

No significant diseases were present in the clinical history of our patient. She reported that, 7 months earlier, she had started intramuscular injections of thiocolchicoside (once weekly) because of a stiff neck, and that the atrophic lesion had appeared after the fourth injection performed at the same point on her right gluteus. When asked, she denied the use of topical or other systemic treatments.

We executed a punch-biopsy of lesional skin. The histopathologic findings of the specimen obtained showed hyperkeratosis, marked atrophy of the stratum malpighii, and edema of the upper dermis with homogenization of the collagen bundles (Fig. 1b). Weigert-stained sections revealed a decrease and fragmentation of elastic fibers, which were thinner than those of normal skin (Fig. 1c). As a control, we injected a placebo (physiologic saline solution) in the contralateral gluteus, without any reaction.

On the basis of these findings and clinical evidence, we diagnosed thiocolchicoside-induced skin atrophy.

Discussion

To assess the likelihood of our conclusion, we used the method suggested by Naranjo *et al.*¹ in our patient. The adverse event appeared after the administration of the suspected drug (two points), no alternative causes of the undesirable effect were present (two points), the reaction did not appear after the injection of placebo (physiologic saline solution) in the contralateral gluteus (one point), and histology confirmed the clinical suspicion (one point), giving a total score of six points. Thus, the causal correlation between thiocolchicoside administration and skin atrophy in our case can be defined as probable.

Thiocolchicoside is a semisynthetic derivative of colchicoside, which acts as an agonist for GABA-ergic (GABA, γ -aminobutyric acid) and glycinergic receptors. Orally or parenterally administered, thiocolchicoside is widely used as a muscle relaxant agent, and its pharmacologic and pharmacokinetic features make it a relatively safe drug. According to data deposited at the Italian Ministry of Health, the adverse events caused by this molecule are rare, and include dizziness (with or without hypotension) or anxiety after intramuscular administration, sleepiness, cutaneous eruption, and erythema; there are no reports of clinical problems caused by overdose.

A patient with hyper-immunoglobulin E syndrome 25 years later

We had the opportunity to control a rare case of hyper-immunoglobulin E (hyper-IgE) syndrome 25 years after the first diagnosis,¹ and to determine its association with chronic mucocutaneous candidiasis (CMC) of late onset. In the literature, there are no studies on the outcome of such patients. Only two cases have been reported.^{1,2}

A 28-year-old woman reported having suffered for many years from recurrent eczematoid dermatitis of the face, neck,

With regard to allergic reactions, only two cases of contact allergy^{2,3} and one case of photocontact allergy⁴ after the topical use of thiocolchicoside are known to date.

Skin atrophy is a possible side-effect of drugs, most frequently reported after the topical or parenteral use of steroids.⁵⁻⁸ In our case, the close correlation between the administration of thiocolchicoside and the onset of the lesion observed, together with clinical and histopathologic data, led us to conclude that the drug may have had a possible causal role in the pathogenesis of skin atrophy.

To our knowledge, there are no previous reports of skin atrophy as a result of intramuscular injection of thiocolchicoside.

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buttocks, and knees, and pustular dermatitis and abscesses all over her body. She had an elevated IgE titer (900 kU/L; normal value, 100-150 kU/L) and a neutrophil chemotactic defect. At the age of 2 years she had been reported as having hyper-IgE syndrome.³

On physical examination, she exhibited multiple pustular lesions and abscesses on the neck, abdominal region, and buttocks, and eczematoid lesions on the chest and thighs (Fig. 1). She also had recurrent thrush and fingernail dystrophy (Fig. 2). She had also suffered from secondary amenorrhea for 4 years.



Figure 1 Pustular dermatitis and abscesses on the thigh



Figure 2 Fingernail dystrophy caused by *Candida albicans* infection

Laboratory tests disclosed a normal full blood cell count and an elevated erythrocyte sedimentation rate (30 mm/h; normal value, < 15 mm/h). The high titer of total IgE (24,621 kU/L; normal value, 100–150 kU/L) was confirmed. The levels of free triiodothyronine (fT₃), free thyroxine (fT₄), and thyrotropin-stimulating hormone (TSH) were normal. The prolactin level was low at 0.10 ng/mL (normal value, 3–20 ng/mL), as were estradiol (29.0 pg/mL; normal value, > 200 pg/mL), progesterone (0.4 ng/mL; normal value, > 3 ng/mL), luteinizing hormone (LH) (0.1 IU/L; normal value, 0.6–16 IU/L), and follicle-stimulating hormone (FSH) (1.5 IU/L; normal value, 1.5–13 IU/L). Anti-ovary and antinuclear antibodies were negative. Both abdominal echography and chest radiography were normal. Nuclear magnetic resonance of the pituitary and hypothalamus showed no change. These data were consistent with a secondary hypogonadotropic amenorrhea caused by a selective LH deficiency, with a normal response of LH, FSH, prolactin, and TSH to

stimulation with LH-releasing hormone and TSH-releasing hormone.

Mycelial filaments of *Candida albicans* were found in the oral mucosal lesions and in the nail bed. *Staphylococcus aureus* from cutaneous lesions of the neck and buttocks was also detected.

CMC in association with hyper-IgE syndrome in a patient with hypogonadotropic amenorrhea was diagnosed. The patient was first treated with systemic fluconazole (200 mg/day for 15 days) and later, because of an allergic reaction to a component of fluconazole, with itraconazole (200 mg/day) for 1 month. The nail lesions improved and thrush resolved in 6 months. Unfortunately, they relapsed twice. The eczematoid lesions were treated with tacrolimus 0.1% (one application per day) and improved in 3 months.

Hyper-IgE syndrome is a rare primary immunodeficiency condition characterized by recurrent bacterial infections, a markedly raised serum IgE level with mild eosinophilia, eczematoid dermatitis, and recurrent skin abscesses frequently caused by *Staphylococcus aureus*. Patients frequently show neutrophil chemotactic defects and abnormalities of cytokine production. Nonbacterial infections also occur. Onychomycosis, thrush, disseminated pulmonary candidiasis, *Candida* endophthalmitis, and endocarditis have been reported.¹ The association of CMC with hyper-IgE syndrome is rare. Only six cases have been reported so far.^{4–7}

CMC is classified into five different types:⁸ (i) autosomal dominant form; (ii) autosomal recessive form; (iii) diffuse form; (iv) form associated with endocrinopathy; and (v) late-onset form. Because our patient presented with candidiasis when she was 25 years of age, she belongs to the fifth group. This form may be associated with thymoma or systemic lupus erythematosus, or may be the initial presentation of human immunodeficiency virus (HIV) infection; all were excluded in our patient. Instead, she was found to be suffering from hypothalamic amenorrhea without hypoparathyroidism and hypoadrenocorticalism, which are the main endocrine abnormalities of CMC associated with endocrinopathy. In addition, she had no other autoimmune abnormalities, such as pernicious anemia, vitiligo, or primary ovarian failure.

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Dermatofibrosarcoma protuberans occurring in the site of prior leishmanization

Several cases of basal cell carcinoma (BCC), squamous cell carcinoma (SCC), malignant melanoma, malignant fibrous histiocytoma (MFH), dermatofibrosarcoma protuberans (DFSP), Bednar tumor, and a dermatofibroma within vaccination scars have been described.¹ It is difficult to prove an etiologic relationship, and if such a relationship exists it may be the result of an unspecified trauma, a biologic agent, or other unknown factor. The authors report a case of DFSP occurring at a previous leishmanization site.

Case Report

On January 1998 a 29-year-old man presented with a large exophytic tumor on his right arm (Fig. 1). The patient reported that the first sign had appeared as a red papule in 1988 at the site of a previous leishmanization, which had been treated 1 year before the onset of this lesion. Examination revealed a large sessile tumor located on the lateral aspect of his right upper arm. The tumor was firm and asymptomatic. It measured 100 × 80 mm and was 70 mm high. In physical examination it had no regional lymphadenopathy, hepatomegaly, nor splenomegaly. The chest X-ray and the routine laboratory tests (e.g. liver function tests) were normal.

Histopathology of a specimen obtained from the lesion demonstrated an atrophic epidermis with highly-cellular spindle cell proliferation in the dermis arranged in a storiform pattern which demonstrated conspicuous mitoses and cytotoxic atypia (Fig. 2). The tumor extended to the subcutis, whereas there was no evidence of leishmaniasis. Immunostaining for CD34 confirmed the diagnosis of dermatofibrosarcoma protuberans.

The lesion was excised with a 30-mm margin and the area was covered with a skin graft. No evidence of tumor recurrence was observed after a 5-year follow-up period.

Discussion

The described histologic features are diagnostic for DFSP, which is categorized as a borderline fibrohistiocytic tumor and is a locally aggressive and rarely metastatic spindle cell tumor. It commonly presents clinically as a reddish-brown,

purple or flesh-colored indurated plaque. The tumor usually appears at the age of 20–50 years and it affects males more than females.^{2,3}

This is the first reported case, to the authors' knowledge, of DFSP occurring in the site of leishmanization. Inoculation of virulent leishmania major to the skin of the deltoid region, producing a lesion and therefore inducing a protective immunity to control cutaneous leishmaniasis, was extensively used during the Iran–Iraq war. The cause of DFSP remains



Figure 1 Large exophytic tumor on the lateral aspect of the patient's arm (January 1998)