Erythema nodosum Following Thalidomide Therapy for Behçet's Disease

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The therapeutic effects of thalidomide in recurrent urogenital ulceration of Behçet's syndrome have been previously reported by Mascaro et al. [1], Saylan and Saltik [2], and Bowers and Powell [3]. Moreover, thalidomide is highly indicated in the treatment of erythema nodosum leprosum [4]. We report a case of Behçet's disease showing dramatic improvement of urogenital ulcers but occurrence of erythema nodosum (EN) following thalidomide therapy.

A 25-year-old Algerian man presented with recurrent thrombophlebitis since 1982. The diagnosis of Behçet's disease was supported by additional relapsing symptoms including aphthae, genital ulcerations, pustules on the buttocks, arthritis involving both knees and ankles. EN was notably absent and ophthalmologic findings were negative. Tissue type was HLA All A28 B5 B12. Therapy was begun on 4 January, 1986, with thalidomide, 100 mg/day. Five days later he developed numerous painful erythema-tous nodules on his legs. Thalidomide was stopped and the patient started a treatment with colchicine, 2 mg/day. On 26 April, 1986, thalidomide was read-ministered because of painful aphtae. Two days after profuse nodules reoccurred involving both the arms and the legs. Clinical examination was normal but hyperreactivity to venous puncture was noted and ocular examination revealed vasculitis. Biological investigations including blood cell count and differential, serum electrolytes, liver function test, urea, creatinine and serum protein were normal or negative. Electrophoresis showed an increase of gammaglobulin with a polyclonal profile on im-munoelectrophoresis. Total T cells and their subsets were determined using monoclonal antibodies. Total T cell count was normal but the ratio of T helper to T suppressor cells was low because of an increase in the number of T suppressor cells.

Histological examination of a recent nodule showed a normal epidermis and dermis. An inflammatory infiltrate was found in the connective septa of the hypodermis around the blood vessels.

Leukomonocytes were only found in the infiltrate without polymorphonuclear neutrophils.

Search for circulating immune complexes and direct im-munofluorescence microscopy were not performed. Thalidomide was stopped and a treatment with in-domethacin, 50 mg/day, was begun. A month later the

nodules had entirely disappeared, ophthalmologic examination returned to normal but regmatogenous disorders were noted on peripheral retina and treated with laser.

Occurrence of EN during thalidomide therapy for Behçet's disease has been previously reported by Saylan and Saltik [2] in 2 cases. These patients had never presented such a symptom before.

Other clinical trials [1, 3] of thalidomide therapy for Behçet's did not mention EN as a side effect of the therapy.

Moreover, incidence of EN eruption is high in Behçet's disease. In our case, EN occurred after each thalidomide administration and disappeared spontaneously.

In all clinical trials [1-3] thalidomide is highly effective on aphthae. Other cutaneous manifestations of Behçet's disease including EN lesion and skin hyperreactivity (pathergy) as ocular symptoms did not respond well to thalidomide therapy. One can consider that selective efficiency of thalidomide is reliable to histological and immunological differences between aphthae and EN manifestations in Behçet's syndrome [5]. In spite of this efficiency on aphthae and EN leprae thalidomide could promote EN eruption, which is relevant to a different immunological mechanism. A careful assessment of thalidomide as a therapeutic agent of Behçet's disease seems warranted to delineate these side effects.

References

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