Gestosis and fetal rejection: immunopathogenetic role of HLA-DR

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Summary: In this study we faced the problem of etiopathogenesis of EPH Gestosis, focusing our attention on the role of immunitary aspects in determining its onset.

We typed HLA-DR in 20 couples with gestosic patient and in 20 control couples. Blood samples were taken into heparin-treated test tubes, from all the couples and HLA typed through standard lymphotoxicity technique in accordance with Terasaky (1).

Our results in couples with a gestosic patient, showed homozygosis in 65% of patients and in 70% of partners; in 35% of cases homozygosis was present in both partners, and these were the most severe cases. It is also worth mentioning that in all the couples with gestosic patient, at least one of the partners resulted homozygotic.

Homozygosis would therefore represent a predisposing factor in the etiopathogenesis of gestosis, and pre-conception HLA-DR typing of the couple could prove to be a valid alarm signal for gestosis risk.

Key words: Gestosis; HLA-DR.

INTRODUCTION

In some former studies (2), we submitted the placentae of gestosic patients and of women with physiological pregnancy to immunohistochemical and HLA-DR monoclonal antibody tests.

HLA-DR recognises all products of DX DQ subregions of the human class II major histocompatibility complex, therefore identifying many of the elements involving immunitary reaction activation and maintenance (monocytes, macrophages, T activated cells, endothelial cells).

Our results showed a marked expression of antigens of class II histocompatibility in gestosic placentae with respect to controls, with a reaction similar to that observed in kidney transplant rejection (3).

The mechanism at the basis of such an evident immunological reaction in gestosis is still unknown. We formulated two hypotheses:

1) on the basis of some pathologies (gestosis, IUGR), whose primum movens escapes us, there might be a modification of the property of "immunologic sentinel"

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Table 1. – *Couples with gestosic patient.*

HLA-DR woman	HLA-DR man
2	5
1	5
5	3
3	2
5	3
7	4
2	1
7	4/14
7	5/14
5	1/3
1	2/4
2	3/5
5	5/7
1/5	5
3/7	2
2/5	14
1/4	5
5/10	3
2/4	14
3/10	2

of endothelial cells, due to several, even temporary, risk factors, such as post-prandial hypercholesterolemia, shear stress, smoke, advanced glycosilated end-products as in diabetes ([4, 5]). Inter-cell junctions breakage, modifications in maternal-fetal barrier and rejection are a consequence;

2) gestosis, as well other diseases (ankylosing spondylitis, insulin-dependent type I diabetes), may correlate to particular, genetically determined HLA haplotypes which increase disease receptivity.

We undertook the present study to verify this latter immunopathogenetic hypothesis. We performed HLA-DR typing in some gestosis patients and in their partners, comparing resulting data with couples with physiological pregnancy.

MATERIALS AND METHODS

Twenty patients with severe gestosis complicated pregnancy, their partners, and twenty control couples were examined.

Patients were primigravidae and aged 24 years on average, had never undergone blood transfusion, and presented negative anamnesis for hypertension, diabetes and renal diseases.

From all patients, their partners and controls, blood samples were taken into heparin-treated test tubes; samples were HLA-DR typed through standard lymphocytotoxicity technique ([6]).

RESULTS

As tables 1 and 2 show, no particular HLA-DR haplotype was found in our case study, thus contradicting the hypothesis.

A relevant data emerging from the pathologic group is presence of homozygosis in one or both partners (65% of women, 70% of men and 100% of couples). In the control group we observed an extremely reduced percentage of homozygosis cases (15% of women, 5% of men, 15% of couples).

Comparing homozygosis and two severity indices of gestosis, such as fetal mor-

Table 2. – *Control couples.*

HLA-DR woman	HLA-DR man
2/5	11/5
1/5	1/3
4/8	5/4
14/5	5/14
1/6	4/12
3/6	3/5
2/3	1/7
6/7	4/6
1/2	4/7
4/7	2/4
1/8	3/14
5/8	1/6
4/7	1/2
4/6	2/5
3/5	7/12
5/8	1/7
2/7	5/6
5	3/4
1	5/6
3	4

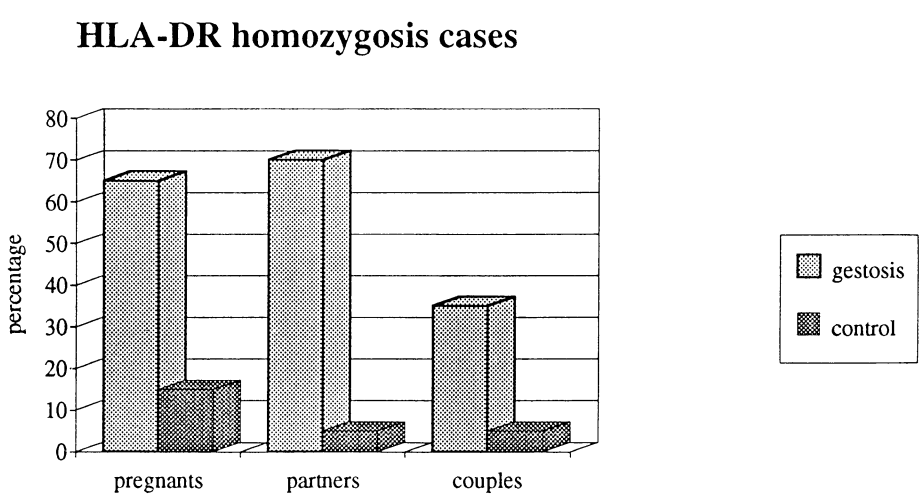

Fig. 1.

bility (IUGR & MIF) and maternal endangering elements (pleural and pericardial effusion, renal damage) we found the most severe cases when both partners were homozygotic (35%).

DISCUSSION AND CONCLUSIONS

Our data, although limited, agree with results obtained by other Authors, who addressed the complex problem of etiopathogenesis of gestosis.

Back in 1978, Redman *et al.* reported a high incidence of HLA-A and HLA-B homozygosis in patients with pre-eclampsia with respect to controls ([7]), asserting that maternal homozygosis reduced antigenic disparity between pre-eclamptic women and their partners.

In 1988 Simon *et al.* postulated an association between HLA-DR and Hypertension risk in pregnancy ([8]).

In 1992 Hoffman *et al.* pointed out a significant correlation between maternal HLA-DR homozygosis and risk of fetal loss ([9]).

It is more and more frequent and significant to observe an immunologic role in gestosis etiopathogenesis. If our data are confirmed through wider case studies, we believe that preconceptional HLA-DR typing in couples may allow identification of risk cases and activation of prophylactic-therapeutic measures as early as possible (low heparin doses) ([10]).

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