Remission of Sézary’s Syndrome with Cyclosporin A. Mild Capillary Leak Syndrome as an Unusual Side Effect

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A case of Sézary syndrome treated with cyclosporin A is reported. A dramatic cutaneous improvement was obtained within a few days after initiation of treatment. Among the side effects produced were linear purpuric lesions in skin folds and friction areas. Key words: Drug toxicity. (Received June 14, 1985.)

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Cyclosporin A is an immunosuppressive drug which acts on T cell helper response. It inhibits the production of Interleukin-2 (1) which is needed to support the growth of this lymphocyte sub-population (2).

Its inhibitory effect on the growth of a human leukemia cell line was reported by Foa et al. (3). Totterman et al. (4) found it was selectively cytotoxic and cytostatic on the Sézary cells. Some authors have used Cyclosporin A in the Sézary syndrome treatment (6, 7).

CASE REPORT

A 49-year-old man, was first examined in August 1983. He suffered from an erythrodermia, with itching, palmoplantar keratoderma, subungual hyperkeratosis, and loss of body hair. A skin biopsy revealed the presence in dermis of an infiltrate of atypical mononuclear cells with epidermotropism and formation of Pautrier microabsceses. White blood cells (WBC) were 20,000, with 70% lymphocytes of which 19% were Sézary cells. Lymph nodes, internal organs, and bone marrow were not affected. Sézary syndrome was diagnosed.

The patient was treated with prednisone (20 mg per day) in combination with low-dose of chlorambucil. Later, the dose of prednisone was increased and 13-cis-retinoic acid was introduced. Subsequently, leukapheresis sessions were performed without showing improvement. Treatment was then changed to Cyclosporin A at the dose of 17.5 mg/kg per day and within a week a dramatic cutaneous improvement was observed. Clearing of the erythrodermia and presence of leukodermic areas were noted. Disappearance of the palmoplantar hyperkeratosis and itching were also observed. Blood count remained unchanged.

During the next few weeks the following symptoms were observed: Epigastric burning, transitory increase of arterial tension, paresthesias, tremor, hypertricosis in the face, thorax and arms, gum hypertrophia, gingivitis ulcerative necrotizing, facial edema and purpuric lesions in friction areas and small skin folds subject to pressure (Fig. 1). Coagulation tests were normal.
After two months of treatment a rise in liver function tests made necessary the reduction of drug dosage to 10 mg/kg per day. These parameters returned to normal limits but the skin symptoms reappeared. Thus the administration of Cyclosporin A was discontinued.

The suspension of Cyclosporin A resulted in the disappearance of the purpura skin pattern. The WBC rises up to 75,000.

DISCUSSION
Cyclosporin A has been used since 1976 for the prevention of the rejection of organ transplants and in the treatment of the skin graft-versus-host-disease. More recently it has been used as an immunosuppressive drug in the treatment of other diseases in which modulation of T cell response is desired (8).

It produces diverse side effects such as decreased appetite, fatigue, paresthesias, tremor, nephrotoxicity, benign breast lumps (9), and development of lymphomas (6).

Some of the skin changes attributed to the use of this drug are: gum hypertrophy, hypertricosis, cutaneous squamous cell carcinoma (10), and hidradenitis (8).

The therapeutic results in our patient were very dramatic concerning the improvement of the skin pattern, although the blood count remained unchanged. Similar results have also been observed by other authors (6, 7).

The presence of serious side effects such as hepatotoxicity, led to a reduction of dosage and to the subsequent cessation of the use of this drug when it was observed that the therapeutic response was not being maintained.

All the secondary effects presented by our patient have been described previously with the exception of the pattern of linear purpuric lesions in friction prone areas. As these lesions are not associated with the Sézary syndrome and cannot be connected with a coagulation disorder, they were interpreted as a phenomenon of capillary fragility attributed to pharmacological toxicity. This interpretation was also supported by the disappearance of the lesions, when Cyclosporin A was stopped.

Harper et al. (5) in their publication concerning skin changes caused by Cyclosporin A described with the name of "capillary leak syndrome" a serious disorder with generalized increase of the capillary permeability, which causes multiple organ damage (pneumonitis,
gastrointestinal bleeding) the skin manifestations being hemorrhagic and necrotic areas. On being consulted concerning our patient, the above mentioned author stated that he had never seen lesions similar to those in our case although he considered them to be due to the same pathogeny (11).

We suggest that the pattern presented by this patient could be considered as a mild form of capillary leak syndrome, not previously described.

In view of the striking effect of Cyclosporin A on the skin manifestations and its very slight or lacking effect on blood count pattern, we consider that this drug would be more appropriate in the treatment of mycosis fungoides than of Sézary’s syndrome.

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The Response of Generalized Granuloma annulare to Dapsone

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Six patients with generalized granuloma annulare were successfully treated with Dapsone. Their ages ranged from 11 to 76. There were no serious side-effects and all were able to cease the drug. Key words: Chronic disease; Anti-inflammatory; Safe. (Received May 20, 1985.)

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