



Breaking Down Preeclampsia: “The HLA Challenge”

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Aim of the study: The placenta acts as an immunological barrier between the mother and the fetal "graft", allowing two antigenically different organisms to tolerate one another.

Moving from a rejective hypothesis of the fetal graft in gestosis, we undertook these studies to evaluate at placental and plasmatic level, the potential etiopathogenetical role of the MHC - HLA antigens, which are implicated in self and non self recognition and in rejective reactions.

Materials and methods: Previously, placentae from gestosis and normal pregnancies were tested by immunohistochemical study of placental endothelium with HLA-DR monoclonal antibodies. Furtherly, a placental ultrastructural and biochemical V-CAM 1 plasmatic study followed and finally laser confocal and electron microscopy assessment was carried out both through immunofluorescence and immunocytochemistry for HLA-G1 antigen and ubiquitin.

Gestosis women, their partners and physiological control couples were also examined for HLA-DR assessment, chronologically performed by serological Terasaki technique, low and high resolution PCR and DNA sequence-based typing.

Results: Our first immunohistochemical study of placental endothelium showed a marked and widespread expression of HLA-DR antigens not occurring in normal pregnancy¹. Subsequently, in placentae from gestosis women, we ultrastructurally demonstrated a placental barrier breakage, leading to the mixing of maternal and fetal different blood. This condition could provoke a triggering of that maternal rejective reaction presumed to be at the basis of gestosis. Thus, we investigated the Human Leukocyte class II DR Antigens (HLA-DR), whose role in self and

non self recognition is well known, in women with gestosis, their partners and in controls, using the serological Terasaki technique. The results showed a statistically significant increase of HLA-DR homozygosity and a reduced antigenical variety in gestosis women and their partners versus control couples. The following update, studying the 2nd exon of the human gene HLA-DR_1 on the short arm of the chromosome 6, by DNA sequence-based typing (S-BT) PCR, in gestosis and control couples, confirmed the significant excess of HLA-DR homozygosity in partners associated with gestosis versus controls.

Discussion: Immunohistochemical and ultrastructural evidence of immunological activation and placental barrier disruption, strongly support the rejective hypothesis supposed occurring in gestosis. From serotyping and genotyping results in gestosis and control couples, it emerges that HLA-DR homozygosity and the reduced antigenical variety seem to be associated to a major risk for this syndrome which furtherly appears to be a “couple's disease”. The preliminary data of an ongoing study, to evaluate by immunofluorescence and confocal laser, the expression and localization of HLA-G in human term normal placentas, are shown for discussion, as an original and comparative study approach, to further understand the fascinating immunological mechanism at the basis of tolerance and rejection in pregnancy

Key Words: Preeclampsia/Gestosis, MHC- HLA Antigens, DNA sequencing, Laser Scanning Confocal Laser, Transmission Electron Microscopy

Bibliographical Synthesis

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