groups, and difference may exist among females from different nations, even in Northern Europe (1, 3).

In this study there was 2 females with climacterium praecox (7.4%), which is consistent with a frequency of 5% in the normal population (1).

The females with systemic sclerosis had presented the known symptoms of physiological menopause, and the cessation of menstruation had a normal pattern with no registered bleedings during the postmenopause. The females with menstruation had a normal cyclic bleeding pattern.

In conclusion, this study indicates that the menopause is normal in females with systemic sclerosis.

The fertility of the females with systemic sclerosis, expressed as 1.5 liveborn infants for each female, does not seem to be diminished, since some of the females with this serious disease may have decided to avoid more children. The frequency of recognized spontaneous abortions of 13 (27.6%) out of a total of 47 pregnancies may be higher than a frequency of 10% in the general population (2). An increased rate of pregnancy wastage has been found in other studies, especially in advanced scleroderma (4).

Seven females could not participate in the study because of earlier hysterectomy. This represents a frequency of 20.5% of the entire group before allocation to study, which is no different from the average frequency of hysterectomy in Danish women (5).

The findings in this study indicate that the ovary is not involved in systemic sclerosis.

REFERENCES

1. Bjøro, K.: Klimakteriet. *In* Gynaekologi (ed. K. Bjøro and P. Kolstad), p. 120. Universitetsforlaget, Oslo, 1979.
2. Brody, S.: Abort. *In* Obstetrik och Gynekologi (ed. S. Brody), 1st ed., p. 191. Almqvist & Wiksell, Stockholm, 1970.
3. Flint, M. P.: Sociology and Anthropology of the menopause. *In* Female and Male Climacteric (ed. P. A. van Keep, D. M. Serr and R. B. Greenblatt), 1st workshop report, p. 1, MTP Press Limited, Preston, 1979.
4. Jablonska, S.: Adrenals, hypophysis and gonads. *In* Scleroderma and Pseudoscleroderma (ed. S. Jablonska), 2nd ed., p. 61. Polish Medical Publishers, Warzaw, 1975.
5. Klemp, P. & Crone, P.: Regional variation i hysterectomifrekvensen i Danmark. Ugeskr Læger *144:* 213, 1982.
6. Medsger, T. A. & Alfonse, T. M.: Epidemiology of systemic sclerosis (scleroderma). Ann Int Med *74:* 714, 1971.
7. Rowell, N. R.: Systemic sclerosis. *In* Textbook of Dermatology (ed. A. J. Rook, D. S. Wilkinson and F. J. G. Ebling). 3rd ed., vol. 2. 1209 pp. Blackwell Scientific Publications, Oxford, 1979.

Behçet's Syndrome in Two Brothers

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Abstract. Two brothers, born in 1944 and 1950, had been brought up in separate homes since 1951. In 1978 they were both afflicted with Behçet's syndrome. This condition is uncommon in Scandinavia, and there are no other known reports of familial cases from the Scandinavian countries. The etiology of the disease is obscure and controversial. In our two cases a hereditary disposition seems more probable than an infectious origin.

Key words: Behçet's syndrome; HL-A antigen; Hereditary diseases

Behçet's syndrome is frequently reported from Japan and the Eastern Mediterranean area, but is an uncommon disease in the USA and Northern Europe (9). The syndrome usually displays protean features, making it "a great imitator". The variability in clinical manifestations and the long delay in involvement of various target organs make the diagnosis difficult. There are no pathognomonic symptoms, but a summary of criteria is necessary to fulfil the diagnosis. The criteria are divided into major or minor, according to the Behçet Syndrome Research Committee (9). The four major criteria are 1) recurrent aphtae; 2) skin lesions—erythema nodosum-like eruption, subcutaneous thrombophlebitis, folliculitis; 3) eye lesions—iridocyclitis, chorioretinitis; and 4) genital ulcerations. Minor criteria may include articular, cardiovascular, intestinal, urologic and neurologic involvement (8, 9). The syndrome is considered complete when all four major symptoms appear in the clinical course; otherwise it is called incomplete (9). The complete form is not necessarily more severe than the incomplete variant. The basis for the symptoms

seems to be a lesion in small vessels (vasculitis), predominantly in venules. An imbalance between B- and T-lymphocytes and an enhanced leukocyte chemotaxis have been observed (5, 8, 9).

CASE REPORTS

The two brothers, C. S., born in 1944, and R. G., born in 1950, were separated in early childhood, when their mother, aged 31, suddenly died of a "heart attack". There was another brother in between them, and the two elder brothers stayed with their father, while the youngest child was brought up by an aunt. C. S. and R. G. then lived completely apart; they met once in 1971, but not until 1981 did they begin to see each other regularly.

C. S., employed as a foreman in a meat-packing firm, had for several years diffuse back-ache. In 1978 he presented with transient ocular symptoms. Later on he suffered from painful recurrent genital, oral and interdigital ulcerations. He also complained of pyoderma of the legs. In 1979 bilateral iridocyclitis was diagnosed and has recurred repeatedly. He was also treated for gonarthritis in 1980. The activity of the disease has required treatment with systemic corticosteroids and cyclophosphamide. At present his vision is somewhat impaired, but he is employed full time.

R. G., working as a waiter, has experienced diffuse arthralgias and muscle pain, mostly from the lower back and the legs since 1978. In addition he has had recurrent symptoms from the skin—nodular subcutaneous swellings (erythema nodosum), thrombophlebitis, acneiform eruptions and hidrosadenitis. Since 1979 he has had recurrent orogenital ulcerations. On some occasions microscopic haematuria has been observed, and he has usually shown a moderate leukocytosis. He has been treated with antiphlogistic preparations, with some degree of effect.

The investigations made at various departments regarding the two brothers have not revealed any evidence of any other disease—dermatologic, rheumatic, ophthalmologic or urologic—than the syndrome of Behçet. The elder brother has all the criteria for the complete syndrome, whereas the younger as yet has the incomplete type. Analysis of histocompatibility antigens, HL-A, shows that C. S. has the haplotype HLA $A_2B_1;W_{21}$, and that R. G. has the haplotype $A_2B_{12}W_{21}$.

DISCUSSION

More than forty years after Behçet's first report of the disease (3), the etiology is still obscure. The syndrome was initially proposed to be of infectious, probably viral, origin, and although theories of a slow virus infection have been suggested, the evidence is not convincing (2, 7, 8). In studies from Japan, environmental pollution is held responsible, at least as a provoking factor, for the high and steadily increasing incidence there (8). Familial incidence is rare, though reported by several authors (1, 2, 4, 5, 6, 7). A family study of probands with Behçet's syndrome showed an increased tendency for orogenital ulcerations in first-degree relatives (6). Association with HLA B_5, especially in males, has frequently been reported by many investigators, and the connection seems to be stronger in familial occurrence (5, 8, 10). The disease tends to be more severe in the familial than in the sporadic cases (2). Andaç et al. described Behçet's disease in two families with evidence of recessive transmission (1). However, there is another study of the syndrome in four generations, postulating a dominant inheritance with variable expressivity (5). Concerning our two cases, they evidently do not support the infection theory, as the brothers had hardly met for 30 years, but rather a genetic disposition. A hereditary factor, possibly linked to the immune system, might explain the tendency to develop the syndrome, perhaps precipitated by viral, environmental, or other toxic factors.

REFERENCES

1. Andaç, K., Pamukçu, K. & Ergüllü, H.: Hereditary Behçet's disease: case reports in two families. International Congress Series 467, p. 138, Excerpta Medica, 1979.
2. Aoki, K., Ohno, S., Ohguchi, M. & Sugiura, S.: Familial Behçet's disease. International Congress Series 467, p. 133, Excerpta Medica, 1979.
3. Behçet, H.: Über rezidivierende, aphthöse, durch ein Virus verursachte Geschwüre am Mund, am Auge und an den Genitalien. Dermatol Wochenschr *105:* 1152, 1937.
4. Berlin, C.: Behçet's disease as a multiple symptom complex. Arch Dermatol *82:* 127, 1960.
5. Berman, L., Trappler, B. & Jenkins, T.: Behçet's syndrome: a family study and the elucidation of a genetic role. Ann Rheum Dis *38:* 118, 1979.
6. Chamberlain, M. A.: A family study of Behçet's syndrome. Ann Rheum Dis *37:* 459, 1978.
7. Goolamali, S. K., Comaish, J. S., Hassanyeh, F. & Stephens, A.: Familial Behçet's syndrome. Br J Dermatol *95:* 637, 1976.
8. O'Duffy, J. D.: Summary of international symposium on Behçet's disease. J Rheumatol *5:* 229, 1978.
9. Shimizu, T., Ehrlich, G. E., Inaba, G. & Hayashi, K.: Behçet disease (Behçet syndrome). Semin Arthritis Rheum *8:* 223, 1979.
10. Yazici, H., Chamberlain, M. A., Schreuder, I., D'Amaro, J. & Muftuoglu, M.: HLA antigens in Behçet's disease: a reappraisal by a comparative study of Turkish and British patients. Ann Rheum Dis *39:* 344, 1980.