LEUCOCYTE CHEMOTAXIS IN NORMAL PREGNANCY AND ECLAMPSIA

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SUMMARY

Neutrophil chemotaxis from normal pregnant and preeclamptic patients were studied using the Wilkinson's modification of Boyden's chamber. Neutrophil chemotaxis was found to be impaired in both the groups. Further, sera obtained from pre-eclamptic patients significantly reduced chemotaxis of normal neutrophils. These observations support the fact that not only the cells (neutrophils) are at fault but also the sera contains inhibitory factors for neutrophilic chemotaxis. However, the random migration of the cells was significantly increased only in patients with eclampsia indicating a non-specific stimulation of chemokinesis in eclampsia.

Maternal immune responses are modulated to retain the foetus during pregnancy (Nicholas 1989). Depression in cells mediated immune response with disturbance in helper-suppressor ratio has been noted. Reduced T cell response to stimulation by the lactin phytohaemagglutinin has been seen (Gerewal et al, 1978), but antibodies against paternal antigens have also been noted in the pregnant women (Nicholas 1989).

Attention has been focussed on the changes in the neutrophil functions in the female during pregnancy. Diminished phagocytosis and chemotaxis of neutrophils due to inhibitory factors in serum was noted by Takechi and Persellin (1980). Intracellular metabolic defects have also been shown in the form of defective bacterial killing (Persillin & Leibfarth 1978). In an earlier study we have shown that serum factors exert inhibitory effect for chemotaxis in normal pregnancy (Datta et al, 1985) but no data are available on abnormal pregnancy. We have now studied the behavior of the phagocytic cells and the serum inhibitory factors in pregnant women, with early and late eclampsia.

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MATERIAL

Patients coming to the Antenatal Clinic of Obstetrics and Gynaecology Department of the Nehru Hospital were taken for the study. The following groups were studied :

(i) 25 normal pregnant women in the last trimester of pregnancy.
(ii) 30 pregnant women suffering from hypertension induced toxemia. These included 15 with mild condition and 15

with severe eclampsia, as defined by Villar & Sibai (1888).

Patients excluded

1. Patients with acute or chronic infection.
2. Patients with immunologically related disease e.g. SLE, RA, etc.
3. Patients with pregnancy complicated with diabetes mellitus or other hormonal disorders.

Controls

The laboratory standards for controls are already available from previous study (Datta et al, 1985). However, a control sample from normal individual was set up everytime alongwith the test to assess the validity of the results and normal cells were also used to see the effect of patient's serum.

METHODS

Blood was collected for serum in the plain vial and for neutrophils in heparin. Wilkinson's modification of Boyden's chamber (Wilkinson, 1983) as described earlier was used (Datta et al 1985) for Chemotaxis and the tests were set up in two groups -

(1) Chemotaxis of cells from normal pregnancy, mildly eclamptic and severe eclamptic patients (each in duplicate).
(2) Normal cells with serum of each of the mentioned group.

Statistics

The result of each group were compared with the control value using students T-test. Each test group was also compared with each other similarly.

RESULTS

1. **Controls :** The mean random locomotion of the neutrophils was 11 $\pm$ μm and directed locomotion was 65 $\pm$ 6 μm. The values for directed locomotion in the control varied from 56 to 80 um.

2. **Chemotaxis in normal healthy pregnant : neutrophils taken from the normal pregnant** women in the last trimester showed random locomotion of 8 $\pm$ 2 which is similar to controls but the directed locomotion was statistically significantly reduced over controls ($p < 0.001$) as shown in table I. The range was 39 to 70 um.

3. **Chemotaxis of neutrophils from severe and mild toxemia patients :** The random locomotion of these patients is significantly higher ($p < 0.001$) than the controls (Table I). This is an interesting finding. The directed locomotion was significantly inhibited compared to controls ($p < 0.001$). There is no significant difference between the severe and mild toxemic nor between the normal pregnant and toxemic pregnant.

Table - I

Chemokinesis (random locomotion) and directed chemotaxis of neutrophils

Subjects (No.)	Chemotaxis of/μm/90 min Mean (SD)	Chemotaxis/μm/90 min Mean (CP)
1. Controls (25)	11 (5)	65 (6)
2. Normal pregnancy (25)	8 (2)	52 (9) *
3. Mild preeclampsia (15)	21 (7) *	46 (7.3) *
4. Severe preeclampsia (15)	20 (9) *	48(11) *

* Statistically significant inhibition ($p < 0.001$) when compared with the control (Student's 't' - test)

Table - II

Effect of sera from preeclampsia patients on normal neutrophils

Group (No.)		Chemotaxis/μm/90 min mean $\pm$ SD	Student's 't' test
1.	Normal neutrophils (25)	65 $\pm$ 6	
2.	Normal neutrophils and sera from mild preeclampsia (15)	36 $\pm$ 9	1 vs 2 : $p < 0.001$
3.	Normal neutrophil and sera from preeclampsia (15)	36 $\pm$ 11	1 vs 3 : $p < 0.001$

4. Effect of serum from toxemic patients on normal cells : Significant inhibition ($p < 0.001$) of the chemotactic activity of the toxemic serum is seen on the normal cells. The mean chemotaxis of normal neutrophils with sera from eclamptic females was 36 μm with SD of 9 and 11 in early and late eclampsia respectively. Although the two situations are not comparable and more work need to be done it seems that the inhibitory factors in serum had more pronounced effect.

DISCUSSION

Survival of the foetus in a partially foreign environment is a remarkable phenomena and demonstrates the complex immunoregulatory state of the pregnant female. There are evidence to support that the mother recognises the foetus as foreign. This is manifested by enlargement of the lymph nodes draining the uterus during pregnancy (Ansell et al 1978) and production of anti-paternal antibodies in some species (Beer & Billingham 1974). However, observation support that mutual feto-maternal acceptance is achieved by immunosuppression (Nicholas 1989). The ameliorating effect of pregnancy on the inflammatory disorders has been observed quite early (Hench 1938) and confirmed by later studies (Persellin & Leibfarth J.K. 1978).

Interest has been focussed on the role of neutrophils in pregnancy (Hempal et al 1970, Persellin et al 1978, Takeuchi & Persellin 1983; Hawes et al 1980). Polymorphonuclear leucocytes are the major effector cells of non-specific host defence and a host of factors are known to modify their ability of cell function, Ginsburg et al (1980). It is observed that the serum from pregnant women stabilise the lysosomal membrane (Hempal et al 1970) hence the decreased inflammatory response. Inhibition of phagocytosis and intracellular killing in pregnancy has been reported (Persellin et al 1978). We have observed no overt phagocytic defect not significant nitroblue tetrazolium reduction defect in our studies (unpublished data).

The effect of pregnancy serum on the directional migration of normal human polymorphonuclear leucocytes in response to standard chemotactic attractant has been studied by Takeuchi & Persellin (1983). Pregnancy sera in direct contact with the polymorphs inhibited their response to standard chemoattractants. This suppressive effect is seen during the third trimester of pregnancy.

Similar observations have been made in this laboratory (Datta et al 1985). The normal serum has minimum and non-significant effect on the chemotactic activity of normal neutrophils, but the sera obtained from pregnant women in third trimester of pregnancy significantly inhibit the chemotaxis of leucocytes. Since in the past study significant alternations were seen in only the last trimester of pregnancy. All the subsequent work

was done in patients in the last trimester of pregnancy. The serum obtained from patients with toxemia of pregnancy have significantly reduced chemotaxis same as seen in healthy pregnant females. The inhibition was upto 45% and the type of toxemia made no difference. The effect of toxemia serum on autologous cells and of normal serum on toxemia cells needs further studies.

The random chemotaxis of neutrophils is raised in patients with toxemia of pregnancy (almost twice of control). This signifies that the cells are in hyperactive stage. The cause of this activity is not clear. One can only postulate that certain peptides liberated by the swollen tubular cells may activate the chemokinesis but the cells still retain their incapacity to respond to directed chemotaxis. Increased monocytes and chemotactic activity was observed by Hawes et al (1980) but the present study is limited to neutrophils. We have observed increased chemokinesis in psoriasis earlier (1986). Here, again one postulated some stimulants by the rapidly proliferating DR + ve keratinocytes. It is clear that more work needs to be done to explain the increased chemokinesis.

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