REM Syndrome: An Immediate Therapeutic Response to Hydroxychloroquine Sulphate

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Received September 24, 1979

Abstract. A 22-year-old woman had been suffering for 11 years with a REM syndrome. Her symptoms were provoked and aggravated by exposure to sunlight. The administration of hydroxychloroquine sulphate had a quick effect. The drug was given for 6 months, and the patient remained symptom-free even in summer, when sunbathing.

Key words: REM Syndrome; Mucinosis; Lymphoreticular proliferation; Hydroxychloroquine sulphate

The etiology of cutaneous mucinoses is unknown. To this group of diseases characterized by similar histochemical alterations, a new clinical variant, the reticular erythematosus mucinosis (REM) syndrome, has been added recently (1, 2, 3, 4, 6, 8, 10, 11).

The clinical picture consists of a sheet-like or net-like, slightly infiltrated erythema on the anterior part of the chest, on the back, and (rarely) on the neck or abdomen. Histologically, parivascular, round cell infiltrates and the deposition of alcian blue positive acid mucopolysaccharides are found in the dermis.

We report here a patient with pronounced perifollicular infiltrations simulating a lymphoproliferative disease.

CASE REPORT

A 22-year-old woman was sent to our clinic for histological examination on 7th January, 1978. She had been suffering from skin eruptions for 11 years. The first lesions appeared on the anterior part of the chest, and had progressed during the last 5 years. Sunlight, perspiration and excitement always aggravated the condition.

On clinical examination a more or less sharply delimited erythema, in some places with tongue-like extensions, was seen on the anterior part of the chest (Fig. 1), on the epigastrium and on the right side supraclavicularly, too. In the erythematous areas follicular papules were discernible.

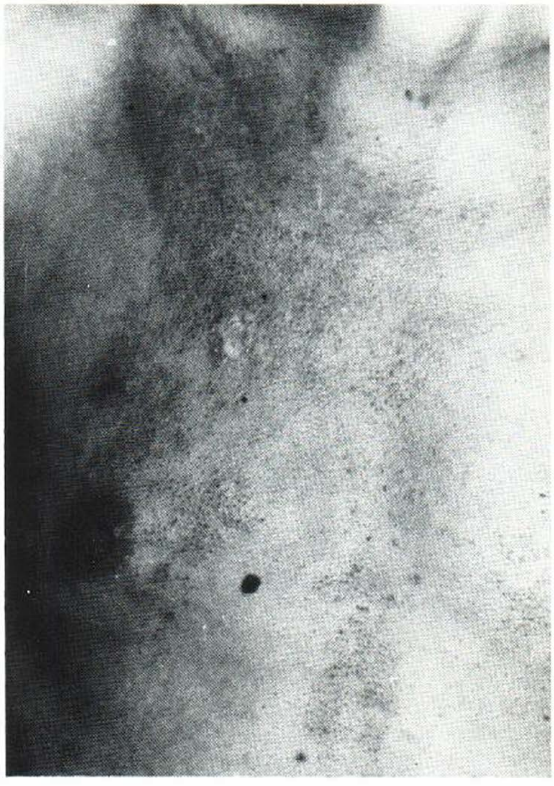

Fig. 1. Skin symptoms before treatment.

Histological examination of a follicular papule on the chest showed cellular infiltrations around the normal-looking hair follicles (Fig. 2). The infiltrate contained two types of cells: lymphocytes with a small, round, dark staining nucleus, and bigger cells with a large nucleus and slightly basophilic cytoplasm. In preparations stained with HE under high-power magnification a net-like or granular structure resembling mucous deposition was seen, but it did not stain either with alcian blue or with cresyl violet. With Giemsa staining cells were seen with a larger, paler nucleus having azurophilie in their cytoplasm. The process was evaluated as a perifollicular lymphoreticular proliferation of benign character and unknown origin. Another biopsy was proposed to investigate the mucous deposition in frozen section. The patient was seen again in April. Her skin symptoms remained unchanged.

Another skin biopsy was performed, from the chest. In paraffin-embedded sections the upper corium had a loosened structure—otherwise the picture was identical with that seen in the first biopsy. No deposition of acid mucopolysaccharides was detectable in this material. However, in unfixed frozen sections the deposition of alcian blue positive filamentous material (Fig. 3) could be observed in the vicinity of the blood vessels and around the cellular infiltrates, or even among the cells. A diagnosis of REM syndrome was established.

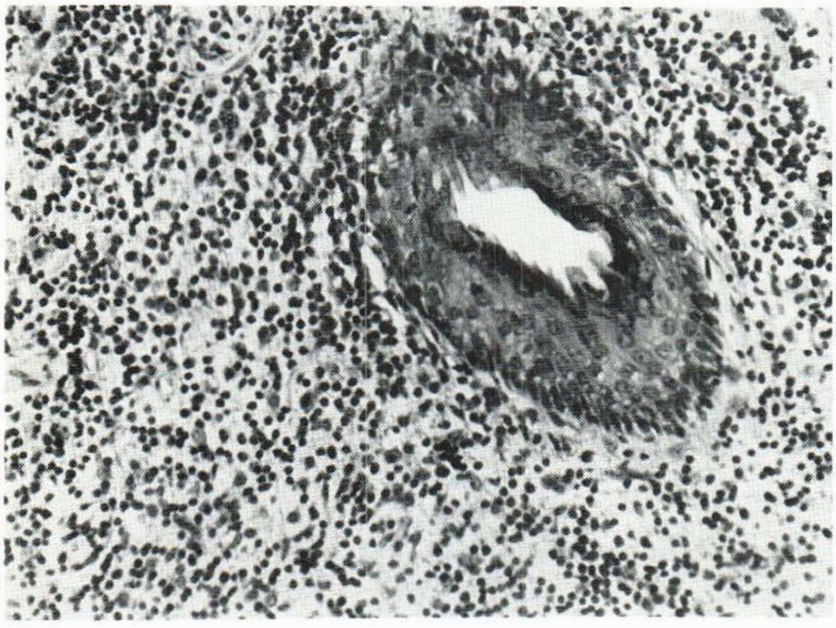

Fig. 2. Perifollicular infiltrate composed of lympho- and histiocytes, a few plasma cells and lymphoblasts. HE. ×100.

Investigations

MED values, thyroid function, chest and skull X-ray, electrocardiogram were normal. ESR 2 mm/h. RBC, hemoglobin, quantitative and qualitative WBC count were within normal limits. Urine analyses were negative. Uro- and coproporphyrin were within normal limits. 17-ketosteroid excretion 19.2 mg/24 h; VMA and 5-hydroxytryptamine, negative. Blood glucose, 100 mg%; BUN, 15 mg%; serum bilirubin, 0.3 mg%; serum alkaline phosphatase, 80 mU/ml; SGOT, 25 U; thymol, 1.05 U. Serum electrolytes, normal. Serum protein, 7.46%; electrophoresis: albumin, 49%; globulins: α_1 5%, α_2 10%, β16%, γ20%. LE-cell, antinuclear antibody test, Rose test, negative. Antistreptolysin 0 titre, 120 U. Serum calcium, 9.6 mg%.

Progress

After having established the diagnosis, Plaquenil (Winthrop) was administered in a daily dose of 400 mg for 3 months, and of 200 mg for a further 3 months. Consider-

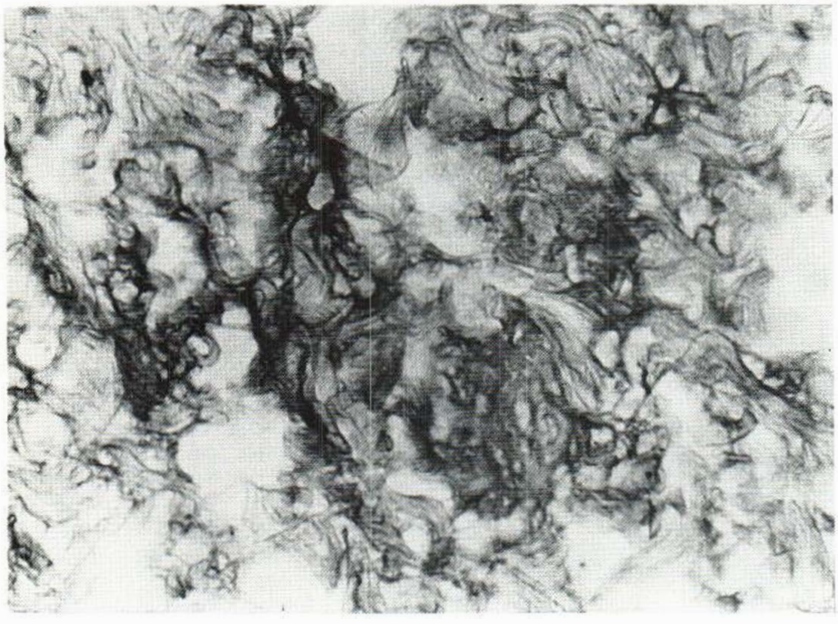

Fig. 3. Alcian blue positive filamentous deposition among the collagen fibres and around the blood vessels. Frozen section, ×200.

able improvement was noted on the 5th day, and the patient became symptom-free on the 10th day. In the summer she was able to sunbathe, yet remained and has been symptom-free up to now.

Discussion

The deposition of acid mucopolysaccharides in the dermis in cutaneous mucinoses and in REM syndrome is most probably a secondary phenomenon due to a hitherto unknown cause. In the first group of diseases it is accompanied by an increased number of fibroblasts; in the second condition by a perivascular or/and perifollicular infiltrate of patchy character. The infiltrate is composed mainly of lymphocytes, but lymphoblasts or stimulated lymphocytes also occur in them (6, 11). These cellular elements may play a part in the deposition of acid mucopolysaccharides in which connection no immunoglobulin deposition was found (1, 2, 4).

The eruptions appear mostly after sun exposure (10, 11) although the MED values are usually normal (1, 2, 11), as in our case. Another interesting point is the good therapeutic response to chloroquine derivates (1, 4, 6, 10, 11, 12). The action mechanism of these preparations in photosensitive eruptions is thought to be the drug's binding to the DNA (9). In REM syndrome the infiltrations contain stimulated lymphocytes (6, 11), and the chloroquine derivates might have something to do with their DNA-rich nuclei. Their action in other forms of mucinoses (5, 7) might be connected with the fibroblasts which normalize their activity.

Investigations into the action mechanism of chloroquine might throw some light on the pathogenesis of mucinoses and REM syndrome.

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Topical Application of Zinc-Solutions: A New Treatment for Herpes Simplex Infections of the Skin?

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Received October 9, 1979

Abstract. Eighteen patients experiencing 22 episodes of recurrent herpes simplex skin infections were treated with topical applications of a solution containing 4% zinc sulphate in water. In all patients, pain, tingling and burning stopped completely within the first 24 hours of zinc therapy. Crusting occurred within 1–3 days and no adverse effects were observed.

Recurrent herpes simplex infections, although usually self-limited, are an annoying source of discomfort and embarrassment. Topical therapy with iododeoxyuridine (6), adenine arabinoside (2), cytosine arabinoside (8) and ether (2) have been shown to be without effect on the clinical course of this condition. Photodynamic inactivation has been reported to be effective in the treatment of orolabial and genital herpes Simplex (4); however, the safety of this form of therapy has been questioned, since photodynamically inactivated herpes simplex virus can induce neoplastic transformation in vitro (10) and in vivo (7).

Solutions of zinc salts have been reported to be effective in the treatment of herpetic keratitis in man (3). More recently, zinc ions have been shown to cause irreversible inhibition of herpes simplex