Primary Cutaneous CD4+ Small- to Medium-Sized Pleomorphic T-Cell Lymphoma: Report of a Case With Spontaneous Resolution

To the Editor:

Primary cutaneous CD4+ small- to medium-sized pleomorphic T-cell lymphoma is included as a provisional entity in the group of primary cutaneous peripheral T-cell lymphomas, both in the latest WHO classification of tumors of hematopoietic and lymphoid tissues and in the WHO-EORTC classification for cutaneous lymphomas.1,2 This lymphoma is defined by a predominance of CD4+ small- to medium-sized pleomorphic T cells, with no prior history of macules or plaques that would suggest mycosis fungoides.1,2

A 35-year-old man visited our department with an asymptomatic lesion on his left cheek; the lesion had appeared 4 weeks earlier and had grown rapidly. The only relevant information in the patient’s past history was that he had taken allopurinol for 3 months to treat asymptomatic hyperuricemia. He had interrupted this medication 3 days before visiting our department. Physical examination revealed an oval, dome-shaped erythematous tumor measuring 3 x 4 cm on the left cheek. The tumor had well-defined borders and a shiny surface and was indurated on palpation (Fig. 1A).

A biopsy of the lesion was taken for histopathology study. The low-magnification view showed that the epidermis was not involved and revealed a dense cellular infiltrate occupying the entire thickness of the dermis and reaching the subcutaneous tissue. The neoplastic infiltrate consisted predominantly of small- to medium-sized lymphocytes with moderate pleomorphism and mild atypia. Numerous histiocytes were also found among the lymphocytes (Fig. 2). Immunohistochemistry showed the cells to be strongly positive for CD3, CD4, and CD5. Furthermore, staining was focally positive for CD8, CD20, and CD68, but negative for CD7 and CD30. The analysis of T-cell clonality using PCR for the T-cell receptor gamma (TCRG) gene showed monoclonal rearrangement. On the basis of these data we established a diagnosis of primary cutaneous CD4+ small- to medium-sized pleomorphic T-cell lymphoma.

Further tests included an analysis of lymphocyte populations and immunoglobulin levels, computed tomography of the neck, thorax, abdomen, and pelvis, and bone-marrow biopsy. All results were normal or negative. The lesion underwent a rapid spontaneous reduction in size and was completely flat after 6 weeks of follow-up (Fig. 1B). The area of residual hyperpigmentation was not infiltrated or hard to the touch. The patient subsequently underwent local radiation therapy using a 6-MeV electron beam, with a total dose of 4000 cGy administered at a dosage of 200 cGy per day. He remained asymptomatic at 7 months (Fig. 3).

Primary cutaneous CD4+ small- to medium-sized pleomorphic T-cell lymphoma is a rare disease and accounts for just 2% of all primary cutaneous lymphomas.2 Clinical pre-
sentation is usually as a solitary plaque or tumor, typically located on the face, neck, or upper torso; it is asymptomatic and fast-growing.\textsuperscript{3,4,5} Spontaneous total remission of the lesions, as occurred with our patient, has been previously reported in only 1 case.\textsuperscript{5}

Histology reveals dense nodular or diffuse dermal infiltrates that tend to infiltrate the subcutaneous tissue. Focal epidermotropism is a possible finding and means that a diagnosis of mycosis fungoides should always be considered.\textsuperscript{1,4,6,7} By definition, there is a predominance of CD4+ small- to medium-sized pleomorphic lymphocytes, although up to 30% of large pleomorphic lymphocytes may be found. Cases where a higher percentage of large cells is found should be classified as peripheral T-cell lymphoma, not otherwise specified. Mixed inflammatory infiltrates have also been reported, consisting of histiocytes, B cells, plasma cells, and, in some cases, CD8+ T cells and eosinophils.\textsuperscript{5,8,9} TCRG analysis shows monoclonal rearrangement in 60% to 70% of cases.

The differential diagnosis should principally include benign lymphoid proliferations (T-cell pseudolymphoma, pseudolymphomatous folliculitis, papules, nodules, and solitary lymphoid tumors) and mycosis fungoides in its unilaterial presentation is usually as a solitary plaque or tumor, typically located on the face, neck, or upper torso; it is asymptomatic and fast-growing.\textsuperscript{3,4,5} Spontaneous total remission of the lesions, as occurred with our patient, has been previously reported in only 1 case.\textsuperscript{5}

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Esomeprazole-Induced Subacute Cutaneous Lupus Erythematosus

Lupus eritematoso cutáneo subagudo inducido por esomeprazol

To the Editor:

We report the case of a 74-year-old woman with a history of hypertension, diabetes mellitus, dyslipidemia, spondyloarthritis, and idiopathic thrombocytopenic purpura for which she had undergone splenectomy 5 years previously. She was being followed up by her rheumatologist for joint pain of inflammatory origin with low titers of rheumatoid factor and was taking lorazepam, ranitidine, domperidone, indapamide, AM3, and ursodeoxycholic acid. She attended our clinic with a pruritic disorder that had begun a week earlier and took the form of well-defined discretely desquamative erythematous papules on her back and, to a lesser extent, on her chest, thighs, and proximal upper arms. She had no blisters or mucosal lesions. These signs first appeared during winter, and the patient reported no previous sun exposure. Of interest, she reported starting esomeprazole during winter, and the patient reported no previous sun exposure. Of interest, she reported starting esomeprazole and a vitamin complex containing B1, B6, and B12 3 weeks before the lesions first appeared. A biopsy specimen of one of the lesions was obtained, and the patient was prescribed a vitamin complex concomitantly with esomeprazole; however, this medication seems a highly unlikely culprit, since there have been no previous reports of drug-induced SCLE with positive anti-SSA/Ro antibody titers, but not with positive antihistone antibody titers. In some cases, these titers become negative once the culprit agent is withdrawn.

In the case we present, it is striking that anti-SSA/Ro and anti-SSB/La antibody titers were previously positive and that this finding was maintained after onset of the skin symptoms. Four of the 8 previously reported cases of SCLE induced by proton pump inhibitors presented positive antinuclear antibody titers before the onset of cutaneous symptoms; however, it is unknown whether anti-SSA/Ro or anti-SSB/La antibody titers were positive. No analytical results were available for the remaining 4 patients (Table 1).

The results of a complete blood count and routine biochemistry were unremarkable. The immunology workup revealed positive titers for antinuclear antibody (1/160), anti-SSA/Ro antibody, and anti-SSB/La antibody. These results had also been positive in laboratory studies performed 2 years previously in the rheumatology department.

Based on a suspected diagnosis of SCLE induced or exacerbated by esomeprazole, treatment with a topical corticosteroid was continued and the culprit medication was withdrawn. The lesions had completely resolved 8 weeks after the interruption of esomeprazole.

SCLE is a well-defined subtype of lupus erythematosus characterized by annular or psoriasiform lesions, limited systemic involvement, and the presence of circulating anti-SSA/Ro antibody. An association has been described between SCLE and various drugs, including thiazides, statins, calcium channel antagonists, phenytoin, griseofulvin, tumor necrosis factor antagonists, terbinafine, and, recently, proton pump inhibitors such as omeprazole, lansoprazole, and pantoprazole. Esomeprazole is the S enantiomer of omeprazole and is used to treat gastroesophageal reflux disease. It came onto the market in Spain in 2002.

Unlike drug-induced systemic lupus erythematosus, which usually involves positive antihistone antibody titers, drug-induced SCLE is generally associated with positive anti-SSA/Ro antibody titers, but not with positive antihistone antibody titers. In some cases, these titers become negative once the culprit agent is withdrawn.

Our patient was taking a vitamin complex concomitantly with esomeprazole; however, this medication seems a highly unlikely culprit, since there have been no previous reports of drug-induced SCLE with positive anti-SSA/Ro antibody titers.