uterine arteries. Anatomy and development of fetal was observed as normal. 1st hour blood glucose was found as 121 on 50 g oral glucose tolerance test (OGTT). In the ultrasonographical examination at 32nd gestational week, fetal measurements were found -2 below standard deviation (SD) according to gestational week. Estimated fetal birth weight was 1,352 g, amniotic fluid volume was normal and the patient detected breech presentation was taken to follow-up by IUGR diagnosis. There was cord coiled around neck two times.

The pregnant was followed up by fetal Doppler and non-stress test (NST) due to IUGR diagnosis until 38th gestational week. Single alive 2,230 gr male baby with 1st minute Apgar score 5 and 5th week Apgar score 9 was delivered by cesarean from the 38-weeks-and-3-days patient through cesarean undergone and breech presentation indications. The existence of cord coiled five times around neck (Figure 1) and true knot (Figure 2) was detected during cesarean. In the umbilical vein blood gas taken during delivery, following values were found: pH 7.36, PCO_2 38, PO_2 46, hematocrit 52. Also following values were found in the umbilical artery blood gas: pH 7.31, PCO_2 50, PO_2 23, hematocrit 53. Postoperative cord length was measured as 105 cm.

In the newborn examination, body temperature was 35.4 °C (axillary) and blood pressure was 55/35 mmHg. There were excessive secretion, certain hypotonia and weakness due to weakness in swallowing muscles. In the radiological examination, chest radiography evaluated as normal. The newborn was dispatched after being followed up for two days in intense care unit. When baby got difficulty to swallow and suck, SMA was suspected. With the analysis of PCR RFLP (Polymerase chain reaction – restriction fragment length polymorphism) SMN 1 (Telomeric survival motor neuron gene) homozygote exon 7 and 8 deletions were found, then SMA type 0 was diagnosed according to these findings.

Patient who was diagnosed as sepsis three times (first one was when only one-month-old) due to pneumonia has still being followed up in pediatric intense care unit by providing respiratory support.

Discussion

The most frequent location of cord coiling which appears beginning from first trimester in the

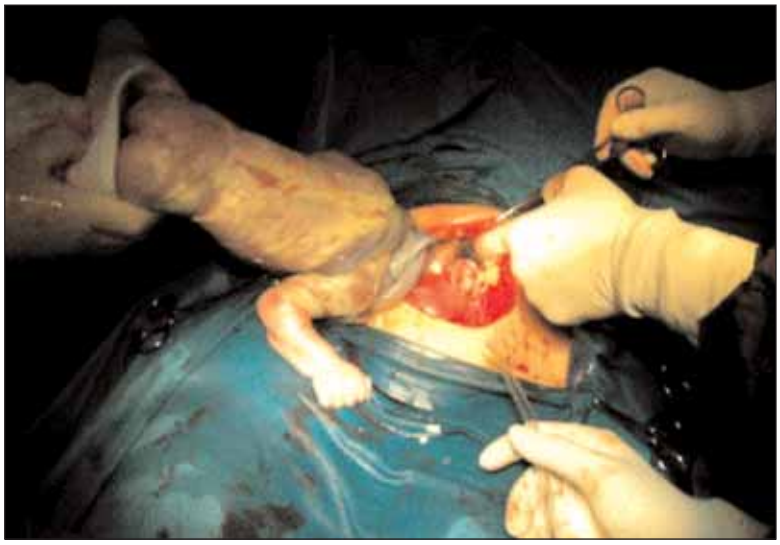

Figure 1. Umbilical cord coiled around neck five times in cesarean section.

pregnancy is the fetal neck circumference.[11] It was reported that cord may coil around neck beginning from the gestational week where cord length reaches 4/5 of fetus length.[12] It was stated that though normal term umbilical cord length is 55-75 cm, it may sometimes be 300 cm and sometimes aplasia may occur.[21] Cord length is considered as associated with coiling number.[13] In our case, cord length was determined as 105 cm.

When fetus was examined in terms of presentation, it was shown that cord coiling was frequently observed in breech presentations.[14] Breech presentation in our case was found as compatible with the literature.

The highest coiling number reported in the literature is nine.[15] In our case, 5 times cord coiling around neck was detected. Cord length, gestational week, placenta localization, fetus weight, fetus mobility and amniotic fluid amount are the factors associated with cord coiling.[12,16] In the literature, there are some studies reporting that placenta being on anterior wall also affects cord coiling.[17]

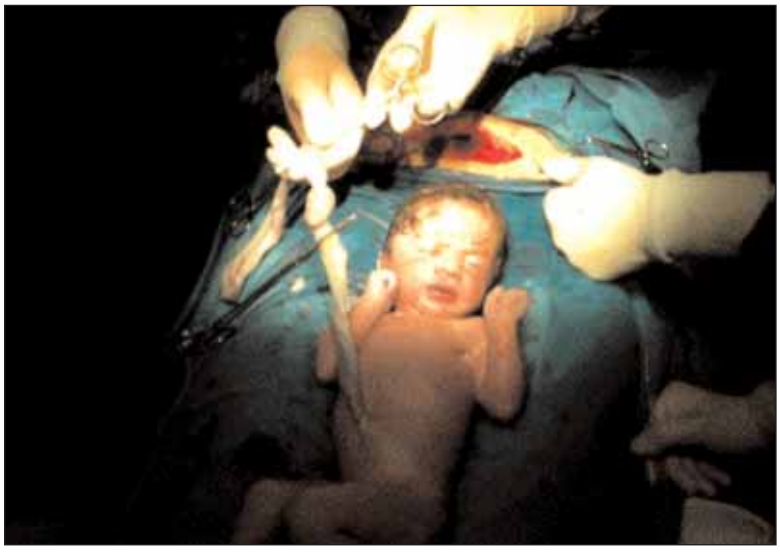

Figure 2. Umbilical cord coiled around neck five times in cesarean section.

In our case, the placenta was found as anterior wall located.

It was reported that increasing mobility of fetus at third trimester was effective on cord coiling.[13] In our case which was SMA type 0, expectation of fetal mobility decrease was not found as associated with cord coil when it was seen in delivery that cord coiled five times around fetus neck.

Clappa et al. reported that coiling rate increased as gestational weeks advanced.[13] In our case, one time cord coiling was first detected on 22nd gestational week. At 32nd gestational week, two times cord coiling was detected at neck. During the cesarean performed on 38th gestational week, five times cord coiling and one true know were detected.

SMA is a frequently seen neurodegenerative disease where it progresses with the degeneration of anterior horn cells of spinal cord and inherited by autosomal recessive. The prevalence in western societies is 1/6,000 – 1/10,000 and the carrier rate of the disease varies between 1/40 and 1/80.[18] SMA's other types as autosomal dominant and inherited according to X were also defined.[19] In patients who are diagnosed as SMA type 0, asphyxia and generalized weakness are observed in newborn period. Most of them require resuscitation and ventilation support. Bulbar muscles are weak as causing weak crying, weak sucking and swallowing, and aspiration as a result of secretion aggregation. There is frequently fasciculation on tongue.[6-9] In our case, minority of intrauterine fetal movements could not be examined clearly during fetal ultrasonographical examination or anamnesis taken from the mother. However, findings such as hypotonia and weakness were clearly observed during newborn examination. Pneumonia and sepsis developed within the first month were the most significant indication of weakness including respiratory muscles. It was shown in some studies that some of the cases who were diagnosed as having SMA after delivery could be followed by fetal IUGR diagnosis.[20] In our case, IUGR was also observed beginning from 32nd gestational week. The diagnosis was established at postnatal period as in similar studies in the literature.

When other fetal hypocinesia cases were investigated in the literature, it was seen that birth dystocia, short umbilical cord, polyhydramniosis, craniofacial malformations, multiple joint contractures and skeletal anomalies displayed association.[20] In our case, cesarean was preferred as delivery method due to the cesarean history. In our case, unlike the literature, short umbilical cord (actually long umbilical cord was observed), polyhydramniosis, craniofacial malformations and skeletal anomaly were not detected.

In our SMA type-0 case where intrauterine fetal movements were expected to decrease, observing cord coiling five times around neck and true knot during cesarean was not found compatible with the literature. Though it is not frequent to see cord coiling five times around neck in SMA cases, measuring cord length as 105 cm was considered as it can be explained by breech presentation of the fetus and anterior located placenta. By a careful ultrasonographical examination performed beginning from 2nd trimester of the pregnancy, it can be detected that umbilical cord is coiled around fetus neck. It should be remembered that this rate increases in weeks approaching 3rd trimester. In our case, cord existence around neck was detected by ultrasonographical examinations performed as of 22nd gestational week.

As seen in our case, SMA type-0 is a disease which should be considered first in differential diagnosis in patients who develop severe weakness, hypotonia and respiratory failure at newborn period. Together with examination findings and molecular study, receiving well antenatal and postnatal histories in newborns that have severe weakness including respiratory muscles will enable to know rare SMA cases and to give required genetic consultancy to families.

Conclusion

By a careful ultrasonographical examination performed beginning from 2nd trimester of the pregnancy, it can be detected that umbilical cord is coiled around fetus neck. It should be remembered that this rate increases in weeks approaching 3rd trimester.

Together with examination findings and molecular study, receiving well antenatal and postnatal histories in newborns that have severe weakness including respiratory muscles will enable to know rare SMA cases and to give required genetic consultancy to families.

References

1. Larson JD, Rayburn WF, Crosby S, Thurnau GR. Multiple nuchal cord entanglements and intrapartum complications. *Am J Obstet Gynecol* 1995;173:1228-31.
2. Ertan AK, Schmidt W. Umbilical cord entanglement and color-coded Doppler ultrasound. *Geburtshilfe Frauenheilkd* 1994;54:196-203.
3. Larson JD, Rayburn WF, Harlan VL. Nuchal cord entanglement and gestational age. *Am J Perinatol* 1997;14:555-7.
4. Kumari S, Saxena A, Monga D, Malik A, Kabra M, Kurray RM. Significance of cord problems at birth. *Indian Pediatr* 1992;29:301-5.
5. Miser WF. Outcome of infants born with nuchal cords. *J Fam Practice* 1992;34:441-5.
6. Dubowitz V. Very severe spinal muscular atrophy (SMA type 0): an expanding clinical phenotype. *Eur J Paediatr Neurol* 1999;3:49-51.
7. Balslev T, Hertz JM, Rackauskaite G, Sorensen LA. Very severe spinal muscular atrophy- type 0. A cause of congenital multiple arthrogryposis. *Ugeskr Laeger* 2001;163:5679-80.
8. MacLeod MJ, Taylor JE, Lunt PW, Mathew CG, Robb SA. Prenatal onset spinal muscular atrophy. *Eur J Paediatr Neurol* 1999;3:65-72.
9. Devriendt K, Lammens M, Schollen E, Van Hole C, Dom R, Devlieger H. Clinical and molecular genetic features of congenital spinal muscular atrophy. *Ann Neurol* 1996;40:731-8.
10. Bürglen L, Amiel J, Voilett L, Lefebvre S, Burlet P, Clermont O. Survival motor gene deletion in the arthrogryposis multiplex congenita- spinal muscular atrophy association. J *Clin Invest* 1996; 98: 1130-1132.
11. Yayla M, Sezer FA, Güngören A, Akdeniz N, Erden AC. Gebelikte umbilikal kordon dolanması. *İstanbul Jinekoloji ve Obstetrik Dergisi* 1997;1:44-6.
12. Collins JH, Collins CL, Weckwerth SR, De Angelis L. Nuchal cords: Timing of prenatal diagnosis and duration. *Am J Obstet Gynecol* 1995;173:768.
13. Clapp JF, Stepanchak W, Hashimoto K, Ehrenberg H, Lopez B. The natural history of antenatal nuchal cords. *Am J Obstet Gynecol* 2003;189:488-93.
14. Giacomello F. Ultrasound determination of nuchal cord breech presentation. *Am J Obstet Gynecol* 1988;159:531-2.
15. Cruikshank DP. Danforth's Obstetrics and Gynecology. Philadelphia: Lippincott Comp., 1994:501-19.
16. Lipitz S, Seidman DS, Gale R, Stevenson DK, Alcalay M, Menczer J, et al. Is fetal growth affected by cord entanglement? *J Perinatol* 1993;13:385-8.
17. Göynümer G, Yayla M. Gebeliğin ikinci trimesterinde boyun çevresinde kordon dolanması sıklığı ve etkileyici faktörler. *Perinatoloji Dergisi* 2004;12:93-5.
18. Pearn J. Incidence, prevalence, and gene frequency studies of chronic childhood spinal muscular atrophy. *J Med Genet* 1978;15:409-13.
19. Kobayashi H, Baumbach L, Matise TC, Schiavi A, Greenberg F, Hoffman EP. A gene for a severe lethal form of X-linked arthrogryposis (X-linked infantile spinal muscular atrophy) maps to human chromosome Xp11.3-q11.2. *Hum Mol Genet* 1995;4:1212-6.
20. Gonzales De Dios J, Martinez Frias ML, Arroyo Carrera I, Fondevilla SJ, Sanchis CA, Hernandez RF, et al. Role of signs of fetal hypokinesia in the diagnosis of spinal muscular atrophy of neonatal onset. *An Esp Pediatr* 2002;56:233-40.
21. Cunningham FG, Gant NF, Leveno KJ, GilstrapIII LC, Hauth JC. Williams Obstetrics. New York: McGraw-Hill Medical Publishing, 2001; 831.

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Non- Hodgkin Lymphoma Diagnosed During Pregnancy: A Case Report

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Abstract

Objective: Lymphomas, a heterogeneous group of disorders caused by malignant proliferation of lymphocytes. Hodgkin and non-Hodgkin lymphoma (NHL) is divided into two. Because of the rarity of NHL in pregnancy, the diagnosis and the management was presented with the literature.

Case: In the 5. gestational week; the symptoms of the patient were sore throat and a palpable mass in the neck. The biopsy was diagnosed as NHL. In the 28. gestational week, syclophosphamid, docsorubicin, vincristin, prednisone (CHOP) chemotherapy was started. In the 39. gestational week, 3,310 gr female baby was delivered. Left ventricular mild systolic dysfunction was revealed in the postnatal echocardiography of the baby. After birth, rituximab was added to the chemotherapy regimen.

Conclusion: The management of the NHL patients during pregnancy, performed with a multidisciplinary approach. Palpable cervical and submandibular masses during pregnancy, certainly should be considered in the differential diagnosis of lymphoma. That patients are showing fast cruise, must be diagnosed and treated as soon as possible.

Keywords: Non-Hodgkin lymphoma, pregnancy, chemotherapy.

Gebelikte tanı konulan Non-Hodgkin lenfoma: Olgu sunumu

Amaç: Lenfomalar, lenfositlerin malign proliferasyonu sonucu oluşan heterojen bir hastalık grubudur. Hastalık Hodgkin ve non-Hodgkin lenfoma (NHL) olmak üzere ikiye ayrılır. NHL'nın gebelikte nadir görülmesi sebebiyle tanısı ve yönetimi literatür bilgileri eşliğinde sunuldu.

Olgu: Beşinci gebelik haftasında, boğaz ağrısı ve boyunda ele gelen kitle semptomları ile gelen hastaya, yapılan biyopside NHL tanısı konuldu. Yirmisekizinci gebelik haftasında siklofosfamid, doksorubisin, vinkristin, prednizon (CHOP) kemoterapisi başlandı. Otuzdokuzuncu gebelik haftasında 3,310 g ağırlığında kız bebek doğurtuldu. Bebeğin postnatal yapılan ekokardiyografisinde sol ventrikülün hafif sistolik disfonksiyonu tespit edildi. Doğum sonrasında kemoterapi rejimine rituksimab eklendi.

Sonuç: NHL olgularının gebelik süresince ve sonrasındaki yönetimi multidisipliner yaklaşım ile gerçekleştirilmelidir. Gebelik sırasında ele gelen servikal ve submandibular kitlelerde lenfomalar ayırıcı tanıda mutlaka düşünülmelidirler. Hızlı seyir gösteren bu olgulara en kısa sürede tanı konulup tedaviye en yakın zamanda başlanmalıdır.

Anahtar Sözcükler: Non-Hodgkin lenfoma, gebelik, kemoterapi.

Introduction

Lymphomas are a heterogeneous group of disorders caused by malign proliferation of lymphocytes. According to the main histological classification, they are separated into two groups as Hodgkin and Non-Hodgkin lymphoma (NHL). Hodgkin disease is the most prevalent lymphoma type seen in pregnancy due to age distribution of patients.[1] But it is very rare to see NHL in pregnancy. Only 75 cases were reported between 1937 and 1985.[2] NHLs establish a very heterogeneous group in terms of hematologic tumors, clinical

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behavior, morphology, cell origin, etiology and pathogenesis. Though it is still not a perfect classification, REAL classification has been used since 1995.[3] NHL constitutes 4% of cancer cases newly diagnosed. It is 6th reason among reasons of newly diagnosed cancers in males and females. Prognosis is bad in a high level NHL and average life period is 1.5 years; but in a low level one, prognosis is better and average life period is 7.5 years.[4] They mostly surround peripheral lymphs and mediastinum.[4]

Lymphomas during delivery are high level. At the same time, they tend to surround organs mostly stimulated hormonally during pregnancy (such as breast, ovary, uterus etc.). Especially NHL has a bad progress in pregnancy since it is together with disseminated intravascular coagulation and aggressive tumors.

In our case, the patient who came to our clinic at her 5th gestational week with sore throat and palpable mass symptoms on neck was diagnosed as NHL in the biopsy. Her chemotherapy began on her 28th gestational week. Since NHL is rare during pregnancy, its diagnosis and management were presented together with the literature information.

Case Report

Thirty-three years old patient (G1, P 0) who did not have a similar complaint before applied to our clinic for the complaint of mass on her right cervical region. Cervical and submandibular lymph node was found in her physical examination. Lymph node biopsy was reported as lymphoma with diffuse major B cell (WHO/REAL). In the biopsy material, it was observed that cells displayed diffuse cytoplasmic staining by CD20 but no staining with CD30 and cytokeratin. In the cervical magnetic resonance (MR) examination of the patient, there were multiple cervical, submandibular and nasopharyngeal masses. Abdominal computed tomography which should be performed for staging purpose could not be done as the patient refused due to her pregnancy. Bone marrow biopsy was reported as normocellular. It was decided to apply 6 cures of CHOP chemotherapy (cyclophosphamide, doxorubicin, vincristine, and prednisone) to the patient as 3 cures would be done during pregnancy and remaining 3 cures would be done after pregnancy.

On 28th gestational week, 750 mg/m^2 cyclophosphamide, 50 mg/ m^2 doxorubicin, 2 mg vincristine and 100 mg prednisone were applied as 1st cure chemotherapy. In the obstetric examination performed after chemotherapy of the patient, amniotic fluid volume was found on placenta posterior wall and as consistent with fetal development week. Umbilical artery Doppler was measured as PI: 086 and RI: 057.

Second cure was applied on 31st gestational week and it was found in the obstetric examination after chemotherapy that fetal development was consistent with gestational week. Umbilical artery Doppler was measured as PI: 083 and RI: 051. 3rd cure of chemotherapy was applied on 38th gestational week. In the obstetric examination performed after chemotherapy, amniotic fluid volume was found within normal volume and as located on placenta posterior wall. Umbilical artery Doppler was measured as PI: 088 and RI: 055.

Four days after last chemotherapy (on 39th gestational week), the patient applied to our obstetrics clinics since her spontaneous contractions began and single alive 3,310 gr baby girl (with 1st minute Apgar score 7.5, and 5th minute Apgar score 8) was delivered by spontaneous vaginal delivery. Baby and mother did not need intense care after delivery. In the postnatal echocardiography of the baby, slight systolic dysfunction of left ventricle was observed. It was decided by Pediatrics Cardiology Department to follow up the patient without providing treatment. One week after delivery, 4th cure of chemotherapy was applied to the mother. 375 mg/m^2 rituximab treatment was added to the CHOP regime. The follow-up of the patient who received totally 6 cures of CHOP chemotherapy and rituximab has still being performed in Internal Medicine Oncology Department.

Discussion

NHL constitutes 4% of newly diagnosed cancer cases. It is 6th among the reasons of newly diagnosed cancer in females and males.[4] The most frequent three NHL types in the USA are lymphoma with diffuse major B cell (31%), follicular lymphoma (22%) and minor lymphocytic lymphoma (6%).[4] In our case, the most frequently seen lymphoma type with diffuse major B cell was observed. NHL is not prevalent in fertile ages;

however, we only see it in the literature as case reports. Lymphomas in pregnancy are high leveled and aggressive. Also they tend to surround organs mostly stimulated hormonally during pregnancy (such as breast, ovary, uterus etc.). It is seen when literature is reviewed that though cases are diagnosed lately and progress aggressively, deliveries with healthy babies born mature are reported. In our case, a healthy baby girl was delivered by spontaneous vaginal delivery at her 38th gestational week.

In NHL treatment, the method to be preferred at delivery varies according to clinical staging and histopathological type. While "wait-and-see" approach can be used in slowly developing and low leveled NHLs, chemotherapy with single agent or local radiotherapy can be also applied.[5]

Lymphoma with diffuse major B cell is more aggressive and may cause life-threatening complications at early period. Since its prognosis is bad and display rapid progression, it is needed to treat by combined chemotherapy regime. CHOP is especially the most frequently preferred combined chemotherapy regime in lymphoma with diffuse major B cell. However, studies about the safe use of this regime in pregnancy are limited. Based upon the data including limited number of case series, no increase in the frequency of fetal malformation was observed in patients who were applied CHOP on 1st trimester.[6-13]

The effects of agents used in CT at NHL over pregnancy results are given in the Table 1 together with the case series.

Our case received totally 3 cures of chemotherapy during pregnancy as first one was on 28th gestational week. It is reported in the literature that disease may grow in postpartum period in some cases. In our case, no grow was observed in postpartum period.

Rituximab is a monoclonal antibody used in the treatment of lymphoma with diffuse major B cell. It is used by combining with CHOP regime. It is reported in the literature that it is used on limited number of cases for treatment of some autoimmune diseases during pregnancy. It was reported by the data obtained from these cases that using it on first trimester did not cause any increase in the frequency of fetal anomaly.[14, 15]

In another case, combined CT was applied with CHOP and rituximab on a 35 years old pregnant

Table 1. The effect of different combined chemotherapy diets on gestational results used on aggressive NHL treatment.[7-21]

Case series	Case number	Pregnancy result
NHL receiving CHOP treatment (on 2nd and 3rd trimesters)	4	Resulted with normal pregnancy progress.
Long-term follow-up results of children who were exposed to various chemotherapy protocols (children of mothers who received alkylating agent and anthracycline agent for NHL treatment on all three trimesters)	33	No congenital neurological or psychological anomaly was observed. Learning and education performances are normal.
Case series receiving combination chemotherapy treatment due to NHL on 2nd and 3rd trimesters (all of them include alkylating agent and anthracycline)	10	Stillbirth in 1 case. No congenital anomaly was observed.
Case series that received bleomycine, vinblastine, cyclophosphamide and prednisone chemotherapy (on 2nd and 3rd trimesters)	3	Resulted with normal pregnancy progress.
The case that received etoposide and cisplatin chemotherapy	1	Resulted with stillbirth at 25th gestational week.
The case that received cyclophosphamide, prednisone and rituximab (on 2nd trimester)	1	Resulted with normal pregnancy progress.
Our NHL (with diffuse major B cell) case that received CHOP chemotherapy on 2nd and 3rd trimesters	1	Resulted with normal pregnancy progress. In postnatal period, slight systolic dysfunction of left ventricle was observed.

and temporary complete deletion in fetal B cells and high rituximab values on cord blood were detected by postnatal examination.[16]

Wider case series are needed to confirm the safe use of rituximab during pregnancy. In our case, the patient and her family was informed in detail about treatment options and side effects. In the light of literature information, it was decided by multidisciplinary approach (Perinatology, Medical Oncology, and Pediatrics) to apply only CHOP treatment during pregnancy and to add rituximab to the treatment in postpartum period. Three cures of CHOP + rituximab were applied to our cases in postpartum 1st week. Remission was detected in the patient according to the physical examination and screening results performed after totally 6 cures of chemotherapy.

According to the limited number of case series in the literature, it was observed that CHOP chemotherapy had no significant effect on pregnancy results and fetal malformations. However, in the postnatal echocardiography of the baby, slight systolic dysfunction of left ventricle was observed but it was decided by Pediatrics Cardiology Department to follow up the patient without providing treatment.

Conclusion

Lymphomas are rare during pregnancy. Hodgkin lymphoma is more frequent than NHL.[17] The diagnosis is generally established lately.[18] The method to be preferred in the treatment varies according to clinical staging and histological type. Those with high leveled lymphoma, those with major tumor mass, and those with systemic symptoms should be treated by combined chemotherapy.[4]

There are limited numbers of data about the reliability of chemotherapy agents during pregnancy. Wider case series are needed to determine optimum treatment options to be used during pregnancy.

The management of cases during and after pregnancy should be performed by multidisciplinary approach which includes the Departments of Perinatology, Medical Oncology, and Pediatrics.

Lymphomas certainly should be considered in the differential diagnosis for palpable cervical and submandibular masses during pregnancy. These rapidly progressing cases should be diagnosed in the shortest time and treatment should be initiated as soon as possible.

References

1. Macfarlane GJ, Evstifeeva T, Boyle P. International patterns in the ocuurence of Hodgkin's disease in children and young adult males. *Int J Cancer* 1995;61:165-9.
2. Beksaç MS. Maternal Fetal Tıp ve Perinatoloji. Ankara: Nobel, 2001;733-4.
3. Harris NL, Jaffe ES, Armitage JO. Lymphoma classification: from R.E.A.L. to W.H.O. and beyond cancer. *Principles and Practise of Oncology Updates* 1999;13:1-14.
4. Haznedar R. Hematolojik Hastalıklar. Ankara: Güneş Kitabevi, 1996;1:10:1298-1312.
5. Horning SJ, Rosenberg SA. The natural history of initially untreated low grade non-hodgkin's lymphomas. *N Engl J Med* 1994;311:1471-5.
6. Koren G, Lishner M, Santiago S. The Motherisk Guide to Cancer in Pregnancy and Lactation. 2nd edition. Toronto: Canada-Motherisk Program, 2005.
7. Aviles A, Neri N. Hematological malignancies and pregnancy: a final report. *Clin Lymphoma* 2001;2:173-7.
8. Peres RM, Sanseverino MT, Guimaraes JL, Coser V, Giuliani L, Moreira RK. Assessment of fetal risk associated with exposure to cancer chemotherapy during pregnancy: a multicenter study. *Braz J Med Biol Res* 2001;34:1551-9.
9. Lishner M, Zemlickis D, Sutcliffe SB, Koren G. Non-Hodgkin's lymphoma and pregnancy. *Leuk Lymphoma* 1994;14:411-3.
10. Guven S, Ozcebe OI, Tuncer ZS. Non- Hodgkin's lymphoma complicating pregnancy: a case report. *Eur J Gynaecol Oncol* 2005;26:457-8.
11. Garcia L, Valcarcel M, Santiago-Borrero PJ. Chemotherapy during pregnancy and its effects on the fetus-neonatal myelosuppression: two case reports. *J Perinatol* 1999;19:230-3.
12. Moore DT, Taslimi MM. Non- Hodgkin's lymphoma in pregnancy: a diagnostic dilemma. Case report and review of the literature. *J Tenn Med Assoc* 1992;85:467-9.
13. Herold M, Schnohr S, Bittrich H. Efficacy and safety of a combined rituximab chemotherapy during pregnancy. *J Clin Oncol* 2001;19:34-9.
14. Ojeda-Uribe M, Gilliot C, Jung G, Drenou B, Brunot A. Administration of rituximab during the first trimester of pregnancy without consequences for the newborn. *J Perinatol* 2006;26:252-5.
15. Temprano KK, Bandlamudi R, Moore TL. Antirheumatic drugs in pregnancy and lactation. *Semin Arthritis Rheum* 2005;35:112-21.
16. Friedrichs B, Tiemann M, Salwender H, Verpoort K, Wenger MK, Schmitz N. The effects of rituximab treatment

during pregnancy on a neonate. *Haematologica* 2006;91:1426-7.

17. Temiz LÜ, Kazancıoğlu TA, Fiar F, Yenigün M. Gebelik esnasında ortaya çıkan Hodgkin Hastalığı: Bir olgu sunumu. *Haseki Tıp Bülteni* 1995;33:249-51.
18. Dasan J, Littleford J, Mc Rae K. Mediastinal tumour in a pregnant patient presenting as acute cardiorespiratory compromise. *Int J Obstetric Anesth* 2002;11:52-6.
19. Falkson HC, Simson IW, Falkson G. Non-Hodgkin's lymphoma in pregnancy. *Cancer* 1980;45:1679-82.
20. Ortega J. Multiple agent chemotherapy including bleomycin of non- Hodgkin's lymphoma during pregnancy. *Cancer* 1977;40:2829-35.
21. Zuazu J, Julia A, Sierra J, Valentin MG, Coma A, Sanz MA. Pregnancy outcome in hematologic malignancies. *Cancer* 1991;67:703-9.

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Fetal Hyperechogenic Bowel and Early Necrotizing Enterocolitis in Three Intrauterine Growth Restricted, Extremely Low Birth Weight Infants

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Abstract

Objective: To discuss the relationship between fetal hyperechogenic bowel, absence of end diastolic flow in umbilical artery with Doppler ultrasound and necrotizing enterocolitis in extremely low birth weight and intrauterine growth restriction infants during early neonatal period.

Case: We presented 3 cases with intrauterine growth-restricted, extremely low birth weight who had absence of end diastolic flow in umbilical artery and hyperechogenic bowel before delivery and developed necrotizing enterocolitis during the early postnatal period.

Conclusion: Hyperechogenic bowel in cases with severe intrauterine growth restriction can be an important finding along with absent or reversed end diastolic flow to make a necrotizing enterocolitis in early neonatal period.

Keywords: Necrotizing enterocolitis, hyperechogenic bowel, extremely low birth weight.

İleri derecede düşük doğum ağırlıklı, intrauterin büyüme kısıtlılığı olan üç olguda fetal hiperekojenik barsak ve erken nekrotizan enterokolit

Amaç: Fetal hiperekojenik barsak ve perinatal izlemde umbilikal arter diastol sonu akımı kaybı ya da ters akım varlığı ile erken neonatal nekrotizan enterokolit ilişkisini, ileri derecede düşük doğum ağırlığı ve intrauterin büyüme kısıtlılığı bulunan olgular dolayısıyla tartışmak.

Olgu: İkinci trimesterde fetal hiperekojenik barsak tanısı alan ve perianatal izleminde Doppler ultrasonografide umbilikal arter diastol sonu akımı kaybı ya da ters akım varlığı saptanan gestasyonal haftaları 28 ile 30 hafta, doğum ağırlıkları ise 760 ile 930 g arasında olan ve postnatal yaşamlarının ilk gününde nekrotizan enterokolit gelişen üç olgu sunulmuştur.

Sonuç: Prenatal izlemde fetal hiperekojenik barsak ve Doppler ultrasonografi ile umbilikal arter diastol sonu akımı kaybı ya da ters akım bulguları, şiddetli intrauterin büyüme kısıtlılığı ile birlikte preterm bebekte yaşamı tehdit eden bir durumdur. Bu bebeklerde, kronik hipoksiye ikincil olarak gelişen nekrotizan enterokolitin, genelde görülme zamanının aksine yaşamın ilk gününde ortaya çıkabileceğini vurgulamak istedik.

Anahtar Sözcükler: Nekrotizan enterokolit, hiperekojenik barsak,ileri derecede düşük doğum ağırlığı.

Introduction

Necrotizing enterocolitis (NEC) is a common acute abdominal condition seen in the neonatal period and most commonly manifests within the second week of life in preterm infants. At the same time the presentations of NEC can be various and are closely related with the gestational age and haemodynamic disturbances of the fetal umbilical artery. In severe intrauterine growth restriction, as a result of these haemodynamic disturbances, the blood flow changes persist in the postnatal life.[1,2]

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We presented 3 cases with extremely low birth weight who had absence of end diastolic flow in umbilical artery (AREDF) and hyperechogenic bowel(HEB) before delivery and later developed early necrotizing enterocolitis postnataly.[3,4] We think that hyperechogenic bowel in cases with severe intrauterine growth restriction can be an important finding for some complications in postnatally. This finding with AREDF can make a necrotizing enterocolitis at early neonatal period.

Case Report

Case 1

Prenatal follow up was done at Baskent University Hospital Perinatology Unit. Absent or reversed end diastolic flow in the umbilical artery as well as hyperechogenic bowel were demonstrated at the 28th week of gestation and the patient was followed up closely. This female infant with IUGR was admitted to Baskent University Hospital Neonatal Intensive Care Unit (NICU) had an extremely low birth weight which was 760 g at the 29th gestational week after delivered by cesarean section because of fetal distress. Later on admission to NICU, surfactant was given because of respiratory distress syndrome (RDS). The infant had abdominal distention and discoloration at abdominal skin without feeding in the first hours. Radiographic grade II NEC was diagnosed in postnatal 2. day then antibiotics and total parenteral nutrition were given. She could not to be fed until the 29th day of life. After then enteral feeding was increased step by step. She was discharged from the NICU at the 81 st day of life.

Case 2

The second case was not followed up at Baskent University Hospital prenatally but was refered to Baskent University Hospital Perinatology Unit because of severe preeclampsia, IUGR, AREDF and evidence of hyperechogenic bowel. An emergency cesarean section was performed and the male infant weighing 930g at the 28th week was born. Then he was admitted to Baskent University Hospital Neonatal Intensive Care Unit after delivery with extremely low birth weight. He also had surfactant therapy just after addmission to NICU because of RDS. He had abdominal distention and discoloration at abdominal skin without feeding in the first day. Grade II NEC was diagnosed by X-ray. Antibiotics and total parenteral nutrition (TPN) were given. He had cholestasis due to TPN. Eventually, enteral feeding could be started at the 23 th day of life. He was discharged from the NICU at 59 th day of life.

Case 3

Third patient's mother was not followed up at Baskent University Hospital prenatally but was referred to Baskent University Hospital Perinatology Unit because of oligohidramnios, severe IUGR, AREDF and hyperechogenic bowel (HEB is shown by Figure 1). Late decelerations were demonstrated by non-stress test and a male infant with extremely low birth weight was delivered by an emergency cesarean section. The gestational age at birth was 30 weeks and the birth weight was 850 g. The infant was admitted to Baskent University Hospital Neonatal Intensive Care Unit. He did not have RDS but he had abdominal distention and discoloration at abdominal skin without feeding in the first day. Grade II NEC was diagnosed by X-ray. Antibiotics and total parenteral nutrition were started, Eventually enteral feeding was started at the 24th day. He was discharged from the NICU at the 50 th day of life.

Discussion

Fetal hyperechogenic bowel (HEB) reveals to increased echogenicity or brightness of the fetal bowel noted on second trimester sonographic examination.[3,4] Hyperechogenic bowel can be found in 0.1-1.8 % of pregnancies as a normal variant in fetuses during the second or third trimester, it has also been described as a prenatal marker for cystic fibrosis, chromosomal aneuploidy and numerous other pathologies such as small bowel obstruction, Hirschsprung's disease, bowel atresia, intra-amniotic hemorrhage and oligohydramnios.[3,4] Some researches refer that in the second trimester HEB is the marker of subsequent suboptimal fetal growth. Intrauterine growth restriction (IUGR) has been expected to complicate 4% to 18% of pregnancies with HEB.[5,6] Strocker et al.[7] examined 131 consecutive pregnancies with fetal HEB and determined that 9 (6.9%) had growth restriction. The association of echogenic bowel with IUGR may be

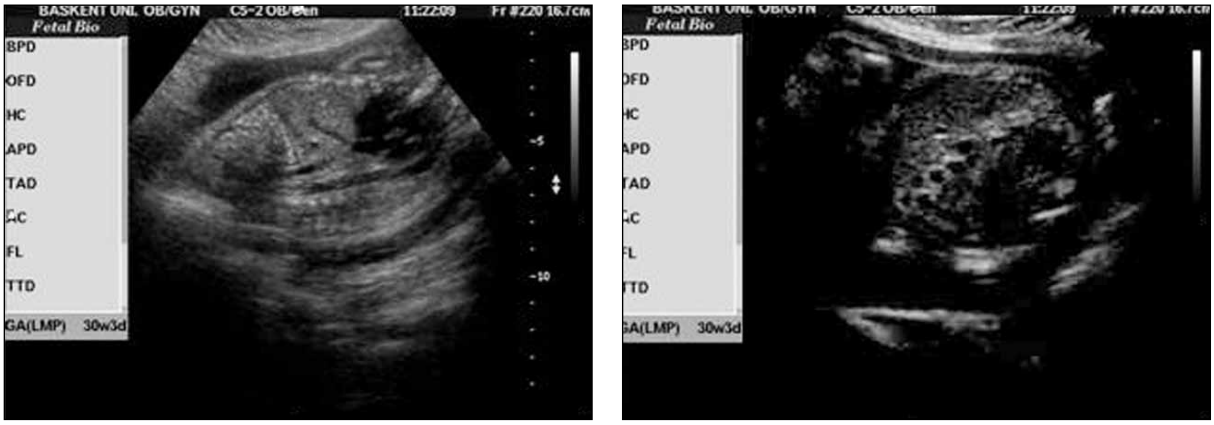

Figure 1. HEB as shown by ultrasonography for Case 3.

caused in part by ischemia from redistribution of blood flow away from the gut.[2] Our three cases were severe IUGR infants and HEB was demonstrated at the second trimester of pregnancy.

Other less common associations are cytomegalovirus, toxoplasmosis, parvovirus. The association of second trimester HEB with metabolic diseases was reported recently.[8] Nyberg et al.[3] investigated the clinical outcomes of 95 second-trimester fetuses with HEB prospectively. They reported that adverse outcomes occurred in 45 of the 95 fetuses (47%) with echogenic bowel compared with eight of the 110 fetuses (7.27%) in the control group, adverse outcomes included chromosomal abnormalities, intrauterine growth retardation, fetal demise, or other fetal anomalies.

Some studies also reveal that absence or reversal of end diastolic flow (AREDF) in the umbilical artery is associated with poor outcome and high incidence of necrotizing enterocolitis (NEC).[9,10] Pregnancies complicated by abnormal umbilical artery Doppler blood flow patterns often result in the neonate being born both preterm and growth-restricted and this situation is at high risk of enteral intolerance, NEC and mortality for newborn infants.[10] Necrotizing enterocolitis is a common acute abdominal condition seen in the neonatal period and most commonly manifests within the second week of life. At the same time the presentations of NEC can be various and are closely related with the gestational age and haemodynamic disturbances of the fetal umbilical artery. In severe intrauterine growth restriction, as a result of these haemodynamic disturbances, the blood flow changes persist in the postnatal life. Malcolm et al.[9] found corrected mortality rate 37 % in fetusus with AREDF and one case died because of fulminant NEC at 42 days. Our 3 cases with HEB had oligohidramnios and IUGR. All of them had absent end diastolic flow in umbilical artery prenatally. We could not be able to feed our cases for at least 3 weeks because of grade II NEC which might end up with intestinal perforation. Feeding could be started after 3 weeks and no complications occurred.

Marianne et al.[11] evaluated 65 pregnant women between 24 and 34 weeks' gestation with pregnancy-induced hypertension prospectively. Fetuses with AREDF were delivered at earlier gestational ages. They had a higher incidence of gastrointestinal complications, bronchopulmonary dysplasia, intraventricular hemorrhage and vascular hypotension than those without AREDF. The presence of AREDF was also associated with a mortality rate of 30%, whereas in fetuses without AREDF there was no mortality.

We think that hyperechogenic bowel in cases with severe intrauterine growth restriction can be an important finding for some complications in postnatally. This finding with AREDF can make a necrotizing enterocolitis at early neonatal period.

Conclusion

We think that HEB and severe IUGR with AREDF together can be an important findings. These findings can make a necrotizing enterocolitis at early neonatal period.

References

1. Hackett GA, Campell S, Gamsu H, et al. Doppler studies in the growth retarded fetus and prediction of neonatal necrotizing enterocolitis haemorrage and neonatal morbidity. *BMJ* 1987;294:13-6.
2. Dorling J, Kempley S, Leaf A. Feeding growth restricted preterm infants with abnormal antenatal Doppler results. *Arch Dis Child Fetal Neonatal Ed* 2005;90:359-63.
3. Nyberg DA, Dubinsky T, Resta RG. Echogenic fetal bowel during the second trimester: clinical importance. *Radiology* 1993;188:527-531.
4. Marcus-Soekarman D, Offermans J, Van den AMW. Hyperechogenic fetal bowel: counseling difficulties. *European Journal of Medical Genetics* 2005;48:421-5.
5. Eddleman KA, Stone JL, Berkowitz RL. Fetal echogenic bowel: the bottom line. *Contemporary Ob/Gyn* 1998;43:53-69.
6. Simon-Bouy B, Satre V, Ferec C, Malinge MC, Girodon E, Denamur E. Hyperechogenic fetal bowel: a large French collaborative study of 682 cases. *Am J Med Genet* 2003;121:209-13.
7. Strocker AM, Snijders RJ, Carlson DE, Greene N; Gregory KD, Walla CA. Fetal echogenic bowel: parameters to be considered in differential diagnosis. *Ultrasound Obstet Gynecol* 2000;16:519-23.
8. Lee M, Cook C. R, Wilkins I. A New Association of second-trimester echogenic bowel and metabolic disease of the neonate. *J Ultrasound Med* 2007;26:1119-22.
9. Malcolm G, Ellwood D, Devonald K. Absent or reversed end diastolic flow velocity in the umbilical artery and necrotising enterocolitis. *Arch Dis Child* 1991;66:805-7.
10. Bromley B, Doubilet P, Frigoletto FD. Is fetal hyperechogenic bowel on fetal sonogram an indication for amniocentesis? *Obstet Gynecol* 1994;83:647-51.
11. Marianne E, Kari A, Pesonen E. Value of absent or retrograde end-diastolic flow in fetal aorta and umbilical artery as a predictor of perinatal outcome in pregnancy-induced hypertension. *Acta Paediatrica* 2008;82:919-24.

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