Sclerosing lymphocytic lobulitis of the breast associated with autoimmune thyroiditis

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Abstract

Background: Sclerosing lymphocytic lobulitis (SLL) of the breast is a rare benign mastopathy, usually associated with diabetes mellitus type 1 or, very rarely, with other autoimmune diseases. The authors describe a patient in whom this condition is associated with autoimmune thyroiditis.

Case report: A 32 year-old woman, with chronic migraine and no history of diabetes or breast cancer, complaining of severe headaches, palpitations, irritability and arterial hypertension. Hyperthyroidism and diffuse goiter due to autoimmune thyroiditis were diagnosed, with positive anti-thyroperoxidase and anti--thyroglobulin antibodies. A 3 cm sub-areolar mass was noted in the right breast, diffuse, firm and slightly painful, with no lymph node enlargement. Several fine-needle aspiration cytologies were negative for malignant cells; core biopsy showed periductal, vascular and lobular phenotypically normal lymphocytic infiltration with severe stromal *fibrosclerosis*. The patient was prescribed thiamazole, which was withdrawn after progression to hypothyroidism. Attempt to treat the SLL with oral corticoid therapy was not successful. About 1.5 years after the diagnosis of autoimmune thyroiditis, mastopathy remains stable with few symptoms without specific treatment.

Discussion: The etiology of breast SLL is unknown, but its strong association with autoimmune diseases and increased expression of HLA-DR in affected epithelial cells suggests that an immune reaction to components of the mammary stroma can lead to fibro-inflammatory changes. To date, there is no evidence of neoplastic potential although data are scarce. It is unknown whether treatment of the underlying autoimmune disease may influence the natural history of this disease. In the absence of targeted therapy, watchful waiting seems to be the most appropriate course of action.

Key words: lymphocytic lobulitis; diabetic mastopathy; autoimmune thyroiditis.

INTRODUCTION

The breast is a complex structure that can be affected by various pathological processes which are not always malignant, but which always have great significance for the patient. The group of proliferative epithelial alterations is particularly heterogeneous, including entities as distinct as fibroadenomas (which have almost zero malignancy potential) and atypical hyperplasia (the presence of which increases the risk of invasive carcinoma by 3 to 6 times). A peculiar lesion was described in various series of patients with type 1 diabetes mellitus – so-called diabetic mastopathy, which generally takes the form of one or more mammary nodules, sometimes painful, and which is histologically manifested as a lobular and vascular lymphocytic inflammatory infiltrate associated with proliferation and fibrosis of the periductal matrix.[1,2] Recently, similar alterations have been identified in women with other autoimmune pathologies, which has led to progressive substitution of this term with the more generic term "sclerosing lymphocytic lobulitis".[3-6] This entity is very rare, and its neoplastic potential is not yet totally clear.[7,8] Due to its form of clinical presentation, it is therefore essential to rule out malignant disease.

The authors describe a case in which this condition is associated with autoimmune thyroiditis.

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CASE REPORT

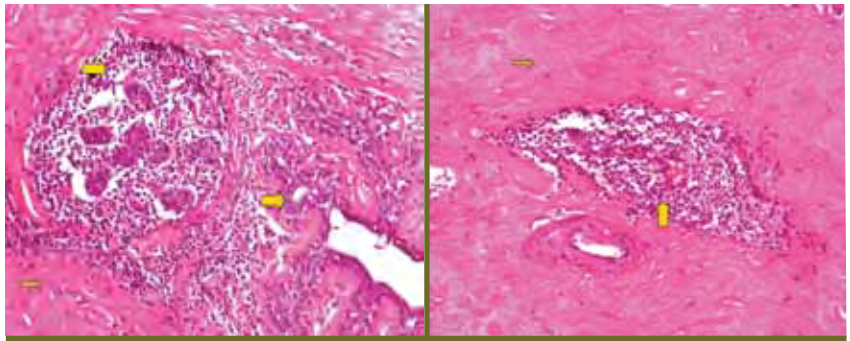
Female patient, aged 32 years on the date of presentation, Caucasian, a nurse. Relevant aspects of the medical history include diagnoses of epidermolysis bullosa in infancy, and chronic premenstrual migraines, controlled with oral antiinflammatories where necessary. The patient has no personal history of diabetes or breast neoplasm; the patient's mother suffered from type 2 diabetes mellitus and hypothyroidism.

At the end of 2007, she presented sub-acute clini-

cal symptoms, evolving for around six weeks and characterized by holocranial headaches of greater intensity and frequency than normal, associated with the episodic sensation of palpitations and irritability. Objective examination showed arterial hypertension, without signs of intracranial hypertension, focal neurological deficits, or other relevant alterations. The study carried out at that time showed hyperthyroidism (analytically) and diffuse goiter (by scintigraphy; no aspiration cytology of the thyroid was performed), leading to a diagnosis of autoimmune thyroiditis with positive anti-thyroid peroxidase and anti-thyroglobulin antibodies.

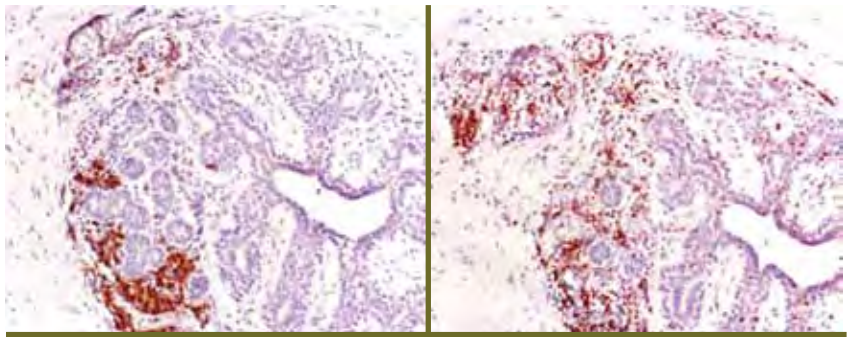
Around 1 month after the start of the initial complaints, the patient noticed subareolar tumefaction of the right breast of around 3 cm it its widest point, with imprecise, poorly-defined edges, firm, and slightly painful on palpation. She did not present adenopathies, weight loss (weight stable at 51kg) or any other sign suggestive of consumptive syndrome, but reported that she felt limited in her daily physical activity due to discomfort in the right breast. The lesion mammographic pattern showed an increased density by predominance of fibroglandular stroma, with homogenous distribution, without distortions or microcalcifications. Echography showed an area of poorly-defined focal hypoechogenicity of around 26 mm at its widest point and a predominantly ductal pattern in the right breast; the left breast had small nodules suggestive of fibroadenomas. The right breast nodule was submitted to two fine-needle aspiration cytologies: Both were negative for malignant cells, and revealed only some monocytes and lymphocytes with benign appearance.

Referred by our Internal Medical department, she underwent complete serum immunology study by flow cytometry of a third aspiration cytology of the breast, and incision biopsy of the lesion. The first exam was positive only for antinuclear autoantibodies (ANA, in titers of 1/640 with mottled pattern) and



Lobular and periductal lymphocytic infiltrate (on the left, large arrows) and vascular (on the right; large arrow); sclerosis of the mammary stroma (small arrows) (HE x100).

FIG. 1



Characterization and distribution of the lymphocytic infiltrate: on the left, immunoreactivity for CD20 (B lymphocytes) and on the right, immunoreactivity for CD3 (T lymphocytes) (x100).

FIG. 2

microsomal antibodies (anti-TPO, in 298 UI/mL); there was no increase in proteins in the acute phase, hypergammaglobulinaemia, complement factor consumption, or positivity for other autoantibodies, namely, rheumatoid factor, anti-dsDNA, anti-neutrophil cytoplasmic antibodies, anti-SS-A and anti-SS-B. The second exam did not identify monoclonality. The third exam, besides ruling out malignancy, showed marked fibrosclerosis of the mammary stroma and intralobular lymphocytic inflammatory infiltrate (lobulitis) *(Fig. 1 and 2)*.

The patient began thyroid therapy with thiamazole, which was suspended a few months later due to evolution to hypothyroidism. In order to reduce the discomfort in the breast and/or the dimensions of the tumor, deflazacort was also initiated in a prednisone-equivalent dose of 1 mg/Kg/day (i.e. 45 mg/day). No clinical or imaging response was observed

after 4 weeks of treatment, therefore corticotherapy was gradually reduced until complete suspension; no relevant secondary effects were noted. Around 1.5 years after the diagnosis of autoimmune thyroiditis and only under hormonal replacement therapy for hypothyroidism did the mastitis remain stable with few symptoms.

DISCUSSION

The definition of a new nosological entity involves a period of "maturation" during which a specific clinical-pathological profile is built up, culminating in the individualization of a "disease". SLL of the breast appears to go through this process.

In effect, sporadic reports are emerging that describe the histological changes that are traditionally termed diabetic mastopathy in patients with other pathologies, such as Graves' disease, Hashimoto's thyroiditis, Sjögren's syndrome and rheumatoid arthritis.[3-6] Although the etiology of these legions has not yet been clarified, data are accumulating that suggest an immunological base. Not only is the association with autoimmune diseases evident, but an increase in HLA-DR3, -DR4 and -DR5 expression has also been observed in the epithelial cells affected, similar to that found in autoimmune lymphoepithelial lesions affecting other glands (as in Sjögren's syndrome, for example). It has been suggested that an abnormal immunological reaction to components of the mammary stroma can lead to fibro inflammatory alterations.[3,4]

The lack of data on the natural history of this rare pathology does not enable the risk of neoplastic transformation to be safely excluded, although there is no current evidence to support this.[7,8] Therefore, faced with a mammary nodule, it is essential to rule out malignant disease. Thus, it is not known whether the treatment of underlying autoimmune disease, or any other type of treatment (notably anti-inflammatory or immunosuppressant) could positively influence the evolution of these lesions. In the absence of targeted therapy, watchful waiting seems to be the most appropriate course of action. ■

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