PATHOLOGICAL CHANGES IN PRODUCTS OF CONCEPTION OF ABORTERS WITH DEFICIEN IMMUNOLOGIC BLOCK FACTOR (S)

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INTRODUCTION

The foetal trophoblast behaves as a homograft in the maternal host, yet it survives. This referes to modulation of maternal immune system to antigenically foreign foetus and placenta. Various investigations demonstrated slight depression of maternal immune system during pregnancy, but the mother does not develop specific immunological tolerance to the foetus. The depression was expressed by increased number of suppressor cells (Moore et al.,1983), reduced activity of natural killer (Gall, 1983).

Rocklin et al. (1976) demonstrate the prescence of immunologic blocking factor in the sera of normal pregnant multigravida women. This factor is absent from the sera of untransfused multipara(Stewart et al., 1984).

It appears in the maternal sera of both primi and multigravidas, as early as the 4th - 5th week of gestation, its activity increased with longer gestation to reach maximum, at the time of delivary, then it begin to disappear (Kasakura, 1971). Johnson et al. (1984) claimed absence of the blocking factor in women suffering from habitual abortion.

To our knowladge the pathological changes in placenta in patients with decreased blocking factor is not described in the work English literature, so the present work is planned to study the pathological changes in the products of conception in patients with deficient blocking factor.

MATERIAL AND METHODS

Patient's Selection :

The study consists of 20 patients with spontaneous abortion. In all the cases, there was no history of maternal diseases e.g. hypertention, diabetes mellitus ... etc. They were sero - ve for $, Rh +ve. All with habitual abortions . The age ranged from 20 - 35 years.

Methods :

I) Serological Study . 5 ccs of blood were obtained from patients. The serum was separated from blood sample under the laminar air flow. The blocking factors was tested for by evaluating the effect of patients sera on the mixed lymphocyte culture (MLC) reaction.

2) The products of conception were obtained, devided into two parts.

a- One part was fixed in 10% formaline and processed for paraffin blocks and sectioned at 6M and stained by H. & E., PAS, V.G. & PTAH.

b- The other part was processed for frozen section of 10M and prepare for staining by direct and indirect immunoflourecence (Bancroft, Stevens, 1977) using IgM and IgG antihuman sera.

RESULTS

(I) Serological Study :

A- Prescence of bloeking factor

i - Effect of patients serum on allogenic stimulated cells The blocking factor was absent in 13 cases (65 %).

ii - Effect of patient's serum on mitogenic stimulated cells

14 cases (70%) does not inhibit these cells. On the contrary, they produce marked stimulation.

B- T-Values of Mixed Lymphocytic Culture :

i - Allogenic stimulated cells :

The mean CPM allogenic stimulated cells was 1109 & S.D. = 1232.4 after adding the patient's serum . The mean CPM become 1152 & S. D. = 1032. The tvalue is 0.22 (statistically non significant). The serum of patients with multiple abortion does not inhibit allogenic Stimulated cells on MLC.

ii- Mitogen stimulated cells :

The mean CPM of mitogens stimulated cells was 1041.4 & S.D. 868.7 after adding the patient's serum. The mean CPM was 7928.1 & S.D. = 7563.5. The t-value is 4./9 (statistically significant stimulation).

(2) Histopathology :

The cases were divided into 2 groups according to presence (7 patients) or obscence (13 patients) of the blocking factor. This pathological change were described as :

a- Regressive changes in the decidual cells in the form of swelling, atrophy of decidual cells or cloudy swelling or hydropic degeneration and iate necrosis. Inter decidual changes in the form of oedema, fibrinoid deposit, and cellular infiltration of plasma cells, macrophages, lymphocytes and eosinophils.

b- Vasculitis with swelling of endothelial cells and cellular infiltrate with late thrombosis all these changes were more frequent in cases with absent blocking factor. For the type of the cellular infiltrate, plasma cells were more frequent in cases in which the blocking factor was present, while the lymphocytic infiltrate, though shows no difference as regard the frequency in the 2 groups, but concerning the intensity of lymphocytic infiltrate it was more marked in cases with absent blocking factor.

Chorionic Villi :

Variable degree of fibrosis was observed in cases in those with blocking factor. In this lesion the corea of chorionic villi were consisting of collagenous fibrous tissue of variable cellularity. No other significant difference could be observed between the two groups.

Immunoflourescence :

Immunoflourescent study by using IgM no flourescence was obtained neither by direct nor indirect methods in both groups with present or absent blocking factor. Using IgG : the negative and weak reactions, were much more frequent in patients with absent blocking factor , while in patients with blocking factor mild and moderate reaction were more frequent.

In positive cases the reaction was seen in foetal stem vessels enothelium, Hofbauer's cells tropoblastic

basement membrane, villous stroma, and sites of fibrinoid changes.

DISCUSSION

The survive of the foetus inspite of the maternal immune system to histoincompetable foetal tissues refers to the fact that such maternal immune system has been adjusted for pregnant to continue undamaged (Gompell, Silverberg, 1985).

In the present study, the prescence or abscence of blocking factor was demonstrated by the effect of the sera of spontaneous abortion cases on allogenic and mitogen stimulated cells in mixed lymphocytes culture.

It was found that the presence of these factors was 65% of cases of multiple aborters which is in full agreement with that recorded by Fizetl Bourquet (1983).

Many possible suggestion are provided to explain the exact role of this blocking factor, Mowbray and Underwood (1985) favoured the opinion that these antibodies may cause modulaton the HLA antigen expression on the trophoblast rather than affecting the cellular immunity.

In present study we compared the pathological changes in the product of conception from aborters who were sera -ve for the blocking factor with these who were sera +ve for anti factor. It was observed that chronic inflammatory cells were more predominantly and more intense in the sero – ve cases. In particular lymphocytes and macrophages. This type of cellular infiltrate may represent immune reaction at the placental site of the cellular immune reaction type.

The observation that the plasma cells were more frequent in cases which were sero +ve for the blocking factor may point to the fact that this blocking factor is AB and that the plasma cells are its source Vasculitis with infiltration of the wall of the arterioles by cellular infiltrate with swelling of endothelial lining may represent a sort of acute rejection in sero-ve cases. This vascular changes eventually lead to vascular thrombosis which lead to the regressive changes observed in decidual cells, swelling, atrophy, oedema, fibrinoid changes in intracellular spaces.

Concerning choronic villi, fibrotic changes in the villi was more frequent in cases which were sero- ve for the blocking factor which may refer to a possible underlying immunological reaction for its Causation similar that in-

volved in certain collagen disease e. g. Scleroderma.

A possibility which was first provided by Strate Ford (1970) who demonstrated elevation of serologic factors similar to that observed in patients suffering from certain collagen diseases in cases of spontaneous abortion associated with evident fibrotic lesion.

The abscence of IgM results was previously mentioned by Johnson et al. (1976). The abscence of IgM is natural in view of the fact that the maternal IgM cannot pass through the placenta and that the blocking factor is IgG (Rocklin et al., 1976).

Using IgG, lesser positive results was observed in sero -ve patients compared to sero +ve patient, for bloking factor (IgG) this may be due to deficiency of the blocking factor in sero -ve patients. Also the intensity of the reaction was less in the sero-ve cases.

Matey and Johnson (1977) reported that endotheliùm of the foetal stem vessels of normal full term human placenta binds to flourescence - congugated heat aggregated human IgG.

Johnson et al. (1977) suggested that the variability of the amount of IgG found in the foetal stem vessels in the placenta may reflect the extent of allogenic in compatibility between the mother and her foetus.

Faulk et al. (1974) suggested that IgG on the trophoblastic basement membrane (TBM) may represent maternal blocking antibodies that protect the placenta from maternal cells mediated immunity. An assumption which fit very will with the present study when the flourescence at the TBM was observed in 16% of cases negative for blocking factor.

Positive flourescence at the villous stroma showęd no difference in relation to the presence or abscence of blocking factor. From this study we can say that in abscence of the blocking factor immune reaction is operated leading either to vasculitis with subsequent thrombosis and degenerative changes in the decidua or fibrosis of choronic villi by mechanism similar to that operating in collagen diseases. However since this changes are not constant, it is possible that the blocking factor are not the only factor in action for protection against the maternal immune rejection and possibly other mechanisms are also involved in the protection.

SUMMARY

The study was performed on 20 aborters 13 of which were seronegative in the blocking factor. The pathological changes especially vasculitis, cellular infilterate of lymphocytes, histiocytes as well as fibrosis of chorionic villi were more frequent and more marked in these seronegative cases than in seropostive ones. The possible role of absence of blocking factor in production of this changes and hence termination of pregnancy was discussed .

Fig.I : Fibrinoid change in the decidua with homogenous, structureless, deeply eosinophilic appearance. The reminants of nuclei are scattered in the area (Hx. & E. X 100)..

Fig. 2 : Focal lymphocytic infiltration in the decidua. (Hx. & E. X 100).

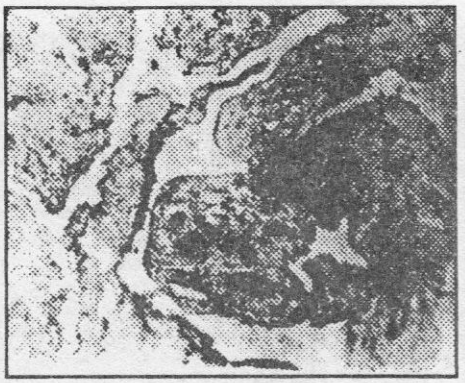

Fig.3 : Concentric perivascular fibrosis together with swelling of the endothelial cells (Hx. & E. X 100).

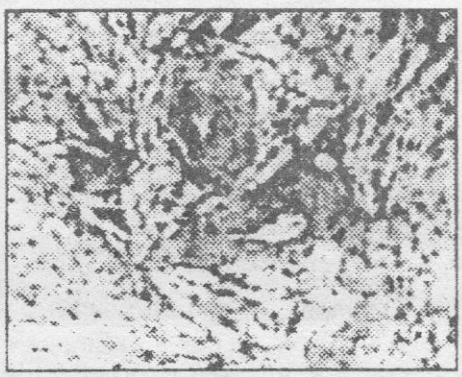

Fig.4 : Perivascular aggregation of chronic inflammatory cells with thick walled blood vessels (Hs. & E. X 150).

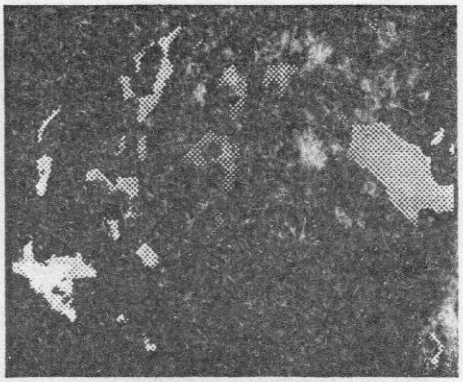

Fig.5 : Direct immunoflourescence for antihuman IgG in a case of spontaneous abortion. Strong positive flourescence is detected in an area of fibrinoid change (F) there is also, some diffuse stromal staining (S). (X 200).

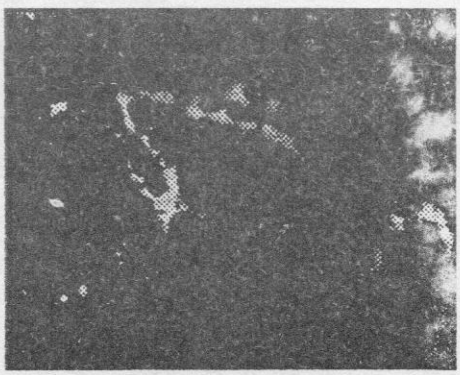

Fig. 6 : Indirect immunoflourescence using anti-human IgG in a case of spontaneous abortion. A weaker reaction is detected in the wall of foetal vessels (V). There is positive staining of some stromal cells (H).

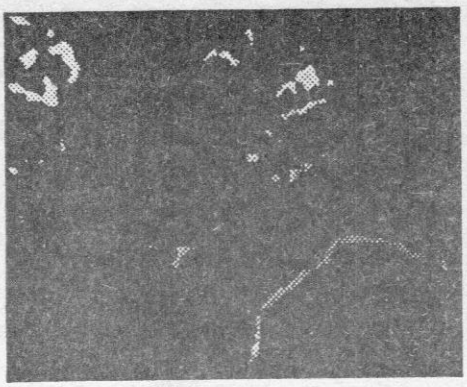

Fig. 7 : Direct immunoflourescence using anti-human IgG in a case of spontaneous abortion. Positive staining is found in a segment of a foetal stem vessel (V) and in an area of fibrinoid change (F).

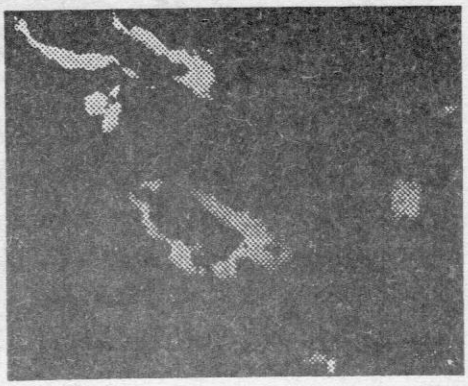

Fig. 8 : Indirect immunoflourescence using anti-human IgG in a case of sporadic abortion in which the blocking factor was present. Strong staining is detected at the trophoblastic basement membrane (T) and in foetal stem vessels (V). (X200).

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الملخص العربى

د. ناديه عبدالمنعم ندا د. نجوى مختار هلال د. فرحه الشناوى

تمت الدراسة على ٢٠ حالة إجهاض، ١٣ حالة كانت سلبية بالنسبة لمانع تعامل الحساسية، ولقد لوحظ أن التغيرات الباثولوچية فى هذه المجموعة والممثلة فى التهاب الأوعية الدموية وتجميع خلايا الالتهاب المزمن مع تليف الزغب المشيمى كان أكثر نسبة وشدة عن المجموعة الإيجابية لعامل منع الحساسية.

ولقد نوقش الدور المحتمل لغياب هذا العامل فى إحداث هذه التغيرات وإنهاء الحمل.