Letters to the Editor

Primary cutaneous large B-cell lymphoma of the legs in a patient with primary Sjögren's syndrome

Sirs,

Sjögren's syndrome (SS) is a chronic autoimmune disease characterized by lymphocityc infiltration of the salivary and lacrimal glands (1). The risk of lymphoma in patients with SS is 44 times greater than in a normal population. Lymphomas complicating SS usually are low grade B cell non-Hodgkin's lymphoma (NHL) and arise frequently in mucosal extranodal sites (2-4). Cutaneous T cell lymphoma and malignant angioendotheliomatosis have also been described in secondary Sjögren syndrome (5, 6). In a multicentre European study (3) of 33 patients with SS that developed malignant lymphoma and in a extensive study of 16 patients with lymphoma occurring in patients with underlying SS (2), the rare variant of cutaneous B-cell lymphoma of the legs (4) was not described nor it was in an extensive literature search (MEDLINE 1966-2002 descriptors [lymphoma], [Sjögren's syndrome],[lymphatic proliferation]).

We report a case of a patient with primary Sjögren's syndrome that developed a B cell NHL in the skin and that clinical and histological criterion allowed the diagnosis of primary cutaneous large B-cell lymphoma of the legs. To our knowledge, the coincidence of these two diseases has not been previously reported.

A 63-yr-old woman was admitted to our hospital with a single tumor confined to the lower part of the right leg of 2 months evolution. Because of subjective dryness of the eyes and the mouth, Sjögren's syndrome was suspected 4 years before. Schirmer's test (2 mm in 5 minutes in both eyes), and positive (+++) rose Bengal dye test confirmed objectively xerophthalmia. Salivary scintigraphy showed an abnormal (grade IV) salivary gland. Immunological studies revealed a positive antinuclear antibody (1/1280, in a homogeneous pattern) and anti-SSA/SSB antibodies. Rheumatoid factor, cryoglobulins and serological syphilis test were negative; C3 and C4 complement levels were within normal ranges (C3 128 mg/dl, normal value: 85 to 170; C4 31 mg/dl, normal value 12 to 52). A salivary gland biopsy showed a lymphocytic infiltration, which consists in a myoepithelial sialadenitis characteristic of SS. Immunohistochemical staining, did not show monoclonality. Therefore the patient fulfilled the new American-European classification criteria (7).

One year after the diagnosis of SS, the patient presented with a severe chronic sensory neuropathy diagnosed by means of electrophysiologic studies. She has been treated during the last 6 months with monthly pulses of immunoglobulins (30 g daily for 5 days, every month), without significative improvement. A sural nerve biopsy showed sparse inflammatory lymphocytic infiltrates without evidence of vasculitis. Two months ago the patient presented with a non-inflammatory nodular lesion on the inner face of right lower leg. On general examination, there was no arthritis or lymphadenopathy. Laboratory analysis on admission revealed a normocytic anemia, polyclonal hypergammaglobulinemia and a high (>100 mm/h) ESR, electrolytes, liver and muscle enzymes including LDH were normal. Virus serology (EBV, HIV, CMV, HCV and HBsAg), timidin-kinase and β-2-microglobulin serum levels were negative or normal. A MR of the leg showed soft tissue tumor that involves skin, vasculature and muscular fascia. A CT-guided fine needle muscle punction showed proliferative large B cells (CD20) that suggest lymphoma, and a cutaneous biopsy showed an infiltration of the dermis by large cells of lymphoid apparence. Immunohistochemical staining showed a neoplastic B cell population (CD 20, CD 21, CD 22, MB1) and strongly express bcl-2 protein and a high Ki 67. Staging procedures, that include thoracic and abdominal CT-scan and bone marrow biopsy were negative. The patient was diagnosed of large B-cell lymphoma of the legs and treatment with 6 cycles of standard chemotherapy (cyclophosphamide [750 mg/m^2], hydroxydaunomycin [75 mg/m^2], oncovin [1.4 mg/m^2] and prednisone [60 mg/m^2, 5 days]) was initiated followed by 30 Gy involved field radiotherapy with complete remission, that remains for two years.

Primary cutaneous large B-cell lymphoma (LBCL) of the legs represents a distinct clinicopathologic entity that mainly affects elderly patients, mainly women, and has been included as a new type of cutaneous B-cell lymphoma with an intermediate prognosis in the recently constituted EORTC classification for primary cutaneous lymphoma (4).

Expression of bcl-2 protein is an important immunohistochemical finding characteristic of cutaneous LBCL of the legs. Moreover, expression of bcl-2 protein has been reported in lymphocytes forming lymphoepitelial lesions of the salivary glands in patients with SS, and may result as a consequence of t(14;18) chromosomal translocation that has been reported in non Hodgkin's lymphoma arising in SS patients (8, 9).

Coexistence in the same patient of primary Sjögren's syndrome and primary cutaneous large B-cell lymphoma of the legs could be explained by a similar mechanism, it means an overexpression of bcl-2 protein that allows the cell to escape a apoptoic cell death resulting into a monoclonal proliferation. The present case suggest that dysregulation in apoptosis could play a role in the multistep development of lymphoproliferative disorders in patients with SS.

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