Abnormal polymorphonuclear leucocyte chemotaxis in Behçet’s syndrome

D. W. JAMES, J. R. WALKER, AND M. J. H. SMITH

From the Biochemical Pharmacology Research Unit, Department of Chemical Pathology, King’s College Hospital Medical School, Denmark Hill, London SE5 8RX

SUMMARY Experiments both in vitro and in vivo have been performed to study the chemotactic response of polymorphonuclear leucocytes (PMNs) in Behçet’s syndrome. The experimental results were apparently contradictory. Using modified Boyden chambers we found that the PMNs from patients with Behçet’s syndrome responded to a greater extent in vitro than normal cells, but with skin chambers placed over abrasions the in vivo response was less than normal. The significance of these findings is discussed and related to the histological appearances that may be seen in this condition.

The first evidence of the increased chemotactic activity of polymorphonuclear leucocytes (PMNs) from patients with Behçet’s syndrome was reported by Matsumura and Mizushima (1975), and because of this they used colchicine in the treatment of Behçet’s syndrome, with apparent success (Mizushima et al., 1977). These findings of increased PMN chemotaxis were supported by Sobel et al., (1977). Using an agarose plate technique these workers produced evidence that both serum and intrinsic cellular mechanisms are responsible for this increase in the chemotactic response.

Patients and methods

Six patients with Behçet’s syndrome were studied by in vitro methods, and 5 of these patients were studied by in vivo methods. The details of the disease manifestations and treatment are shown in Table 1.

Table 1  Details of patients, symptoms and treatment

<table>
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<th>Case no.</th>
<th>Sex</th>
<th>Age</th>
<th>Mouth ulcers</th>
<th>Genital ulcers</th>
<th>Uveitis</th>
<th>Skin lesions</th>
<th>Arthritis</th>
<th>Venous thrombosis</th>
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<td>Steroids</td>
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</table>

*Case 6 not studied in vivo

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Correspondence to Dr D. W. James, Department of Rheumatology, The London Hospital, London E1 1BB.

Results

IN VITRO

The PMNs from patients with Behçet’s syndrome migrated to a significantly greater degree towards normal activated plasma than did control cells, as shown in Fig. 1.

Control: Mean $\pm$ SE = 66 $\pm$ 3 PMNs/high power
field. Behçet’s syndrome: Mean ± SE=113·1 ± 11·8 PMNs/high power field. 72% increase, P<0·001 (Student’s t test).

There was no significant difference in the response of normal cells towards activated plasma of either control patients or of patients with Behçet’s syndrome.

**IN VIVO**

As shown in Fig. 2, there was a clear reduction in the number of PMNs which migrated into skin chambers compared to the control results.

Control: Mean ± SE=41·1 ± 3·7 × 10^6 PMNs/cm^2/1 ml serum/24 h. Behçet’s syndrome: Mean ± SE=11·8 ± 2·7 × 10^6 PMNs/cm^2/1 ml serum/24 h. 72% decrease, P<0·001 (Student’s t test).

**Discussion**

There is an apparent paradox in our results. When the PMNs from patients with Behçet’s syndrome migrate through filters in vitro there is evidence of increased responsiveness to normal chemotactic stimuli, as has been reported previously (Matsumura and Mizushima, 1975; Sobel et al., 1977). This overactivity may explain the marked PMN infiltration into the synovium and synovial fluid which has been reported to occur in patients with Behçet’s syndrome who have an arthropathy (Vernon-Roberts et al., 1978; Gow, personal communication), and also into the uveal tract and aqueous humour in patients with uveitis (Oniki et al., 1976; Shimada et al., 1972).

Despite the increased responsiveness of PMNs detected in vitro there was a reduction in the number of PMNs which migrated through skin abrasions into chambers in vivo. We have found that in patients with rheumatoid arthritis the in vivo findings reflected the in vitro results (Walker et al., 1979), but the situation in Behçet’s syndrome is obviously different.

Histological studies of lesions of the oral mucosa (Lehner 1969) and of induced skin lesions (Haim et al., 1976) show a completely different picture from the synovial histology. The histology of recurrent oral ulceration in Behçet’s syndrome shows a predominantly lymphomonocytic picture with a raised mast cell count. Similar appearances are seen in the dermis 12–48 h after a lesion has been induced by needle prick or injection of normal saline.

Skin and oral mucosa are ectodermal in origin, and the synovium and uvea are mesodermal in origin. There are obvious structural differences such as the
absence of basement membrane in the synovium and uvea. It appears that in patients with Behçet's syndrome tissues of these different embryological origins show different inflammatory reactions. A predominantly lymphomonocytic picture is seen in skin lesions and recurrent oral ulceration, which may represent a form of delayed hypersensitivity (Lehner, 1969), responding to an immunomodulatory drug such as levamisole (Lehner et al., 1976).

The predominantly PMN infiltrate in the synovium and uvea, however, may represent an Arthus reaction (Oniki et al., 1976) enhanced by the abnormally high PMN chemotactic response seen in vitro, which may be suppressed by colchicine. These histological observations may explain the paradoxical results obtained in this study.

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References


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