Hyperkalaemic periodic paralysis without myotonic features is uncommon (Layzer *et al.*, 1967). However, though the cases described by McArdle (1962) all showed some form of myotonia at some time, in a proportion of the cases myotonia was commonly absent. In our patient a characteristic feature of the attack was his difficulty in moving his eyes. This observation has already been made by Gamstorp (1956).

Commonly there is a rise in serum potassium during attacks, though some patients have severe weakness when the level is no higher than 4 mEq/l., whereas in normal people a level of 8 mEq/l. is necessary before weakness develops (Walton, 1966). The serum potassium levels obtained during attacks in this case were on the whole higher than those usually recorded. We checked with control specimens submitted for electrolyte estimation at the same time as blood from the patient, and the results obtained were normal. His potassium levels in between attacks were always within normal limits.

Attacks of hyperkalaemic periodic paralysis usually start in infancy and early childhood (McArdle, 1962 ; van't Hoff, 1962), though in one recorded case the initial attack occurred at the age of 20 (Layzer *et al.*, 1967). The attacks in our patient started at a much later age than those reported. Most of the cases described in the literature have a familial history, but sporadic cases, though rare, have been reported. Investigation into a possible familial tendency has been negative in the above case. The patient's father died at the age of 83 from bronchopneumonia, and his mother died from myocardial infarction at the age of 68. Four of his siblings are abroad but are reported to be well. The remaining five were investigated, with negative results, though his 37-year-old sister had a serum potassium level of 6.2 mEq/l. on one occasion. She was completely symptom-free. It is still possible that she may develop the condition at a later age.

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Behçet's Syndrome with Neurological Manifestations in Two Sisters

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The association of oral and genital ulceration with ocular lesions, usually uveitis with hypopyon, was originally pointed out by Planner and Remenovsky (1922) and again by Adamantiades (1931), but the recognition of the syndrome as a disease entity rightly belongs to Behçet, who earned his eponym with a series of publications from 1937 to 1939. Feigenbaum (1956) has drawn attention, however, to a translation from a paragraph of the Hippocratic Third Book of Endemic Diseases, which almost certainly refers to this condition, raising the possibility that a contemporary sporadic disease was endemic in Ancient Greece.

Manifestations other than orogenital ulcers and inflammation of eyes include skin conditions such as furunculosis, pyoderma, and erythema nodosum ; connective tissue affection with synovitis, arthritis (Strachan and Wigzell, 1963), and pericarditis (Lewis, 1964) ; aortic aneurysms (Hills, 1967), thrombophlebitis and vena caval thrombosis, hepatomegaly, splenomegaly, and gastrointestinal ulcers (Bøe *et al.*, 1958) ; and involvement of the central nervous system. Curth (1946) has suggested that the diagnosis may still be entertained if only two of the classical manifestations are present, and she noted that there was often a long interval between the appearance of the various symptoms.

A familial incidence, though extremely rare, is recognized in this condition, and the present report concerning two sisters provides a further example. These sisters, who were married and lived apart in Birmingham, presented originally with recurrent orogenital ulceration and later developed central nervous system disorder within three weeks of each other.

CASE 1

The patient, aged 31, gave a two-year history of recurrent vulval ulceration and a three-week history of orogenital ulceration of such severity as to necessitate her admission to the Birmingham and Midland Hospital for Women in August 1965, where the diagnosis of Behçet's syndrome was made. She required tube-feeding initially, but her ulcers responded to treatment with chlortetracycline and topical oestrogens with hydrocortisone. During the week after her discharge she complained of headache and dim vision, and over the 48 hours preceding her admission to Dudley Road Hospital she developed a right hemiparesis.

On admission she was drowsy, with bilateral optic papillitis and a right upper motor neurone hemiparesis. She had necrotic labial and foot ulcers, oral ulcers appearing later. Her blood pressure was 95/60 mm. Hg, and at the height of her illness she showed the marked sensitivity to needle-prick described by Blobner (1937) and Jensen (1941) and later confirmed by Katzenellenbogen (1946), but no response to intracutaneous saline.

Abnormal findings included an erythrocyte sedimentation rate of 54 mm. falling to 7 mm., and a hypochromic anaemia of 10.7 g./100 ml. Her cerebrospinal fluid and plasma fibrinogen were normal, blood W.R. was negative, and viral studies and search for tissue antibodies showed no abnormality.

She was treated with large doses of A.C.T.H., initially 60 units b.d., but following a dramatic recovery this was reduced to 40 units b.d. after five days and to 40 units daily after a further week. Thereafter 40 units were given thrice weekly for three weeks ; subsequently the dosage was further reduced, to be discontinued four months after her admission, when she had no disability and only minimal right-sided signs. Three weeks later she was readmitted because of a relapse with severe labial ulceration and a small patch of ulcers on the hard palate. Examination on this occasion showed early pallor of the optic discs with a clear right upper motor neurone hemiparesis. The C.S.F., including an electrophoretic study, was normal. Again there was rapid improvement with A.C.T.H., which was given on this occasion at an initial dosage of 40 units b.d. for one week, and then gradually reduced, to be discontinued three months later.

CASE 2

This patient, aged 34 and sister of the above patient, gave an eight-year history of orogenital ulceration for which she attended the Birmingham and Midland Hospital for Women as a case of Behçet's syndrome. The ulceration showed some response to oestrogens given in a dosage sufficient to cause amenorrhoea. In August 1963 and January 1964 she had episodes of thrombophlebitis, which were treated with anticoagulants.

Three weeks after her sister's admission she first developed blurred vision in the right eye and intermittent headaches, and six weeks later was admitted to Selly Oak Hospital under the care of one of us (A. M. N.). At the onset of the visual disturbance she had been examined at the Birmingham and Midland Eye Hospital and found to have a right optic papillitis and a visual acuity on that side of 6/18 ; this resolved in two to three weeks, though her E.S.R. remained raised at 35 and 42 mm. in the first hour. On admission she was pyrexial, looked extremely ill, and was dysphasic with a right upper motor neurone hemiparesis. There were necrotic oral ulcers, perforation of one labium minorum due to old ulceration, and, in addition, a follicular rash over the trunk and thighs. Initially she deteriorated, becoming comatose, but on prednisolone 20 mg. and tetracycline 1 g. daily she made a striking improvement.

Investigations revealed an E.S.R. of 12 mm., a hypochromic anaemia (Hb 10.9 g./100 ml.), a total white cell count of 11,900/cu. mm. with a normal differential, and a C.S.F. which contained 20 cells, 17 of which were lymphocytes, per cu. mm., and a protein of 38 mg./100 ml.

By the time of her discharge from hospital six weeks after admission the prednisolone had been reduced to 5 mg. b.d., but two weeks later she developed a fresh crop of vulval ulcers and a sore mouth, with a transient pyrexia of up to 104° F. (40° C.). This recurrence settled on increasing the prednisolone to 20 mg. daily ; but some four weeks later, when once again she was being maintained on 10 mg. of prednisolone daily, a further neurological incident occurred. On this occasion there was left-sided long-tract involvement. Increased steroid dosage led to some recovery, but this has remained far from complete, the patient continuing to be dysphasic and emotionally labile. Fracture of a femur, which occurred when she tripped, united satisfactorily.

Discussion

Wolf *et al.* (1965), who reviewed 64 cases with neurological disturbance, and added a further case of their own, concluded that the frequency of neurological complications lay between 10 and 25%. In their series 49 were male and only 16 female. The age at onset of the syndrome varied from 16 to 61, with an average of 35 years, and this preceded the central nervous system condition by periods ranging from two weeks to seven years. Neurological and ocular complications in Behçet's syndrome appear to be much more common in males than in females, but the generally held belief in a male preponderance cannot be sustained if the frequently reported cases of orogenital ulceration alone in women are accepted as examples of this condition (Dowling, 1961).

The most common ocular lesions in Behçet's syndrome are uveitis or iridocyclitis with hypopyon, but conjunctivitis, haemorrhagic retinitis, papilloedema, and optic atrophy may occur. France *et al.* (1951), in a review of 32 cases, found 30 had progressive loss of vision, many terminating in blindness.

The spectrum of neurological declaration may be protean, but a brain-stem syndrome, a meningo-encephalo-myelitic picture, and an organic dementia and confusional state have all been recognized. It is noteworthy that the peripheral nerves and cerebellum almost invariably remain unaffected. The most consistent pathological findings have been perivascular and meningeal infiltration with lymphocytes, plasma cells, and macrophages as well as small foci of softening in the grey and white matter, often in relation to blood vessels. The blood vessels themselves are usually found to be normal and demyelination is rare. The cerebrospinal fluid may be normal throughout, but in acute neurological conditions it may be distinguished by a high cellular count of a level to help in the differentiation of those cases in which multiple sclerosis may be under clinical consideration.

The course of cases in which the nervous system is affected is usually characterized by remissions and exacerbations, but it may be one of progressive deterioration. The mortality rate rises if the nervous system is involved (Schotland *et al.*, 1963) ; 41% of the series of Wolf *et al.* (1965) terminated fatally, and 59% of these deaths occurred within a year of onset of the neurological signs. Alemà and Bignami (1964) quote a similar figure for their series. To date the only form of therapy which has been of some value is the use of steroids or A.C.T.H., but the response is variable: two of the three patients of Evans *et al.* (1957) died in spite of steroids ; one case of Wadia and Williams (1957) showed no response, while another improved. Our two patients showed an initial striking response—the one to A.C.T.H. and the other to prednisolone.

Published records of familial incidence of the syndrome are very few. Berlin (1960) described the case of a man of 28 who had the classical triad with thrombophlebitis and who later developed an organic mental syndrome and convulsions, deteriorated rapidly, and died in coma. Five years later his sister, who was then 36, developed an ocular lesion and oral ulceration, pyoderma, and joint involvement. Sezer (1956) saw the syndrome in three brothers, but these were without neurological involvement, and he has suggested that the disease is communicable.

Comment

Involvement of the nervous system in Behçet's syndrome is relatively uncommon, particularly in women, while a familial incidence is extremely rare.

The cases of two sisters with the syndrome, including neurological manifestations which they developed within three weeks of each other, are described. Both presented with an optic papillitis and an upper motor neurone hemiparesis, and showed an initial good response to treatment—the one to A.C.T.H. and the other to prednisolone—although relapses occurred later.

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