BEHCET'S SYNDROME

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RECURRENT genital and oro-pharyngeal ulceration together with hypopion iritis was recognized as a distinct clinical syndrome by Behçet (1937, 1938 and 1939). Although an uncommon condition it is by no means rare, most cases being seen in ophthalmic, skin or venereal disease departments or by our dental colleagues.

The following case shows many characteristic features of the illness.

Record Number L.H. 24124/52

A married woman, aged 29 years, was admitted in July, 1952, with a two month history of vaginal discharge, painless vulvar ulceration and recurrent painful mouth ulcers. She had lost two stones in weight. The mouth ulcers were of the simple aphthous type; the vulvar ulceration involved both labia with sloughing non-indurated bases and undermined edges. There was also a cervical ulcer surrounding the external os and extending to the vaginal vault anteriorly.

She was pale and ill and exhibited pyrexia (temperature 102°F) tachycardia (pulse 112 per minute) polymorphonuclear leucocytosis (12,500 per c.mm.) and raised E.S.R. (97 mm. 1 hour). Chest X-ray was clear. Vulvar and cervical biopsies showed pyogenic granulation tissue only and all specific tests, including W.R., G.F.T., Kahn, Demelos, and Frei were negative. The L. G. V. Complement Fixation test suggested previous infection with some virus of the psittacosis lymphogranuloma group.

She gradually improved over a period of five weeks, regaining weight, intermittent fever subsiding, E.S.R. falling and the vulvar ulcers healing spontaneously. Sulphatriad did not affect the course of the illness.

In October, 1952, she was readmitted with a relapse of vulvar ulceration. The clinical picture was similar but this time ulceration and recurrent pyrexia persisted for three months. All tests, including blood cultures and rectal swabs for ova, were again negative. It was thought that penicillin therapy twice produced a remission.

In 1955 she had a minor recurrence of vulvar ulceration lasting for a few weeks.

In April, 1958, then aged 35 years, she was admitted to the E.N.T. Department having lost more than two stones in weight in a period of two months. For one month she had experienced increasingly severe pain in the right side of the throat on attempting to swallow.

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The general picture was the same as in 1952 with fever, tachycardia, W.B.C. 15,500 per c.mm., E.S.R. 104 mm. in 1 hour, Hb. 74 per cent, Chest X-ray normal and all serological tests negative. Indirect largygoscopy revealed a white "slough" in the right piriform fossa and œdema of the right ary-epiglottic fold. When examined under anæsthesia the lesion was found to involve the whole of the right piriform fossa and resembled a widespread leukoplakia without naked eye evidence of ulceration. There were no palpable cervical lymph glands. Biopsy showed acutely inflamed and partially necrotic granulation tissue. There was destruction and scarring of both labia minora but no active vulvar ulceration.

Penicillin therapy failed to change the picture, but dramatic relief from pain and dysphagia was obtained after starting treatment with three hourly lozenges of hydrocortisone hemisuccinate 2·5 mgm. as described by Truelove and Morris-Owen (1958).

During the next three weeks the temperature was intermittent, finally remaining normal, yet the E.S.R. was persistently high (over 80 mm. in 1 hour). Pain did not return, despite the fact that the "slough" persisted, and she started regaining weight.

Two weeks after discharge severe dysphagia returned, this time not controlled by local hydrocortisone. It did, however, respond rapidly to oral prednisone acetate 5 mgm. q.d.s. which was started in June 1958, and which she is still taking. Several attempts were made to reduce the dosage of prednisone but each time there was a return of symptoms.

Since June, 1958, the patient has remained well, and has more than regained her lost weight, now showing the classical moon-face from prolonged steroid therapy. There has been no recurrence of oral, pharyngeal, or genital ulceration, and so far she has shown none of the eye or skin lesions found in Behçet's Syndrome. In October, 1958, a right Horner's Syndrome developed and this is taken as evidence of neurological involvement. The prognosis is considered to be poor.

Discussion

The fully developed Syndrome, seen mainly in young adults of either sex, is characterized by recurrent episodes of genital and oral ulceration together with inflammatory eye changes, the various sites being affected during the same or different relapses. Attacks are usually acute and associated with malaise, fever, leucocytosis and raised E.S.R. and, in the case of oro-pharyngeal ulceration and eye involvement, by severe local pain. The loss of weight can be a striking feature.

The oral ulceration consists of typical aphthous ulcers though these are usually more numerous, larger and more persistent than the commoner simple variety. Behçet's Syndrome has also to be differentiated for a heterogeneous group of conditions which affect principally the skin and mucous membranes of the body.

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Behçet's Syndrome

In erythema multiforme (Alm and Öberg, 1945) and especially in its variant, the Stevens-Johnson Syndrome (Church and Sneddon, 1955) there are circular erythematous or bullous eruptions of the skin, conjunctivitis, urethritis and widespread ulceration of the oral mucosa. Systemic upset and joint pains are also seen.

Recurrent non-specific urethritis, polyarthritis and conjunctivitis, with occasional oral ulceration and pleomorphic skin lesions are seen in Reiter's Disease which also responds to steroid therapy (Larson and Zoeckler, 1953).

Mucous membrane pemphigus, in particular, may be confused as ocular oral and genital lesions are frequently found together. Gibb (1958) recently described the types encountered and reported favourable response to steroid treatment.

Another condition worthy of mention is lichen planus. Sometimes there is oral ulceration as opposed to the commoner white patches, and the skin lesions may be confined to the glans penis or vulva (Warin *et al.*, 1958).

Oral ulceration and ano-genital pruritus are seen in certain hypovitaminoses notably pellagra.

France *et al.* (1951) claimed that when ulceration affected the pharynx its appearance was identical to the oral aphthae. In this case, however, that was not so, the area resembling a widespread leukoplakia; it could even have been mistaken for a submucosal non-ulcerated squamous carcinoma or a carcinoma *in situ*. This difference is in keeping with Behçet's original description of the pharyngeal as opposed to the oral lesions.

The genital ulcers, usually large, are found mainly on the labia minora and cervix uteri or on the penile urethra, glans and scrotum; pain is a variable feature and healing occurs with considerable scarring. (Phillips and Scott, 1955 and Berlin, 1944.)

The diagnosis of Behçet's Syndrome can be made, as in this instance, without eye involvement, for the syndrome is often incomplete at least for a period of many years. Typical lesions in any two of the three sites is sufficient for diagnosis (Phillips and Scott, 1955). Iritis, with pus in the anterior chamber, is the commonest but conjunctivitis, keratitis and retinitis also occur. Retinal thrombophlebitis and retinal hæmorrhages are not uncommon.

Skin lesions have not so far been seen in this case; the commonest are an acne-like pyoderma and erythema nodosum (France *et al.*, 1951). Frank ulceration of the skin is also reported.

During the course of the disease isolated or recurrent thrombophlebitis may occur. The case reported by Carr (1957) is a good example of this.

Neurological manifestations, less common and usually starting many years after the onset of symptoms, indicate a poor prognosis. Pallis and Fudge (1956) and Wadia and Williams (1957) have reviewed these. There

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is commonly evidence of acute widespread nervous system involvement ushered in by intense headache. The picture may be one of acute encephalitis or meningo-encephalitis, acute brain stem lesions or acute dementia. Pyramidal signs are common and the cerebrospinal fluid usually has a raised protein and cell count, mainly lymphocytes.

As this single case does not contribute to the question of ætiology, it is not proposed to discuss it in detail. The L.G.V. Complement Fixation Test suggesting previous virus infection is of doubtful significance. Sezer (1953 and 1956) has been the principle upholder of the virus infection theory, while Koch (1950) and Wadia and Williams (1957) give preference to an allergic basis. Many of the individual lesions can be explained by a localized thrombophlebitis (France *et al.*, 1951) but this in itself does not explain the cause of the disease, which, for the present, remains unknown.

Treatment must be largely symptomatic until a remission occurs. For the painful oro-pharyngeal ulcers local hydrocortisone lozenges, which have almost no systemic action, should be tried first. If necessary, systemic steroids should be used and in adequate dosage. Phillips and Scott (1955) and Wadia and Williams (1957) obtained excellent responses in severely ill patients, as also occurred in this case.

It would appear that at least 100 mgm. oral cortisone daily is required. This is approximately equivalent to 20 mgm. oral Prednisone daily, with which analogue there is less salt and water retention. Maintenance therapy may be required temporarily or permanently depending upon the severity of the case.

The eyes are usually affected separately and after an interval of some years. Enucleation may be required for blindness and persistent pain.

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