Cyclofenil in Childhood Scleroderma

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Treatment with cyclofenil for 9 months of a 10-year-old girl with localized scleroderma is reported. No clinical improvement was achieved. The drug was discontinued due to hepatotoxicity. *Key words: Cyclofenil; Childhood scleroderma.* (Received December 8, 1982.)

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Scleroderma is a connective tissue disease of unknown etiology. Despite many therapeutic attempts with different groups of drugs, no treatment has been found effective in preventing the progress of the disease in childhood.

Cyclofenil (Sexovid®, Ferrosan, Malmö, Sweden), a non-steroid, very weakly estrogenic compound with anti-estrogenic properties has been shown in animal studies to inhibit sulphate incorporation in cartilage (1), and promising results in the treatment of adult scleroderma patients have been reported (2–5).

CASE REPORT

A 9-year-old girl was first seen in July 1976 with a band-like skin lesion over the medial surface of the right leg, which was depigmented, shiny and felt thickened and taut. There was muscular wasting of the right calf and contracture in the right ankle joint, and areas of depigmentation were seen on the trunk. The findings of the remaining physical examination were normal.

Initial laboratory data

Hb, 109 g/l; ESR, 36 mm/h; WBC, platelets, S-LD, S-ASAT, S-ALAT, S-CK, and S-creatinine were all normal. Serum immunoglobulin electrophoresis showed normal IgA, while IgG was 22.0 g/l (normal range 6.5–14.0 g/l) and IgM 2.4 g/l (normal range 0.5–1.8 g/l). Antinuclear antibodies were positive to a titre of IgG 1/400 with a homogeneous fluorescent pattern and IgM 1/400. Tests for antibodies to extractable nuclear antigen, DNA-antibodies and rheumatoid factor all proved negative.

Electromyography gave evidence of peripheral nerve damage. A skin biopsy from the right leg showed increased thickness of the dermis with only a few fibroblasts. Abundant hyalinized collagen and some sweat glands were seen, but no hair follicles or sebaceous glands. There were no inflammatory or perivascular infiltrates.

THERAPY AND COURSE

In August 1976 D-penicillamine treatment was initiated. After 16 months of therapy no signs of improvement could be observed and the clinical condition continued to progress.

Cyclofenil treatment was commenced in December 1977. The patient, who weighed 35.2 kg, received cyclofenil 200 mg t.i.d. After 1 week of treatment the patient had fluor vaginalis and slight tension in her breasts. These side effects disappeared after reduction of the dose to 200 mg b.i.d. After 4 months of treatment the transaminases were elevated to S-ASAT 4.60 μkat/l (normal range<0.75 μkat/l) and S-ALAT 5.70 μkat/l (normal range<0.75 μkat/l). The drug was withdrawn for 3 weeks and the transaminases normalized. Rechallenge with the drug was tried three times but in spite of reducing the dosage successively to 100 mg cyclofenil b.i.d., the transaminases rose again to S-ASAT 3.55 μkat/l and S-ALAT 4.10 μkat/l. As the patient's symptoms were slowly progressing and the drug showed marked hepatotoxicity even at a low dosage, the cyclofenil treatment was discontinued after a total period of 9 months. Except for the transaminases, no other laboratory parameters changed during the cyclofenil treatment. Since then the patient has received no drug treatment and has been given physiotherapy only.

The disease shows a slow progressive course. New areas of skin involvement have appeared, the latest in November 1981 with a morphea on the left side of the abdomen. Laboratory investigations in

September 1982 showed a normalized ESR and serum immunoglobulin electrophoresis. Antinuclear antibodies were positive to a titre of IgG 1/400 and IgM 1/100. Tests for rheumatoid factor and DNA-antibodies remained negative.

DISCUSSION

It is conceivable that although the clinical differences between LS (localized scleroderma) and PSS (progressive systemic scleroderma) are significant, it may be essentially the same etiology with different manifestations. It seems reasonable therefore to suggest that a drug effective in PSS will also be so in LS.

In open clinical studies with a total of 29 adult patients with PSS, improvement during cyclofenil treatment was recorded in the skin condition, joint pain and stiffness (2–4). A 1-year double-blind crossover study of cyclofenil versus placebo in two 6-month periods in 27 adults with PSS has shown improvement in oesophageal peristalsis, joint pain and stiffness. Other parameters did not change significantly (5).

In another double-blind crossover study of cyclofenil and matching placebo in two 4-month periods in 11 patients with scleroderma, none of the variables showed consistent change in favour of cyclofenil (6).

We have not been able to demonstrate any beneficial effect of cyclofenil in our patient as she showed a slow progression of the skin manifestations and no significant alteration in the serological tests.

The hepatotoxicity of cyclofenil as seen in our patient has also been noted by others (5, 6). Fluor vaginalis and tenderness of the mammary glands were also registered by others (5). The possible growth-retarding effect of cyclofenil (1) was not seen in our patient, as she grew 7.5 cm/year during the period of cyclofenil treatment (normal range 6–9 cm/year).

REFERENCES

1. Herbai, G.: Separation of growth inhibiting potency from oestrogenicity in different weak oestrogenic drugs of various chemical structures. Acta Endocrinol *68:* 249–263, 1971.
2. Herbai, G.: Treatment of progressive systemic sclerosis with a synthetic weak estrogen: cyclofenil (Sexovid®). Report of a case. Acta Med Scand *196:* 537–540, 1974.
3. Herbai, G., Blom, B. & Boström, H.: Treatment of progressive systemic sclerosis (scleroderma, PSS) with a new drug influencing connective tissue. Acta Med Scand *201:* 203–206, 1977.
4. Blom-Bülow, B., Boström, H., Herbai, G., Persson, B., Wollheim, F. A. & Öberg, K.: Cyclofenil in the treatment of scleroderma—a general view on the results after treating 29 cases. Z Rheumatol *39:* 1–8, 1980.
5. Blom-Bülow, B., Öberg, K., Wollheim, F. A. et al.: Cyclofenil versus placebo in progressive systemic sclerosis. Acta Med Scand *210:* 419–428, 1981.
6. Gibson, T. & Graham, R.: Cyclofenil—a treatment for scleroderma? Ann Rheum Dis *40:* 627, 1981.