Behçet's syndrome: unusual multisystem involvement and immune complexes

N. M. HYMAN
M.B., M.R.C.P.

H. J. SAGAR
M.A., B.M., M.R.C.P.

Department of Neurology, Radcliffe Infirmary, Oxford

Summary

A case of Behçet's syndrome is described in which, in addition to the usual features of the condition, there was evidence of renal, gastric and cardiac involvement. Neurological involvement presented as hemisphere, transient ischaemic episodes. Immune complexes were detected and the patient responded promptly to prednisolone.

Introduction

Behçet's syndrome is a clinical diagnosis which bears the name of the Turkish dermatologist who, between 1937 and 1940, described a relapsing iritis in association with oral and scrotal ulceration, although the original description was made by Blüthe in 1908. Multiple organ involvement has been described and in particular, arthritis, dermal vasculitis, thrombophlebitis, peripheral arterial disease and central nervous system disease have all been reported. The age of onset is usually below 40 years old but there is a wide range. The prevalence of this rare condition in a recent series from Yorkshire (Chamberlain, 1977) was 0.064 in 10 000 which probably represents the frequency in the United Kingdom, although it is far more common in the Eastern hemisphere.

An acute fulminating case of the condition is described in which there is unusual and widespread systemic involvement associated with circulating immune complexes.

Case report

A 53-year-old right-handed engineer presented with a progressive 3-week history of balanitis, pain in the left wrist, right knee and around the left shoulder muscles. Two days before presenting to the out-patient department he developed a painful, red left eye. In the 4th week of his disorder he complained of severe buccal ulcers which were pale, deep and sharply circumscribed. The following day he had a 4-hr episode of central abdominal pain with associated abdominal guarding and this recurred 48 hr later. Investigations revealed an ESR of 40 mm/first hour (Westergren); haemoglobin was

11.4 g/dl; WBC $11.9 \times 10^9/l$ with neutrophilia. The urine contained 240 red cells per high-power field and protein of 5 g/l; blood urea was 7.7 mmol/l. Five weeks after his original presentation he suffered 4 episodes, within 12 hr, of acute profound weakness of the right arm and right leg with associated dysphasia. Each episode lasted about 2 hr and there was no residual deficit. A presumptive diagnosis of Behçet's syndrome was made and he was transferred to the neurological unit at the Radcliffe Infirmary, Oxford. Examination revealed an ill-looking man. The left eye was mildly injected. The right knee and left wrist joints were tender and swollen. The left deltoid muscle was slightly tender to palpation. Vasculitic purpura was observed over the anterior aspects of both ankles. He had painful penile, perianal and buccal ulcers. The BP was 110/80 mmHg and the pulse 88/min. All peripheral pulses were present without bruits. Examinations of the abdomen and CNS were both normal. Shortly after admission he developed retrosternal chest pain at rest with associated pallor and sweating, lasting several hours. An ECG indicated T wave inversion in the lateral chest leads (a previous recording was entirely normal). Prednisolone 60 mg daily was started but after 4 days the patient developed melaena stools and the Hb fell to 7.9 g/dl. He was transfused with 2 pints of whole blood and given cimetidine. Further investigations were as follows: WBC $25 \times 10^9/l$ with neutrophilia; platelets $600 \times 10^9/l$; blood urea (maximum) 12.5 mmol/l; creatinine clearance 78 ml/min (100-120 normal); alkaline phosphatase 247 KAU. Urine (7 estimations): protein 2-13.5 g/l, red cells 20-80 per high-power field. Chest X-ray, anti-nuclear factor, fasting cholesterol and triglycerides, Coombs' test, blood cultures, WR and serum immunoglobulins were all normal. Rose-Waaler < 1 in 8 and Rheumatoid negative; Australia antigen negative; serum C₃ 0.83 g/l (0.65-1.25 normal); cryoglobulin negative; serum immune complexes detected by indirect method using neutrophil activation test with positive control of aggregated IgG, serum 31% of positive control (normal less than 10%). Left deltoid biopsy within normal

limits. Rectal biopsy revealed oedematous mucosa with patchy fresh haemorrhages within the wall and widespread loss of surface epithelium. A barium meal revealed a ragged antral mucosa and gastroscopy showed prepyloric ulcerated raised areas. Gastric biopsy showed mild to moderate chronic inflammatory infiltration in the lamina propria. The surface was covered by a single layer of cuboidal epithelial cells which were infiltrated by polymorphonuclear neutrophils. Below that epithelium there was a fibrous reaction with associated lymphocytic cells (Fig. 1). His condition gradually improved and he was discharged on prednisolone 20 mg daily. The ESR fell to 3 mm/first hour; the WBC fell to $6.4 \times 10^9/l$ and the Hb rose to 15.2 g/dl. The urine became free of protein and red cells. Eight months after discharge serum immune complexes could still be detected but had fallen from 31% to 18% of positive control. He remained well apart from some pain in the knees and wrists.

Discussion

As the spectrum of Behçet's syndrome has broadened with increasing recognition of multi-system involvement, so has confusion increased as to the clinical criteria for the diagnosis. Mason and Barnes (1969) suggested a series of major and minor

criteria for recognition and accordingly the present patient would definitely justify a positive diagnosis.

The wide and unusual multisystem involvement of this case is of interest. Gastric involvement was shown radiologically and at gastroscopy, and additional rectal involvement was shown histologically. The changes of the patient's gastric mucosa were similar to the non-specific changes of the buccal lesions but its clinical manifestation was profound, as it was the likely source for the melaena stools and rapidly developing anaemia. The prednisolone may have been an aggravating factor. Intestinal involvement was present in 2 of the 32 patients of Chamberlain's series (one with a caecal ulcer and the other with both rectal and anal ulcers), and in 3 of the 35 patients of Mason and Barnes's series (all with duodenal ulceration). Ulcers of the intestinal tract have been shown at operation (Tsukada, 1964). This 'intestinal Behçet's syndrome' is in contradistinction to the finding of ulcerative colitis (Bøe, Dalgaard and Scott, 1958; Empey and Hale, 1972) or Crohn's disease (Chamberlain, 1977) in the presence of Behçet's syndrome.

Cardiac involvement in this case was suggested by the chest pain and non-specific electrocardiographic changes, reflecting either myocarditis or ischaemia due to coronary artery disease. Chajek and Fainaru's (1975) analysis of 683 cases of Behçet's syndrome in

FIG. 1. Gastric biopsy: surface covered by single layer of cuboidal epithelial cells with sub-epithelial fibrous reaction (HE, $\times 168$).

the literature revealed only 2 of myocarditis, one of paroxysmal atrial tachycardia and 2 cases of pericarditis. There was post-mortem evidence of myocarditis in another case (Kansu *et al.*, 1977) with scattered foci of chronic inflammatory cells within both ventricles.

Renal involvement in the present case was shown by 8 recordings of microscopical haematuria and proteinuria over a duration of 8 weeks with a fall in creatinine clearance to 78 ml/min and a rise in blood urea to 12.5 mmol/l; (although blood loss into the bowel contributed to this urea level). The urinary abnormalities settled as his clinical condition improved and his creatinine clearance rose to 101 ml/min. There have been only 3 previous reports of glomerulonephritis in Behçet's syndrome (Kansu *et al.*, 1977; Piers *et al.*, 1977; Mace and Jones, 1977), 2 of which came to post-mortem and revealed florid fibrinoid necrosis of the glomeruli. There have been occasional cases of the nephrotic syndrome secondary to amyloidosis (Rosenthal *et al.*, 1975).

The neurological presentation in the present patient was of 'hemisphere transient ischaemic attacks', more usually associated with emboli from the internal carotid into the middle cerebral arterial system. In several reviews of neurological involvement in Behçet's syndrome (Pallis and Fudge, 1956; Whitty, 1958; Schotland *et al.*, 1963; Kawakita *et al.*, 1967) this type of presentation is not described, although neurological manifestations are extremely varied. The onset is usually acute and > 50% have a residual deficit.

The aetiology of Behçet's syndrome is unknown although in recent years abnormalities of the immune mechanism have been recognized and antibodies to oral mucosa have been demonstrated (Lehner, 1969; O'Duffy, Carney and Deodhar, 1971). In a series of 18 patients (Gupta *et al.*, 1978), 8 had high levels of immune complexes. Another series (Williams and Lehner, 1977) revealed that 6 out of 9 patients with the neuro-ocular type of Behçet's syndrome had immune complexes and they suggested that the transition from focal oral ulceration to multifocal Behçet's syndrome might be mediated by immune complexes. However not all cases of the syndrome (including the present report) are preceded by oral ulceration. Nevertheless, immune complexes were detected in the patient who showed very widespread multisystem disease and the complexes fell as his condition improved.

Corticosteroids and immunosuppressives have been used for Behçet's syndrome but the results are inconsistent and confused by the relapsing nature of the condition. The brisk response to corticosteroids

in this case may be associated with the demonstrated immunological abnormalities.

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