Case report

KERATOSIS LICHENOIDES CHRONICA

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ABSTRACT

Keratosis lichenoides chronica is a chronic dermatosis, generally of benign nature, yet refractory to treatment. Our 54-year-old man patient, who is the 40th case reported in the literature, presented with a 15-year history of skin lesions, which were clinically, histopathologically, immunohistologically and electron microscopically compatible with keratosis lichenoides chronica. As a child he was taking antimalarial drugs and later on he was treated with antituberculous drugs. For the past 18 years he has presented with signs of periodic allergic rhinitis. The Re-PUVA therapy produced some improvement in some areas, keratotic papules with keratotic plugs had disappeared and the papules flattened. The results were superior to those obtained by local selective phototherapy or by systemic treatment with etretinate (Tigason). The patient was therapeutically unresponsive to topical application of steroids, 0,5% tretinoin and tar preparations. Systematically administered therapy had only a temporary effect on the dermal lymphocytic and histiocytic infiltrate. Considering the pathogenesis of keratosis lichenoides chronica and the composition of the dermal infiltrate, we think it reasonable to try cyclosporin A but our patient refused it.

KEY WORDS

keratosis lichenoides chronica, histopathology, ultrastructure, treatment

INTRODUCTION

Since 1886, when Kaposi first described keratosis lichenoides chronica (KLC) until 1991, 38 cases of KLC had been described (1). In 1992, a new case of KLC was reported (2). As it is still unclear whether the dermatosis is an independent disease entity, or solely a variant of lichen ruber planus, it has been described under a wide variety of names, such as lichen ruber moniliformis (Kaposi 1886), lichen ruber acuminatus verrucosus et reticularis (Kaposi 1895), porokeratosis striata (Nekam 1938), dermatose papulohyperkeratosique en stries (Bureau, Barrière 1970), keratose lichenoide striée (Degos 1974), lichenoid trikeratosis (Pinol-Augade 1974), and keratosis lichenoides chronica (Margolis 1972) (1).

* *Anica Smrkolj MD, PhD has passed away unexpectedly. A short obituary is included in this issue.*

The disease runs a chronic course without spontaneous remissions. It is most refractory to treatment and affects patients of both sexes and all age groups. The disease is characterized by keratotic papules and plaques, commonly involving the limbs, and by erythematosquamous foci, noticed generally on the face. Nail lesions, keratosis of the palmar and plantar skin, erosions and cellular infiltrations involving the mucous membrane of mouth, genitals, eyes, upper respiratory tract and oesophagus may be also present. There is no systemic involvement and the lesions leave no scarring. Histologically, KLC frequently resembles lichen ruber planus. In the differential diagnosis Reiter's disease, Kyrle's disease, psoriasis vulgaris, keratosis follicularis, lichen ruber verrucosus, pityriasis rubra pilaris and lupus erythematosus have to be ruled out (1-4).

CASE REPORT

A 58-year-old patient, born in Macedonia, presented with a 15-year history of non-itchy skin lesions involving the upper and lower extremities and the gluteal area. The lesions were slowly progredient, unresponsive to local treatment and of seasonal character. The patient used to squeeze whitish comedo-like material from keratotic papules, which tended to suppurate in the summer. The plaquelike lesions were scaly and severely inflamed. His nails had reportedly become thicker and brittle during the past year.

He gave a history of whooping cough in childhood. As adolescent he had endemic malaria, which was treated by antimalarial agents. At the age of 23 he developed pulmonary tuberculosis and was placed on a 9-month course of antituberculous drugs. His history also revealed urethritis of unexplained etiology, which had never recurred. Since the age of 30 he has been taking antihistamines to treat allergic rhinitis which tended to occur in the spring due to exposure to pollens, as confirmed by the prick tests. Five years before present admission he was taking antacids for erosive gastritis. He also gave a history of pain in the right elbow and shoulder for 2 years. The patient is by profession a cellist. He denied drinking alcohol and smoking.

In 1993 he was admitted to the hospital twice. Since 1985 he has been treated at the Department of Dermatology on an outpatient basis, for atopic dermatitis.

On admission, the patient had erythematosquamous, moderately infiltrated plaque-like lesions, some of them reaching the size of a palm. They consisted of keratotic papules with horny plugs involving extensor, side of the arms, cubital fossae, thighs, popliteal fossae and knees (Figs. 1,2). There were individual keratotic foci over the dorsal aspect of the hands. The distal parts of the nails were thickened and split. The scalp showed diffuse scaling. Tiny pink, scaly papules were noted on the lateral borders of the eyebrows. All visible mucous membranes were normal.

Erythrocyte sedimentation rate, blood screen, serum electrolytes, bilirubin, transaminases, alkaline phosphatase, serum amylase, lipid count, urea and creatinine levels were within normal limits. Faecal smears for parasites and stool cultures for Cryptosporidium, fungi, Mycobacterium tuberculosis were negative. No tubercle bacilli were isolated from the urine and sputum. From the throat smear normal flora was recovered. The serologic test for syphilis was negative, while the tests for rheumatoid arthritis were positive (AST 1:240 IU/ml, Latex 240 IU/ml, Waaler-Rose test 1:512 IU/ml; other tests were negative). The serologic test for toxoplasmosis was negative. Total serum IgE levels were elevated to 210 IU/ml. Specific IgE to Phleum pratense and Dermatophagoides pteronyssinus were found positive. Chest X-rays and ultrasound of the abdomen were normal. Roentgenologic examination of the right elbow and right shoulder showed degenerative lesions of the joints.

Histopathology of a plaque on the right upper arm revealed a predominantly atrophic epidermis with intermittent areas of normal thickness. An area of acanthosis and a large invagination of the epidermis, filled out with abundant hyperkeratotic masses, were noticed (Fig. 3). A narrow streak of parakeratosis was seen at the upper border. There were areas of liquefaction degeneration of the basal cells. In the upper dermis, a dense lichenoid infiltrate was noticed, composed of lymphocytes, histiocytes and a few eosinophils (Fig. 4). The Kongo red stain failed to reveal amyloid.

Electron microscopic examination showed cytolytic changes of keratinocytes of the basal layer and lower spinous layer (Figs. 5,6). There was an intercellular oedema. Numerous lymphocytes, monocytes, macrophages and some basophilic, eosinophilic and neutrophilic granulocytes, otherwise forming dense infiltrates in the dermal papillary layer, were found in those areas (Fig. 5). There was a focal thickening of the granular layer of the epidermis with keratinocytes containing thin tonofilament bundles and

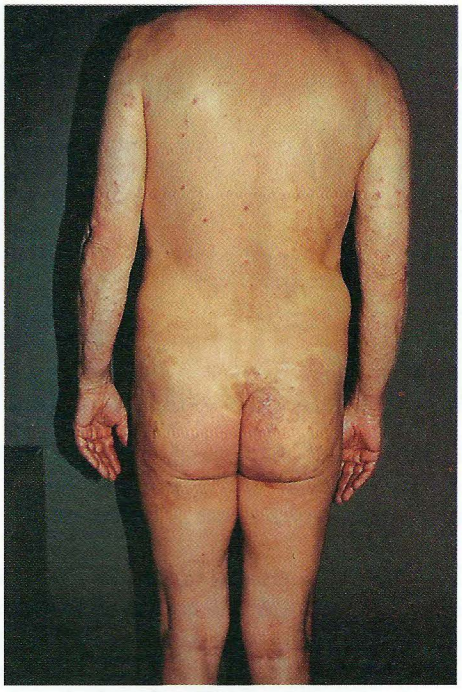

Fig. 1. Distribution of skin lesions.

sparse, rounded keratohyalin granules. The thickened horny layer showed no abnormalities, apart from focal parakeratosis. Other epidermal and dermal elements had normal ultrastructure.

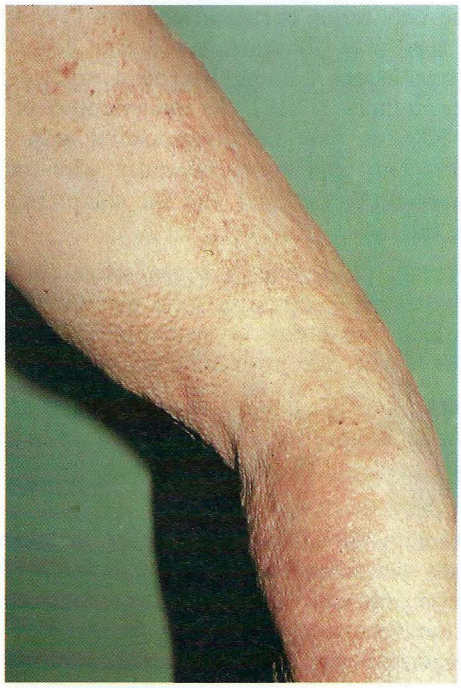

Fig. 2. Keratotic papules and plaque-like lesions on the left upper extremity.

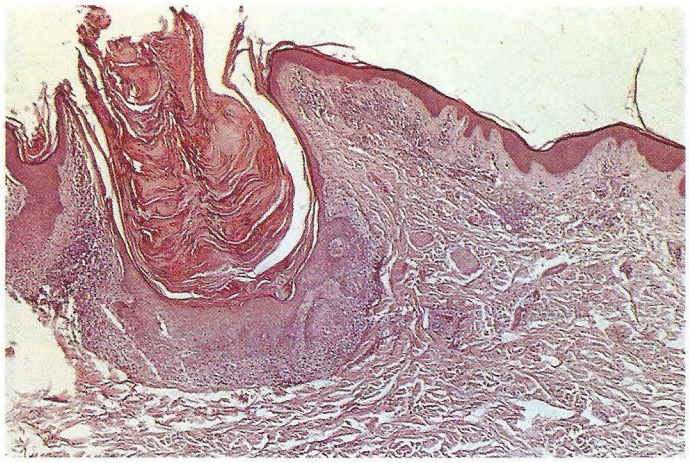

Fig. 3. Massive hyperkeratosis with a narrow streak of parakeratosis. Areas of thinned epidermis. Under the epidermis, dense band-like dermal cellular infiltrate. HE, 25x

Direct immunofluorescence studies demonstrated band-like deposits of fibrin, IgG and C3 at the dermo-epidermal junction and globular IgM deposits in the upper dermis.

Prior to admission to this Department, the patient had been treated by PUVA on several occasions, yet he noticed no improvement.

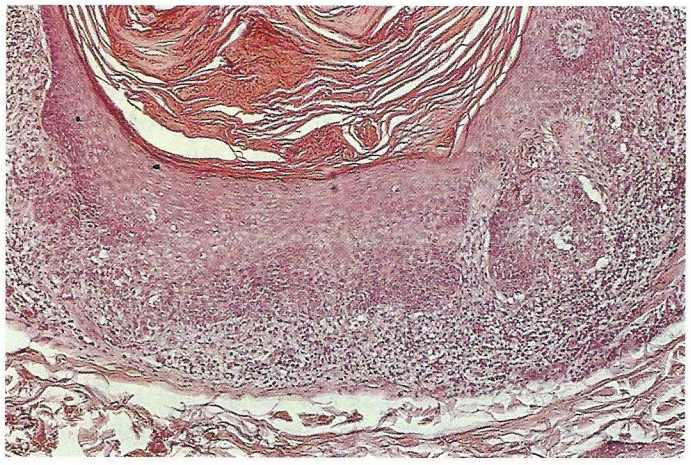

Fig. 4. Higher magnification of features in Fig. 3 showing the dense lichenoid infiltrate, consisting of lymphocytes and histiocytes. Signs of initial liquefaction degeneration in the acanthotic epidermis. HE, 63x

Treatment with nonspecific topical ointments, local steroids and orally administered antihistamines from October 1985 to November 1992 produced no clinical improvement either. Also, the patient was therapeutically unresponsive

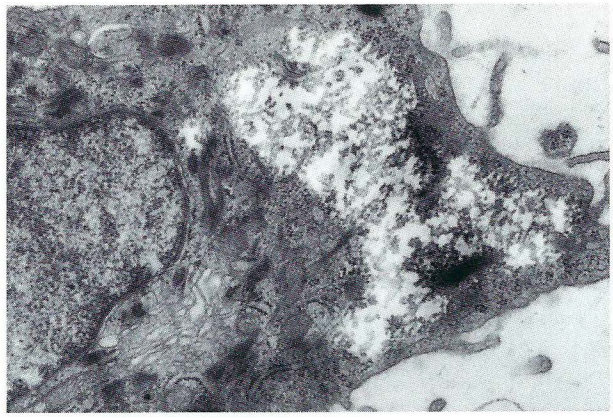

Fig. 5. Cytolytic changes in a keratinocyte of the lower spinous layer. Electron micrograph, 13000x

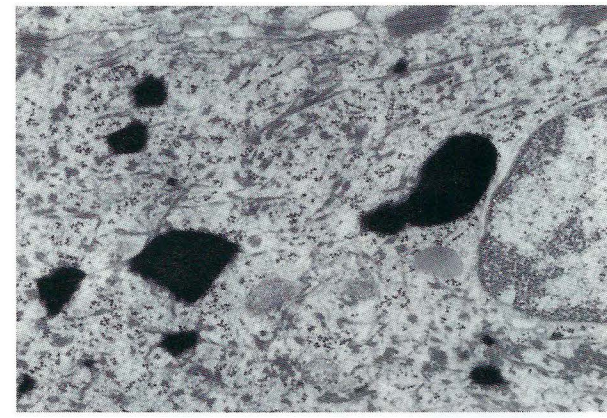

Fig. 6. Keratinocyte of the granular layer with thin tonofilament bundles and sparse pounded grains of keratohyalin. Electron micrograph, 13000x

to local selective phototherapy (long-wave UV-B and UV-A) received in 1985. Another course of 30 irradiations given in 1992 caused temporary deterioration of the dermatosis.

After the histopathologic diagnosis of KLC was established, the patient was placed on a 2-month course of oral etretinate 30 mg/day. The dose was then increased to 40 mg/day (0,5 mg/kg BW) for 2 months and thereafter reduced to 30 mg daily for another 2 months. Later, the patient was placed on etretinate 20 mg/day and Re-PUVA therapy; two hours before each irradiation he received Oxsoralen 40 mg. The patient was given 29 irradiations on the PUVA 4000 (Waldmann) apparatus. The total dosage received was 119 J/cm^2. The therapy produced flattening of papules and plaques, and arrested desquamation. Some areas of papules with horny plugs on the upper limbs had disappeared. At the end of therapy the patient began to experience occasional itching and burning. After the discontinuation of the therapy, sparse fresh papules reappeared. During the treatment, the test for lipids became slightly pathologic. Other side effects included loss of hair, and dryness of the mouth and buccal mucosa. The therapy had no effect on nail lesions.

DISCUSSION

The term KLC summarizes the leading clinical characteristics of the disease (5), but it does not clarify its etiology (6) nor does it imply that KLC is an independent disease entity (3,4,6,7,9).

In the literature there is a disagreement concerning the factors causing KLC. These seem to include antimalarial and antituberculous agents (3,8) - taken also by our patient - tetanus antiserum (9), skin damage and coverage with skin grafts (6). KLC may be associated with other diseases, such as atopic dermatitis (5,10), allergic rhinitis (3), pulmonary tuberculosis (5), hepatitis A (3), chronic lymphatic leukemia (2), neurologic disorders (11), clinically manifest toxoplasmosis, or positive serologic tests for toxoplasmosis (12-14). Chronic asymptomatic course of KLC without spontaneous remissions, with the onset in adult age was characteristic of our case. The disease only rarely occurs in children (10,15,16). It usually lasts over 10 years. A 15-year history of KLC, as seen in our patient, has been reported by some other authors (17,18). As documented in the literature, KLC is only rarely associated with skin itching (9,19). Our patient experienced it after topical application of 0,1% tretinoin and on completion of Re-PUVA therapy.

Arthralgia was partly due to degenerative changes. He also had positive serologic tests for rheumatoid arthritis, which constitutes a symptom only rarely described in connection with KLC (5,18).

The course of the illness, the distribution and quality of skin lesions are similar to the description by Margolis et al. (17) and by other authors (2-8, 10, 12, 1 7-25).

Histopathological findings, including acanthosis, parakeratosis and subepidermal lichenoid lymphocytic and histiocytic infiltrate agree with most observations found in the literature (5,6,8-10,16,20,24). Another feature reported by some investigators was a perivascular infiltrate in the upper dermis (3,13,17). Infiltrate composed of eosinophils has also been found in some previous studies (3,20). Liquefaction

degeneration of the basal layer has been widely reported in the literature (5-7,10,14,17,18,22), and so have been hyperkeratotic plugs in the invaginations of the epidermis (5,7-9, 11,21,24). Electron microscopic results resemble those in lichen ruber planus (26,27). Like Dupperat et al. (23), we found no viral particles. As previously observed by some other investigators, the results of direct immunofluorescence microscopy of skin lesions partially resembled the findings characteristic of lichen ruber planus (1,6,7,9,16,24).

The treatment modalities described so far do not afford complete cure of the disease. Topical application of steroids produced no evidence of benefit, regardless of the concentration of the glucocorticoid used; other authors reported a poor or no response to treatment with local mercury preparations, iodine compounds, salicylic acid preparations and numerous systemic agents, including vitamins A and B, chloroquine sulfate, antibiotics, gold salts, griseofulvin, methotrexate, zync sulphate, glucocorticoids, sulphonamydes, dapsone and levamisole (3,14,17,18,24,25). In the literature there are no reports on successful treatment with selective phototherapy, while some authors described fair improvement after PUVA therapy (10,25); in our patient selective phototherapy and PUVA failed to produce clinical improvement. On the other hand, systemically administered etretinate afforded the expected improvement (14,21,22,25), yet it was only partial, temporary and dependent on the dose given. Fairly good response to Re-PUVA therapy was reported by Duchet et al. (12). In our case, we observed better results of this treatment modality than those yielded by administration of etretinate alone. Some keratotic plugs disappeared and the flattening of skin plaques was noticed; however, sparse fresh papules reappeared one month after the completion of the therapy.

In view of the established pathogenesis and the predominance of T4 lymphocytes in the cellular infiltrations of KLC (12,21), we think it reasonable to introduce cyclosporin A in the future treatment of KLC. It helps regulate the T4 (helper) / T8 (suppressor) ratio, and depresses the function of T4 lymphocytes (28,29). Cyclosporin A is also recommended in the management of other chronic infiltrative dermatoses (30,31,32). Our patient refused it because of the possible renal side effects.

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