Lymphocytic mastitis: Review of three cases

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Resumen
La mastitis linfocítica, también conocida como mastopatía diabética o lobulitis esclerosante linfocítica, es una inflamación fibrótica de la mama. Se presenta más frecuentemente como complicación de la diabetes insulino-requiriente de larga evolución, aunque se ha visto su relación con algunas enfermedades autoinmunes y endócrinas, como así también en paciente sin ninguna de estas comorbilidades. Su importancia radica en la similitud clínico-radiológica que esta patología tiene con el cáncer de mama. El propósito de este trabajo es describir los hallazgos clínicos, radiológicos y anatomopatológicos de tres casos confirmados de mastitis linfocítica, uno de ellos en paciente sano.

Palabras clave: Mastitis, linfocítica, ecografía, mamografía.

Abstract
Lymphocytic mastitis, also known as diabetic mastopathy or sclerosing lymphocytic lobulitis, is a fibrotic inflammation of the breast. It is often a complication of long-standing insulin-dependent diabetes, although it has been found in patients with autoimmune and endocrine diseases, as well as in patients without any of these conditions. It is important to know the characteristics of this pathology since it has many clinical and radiological similarities with breast cancer. The purpose of this paper is to describe the clinical, radiological and pathological findings in three confirmed cases of lymphocytic mastitis, one of which is a healthy patient.

Key words: Mastitis, lymphocytic, ultrasound, mammography.

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Case review
The first case was a 33-year-old female patient without history of diabetes or autoimmune diseases. She had palpable tumors in both breasts. They were hard, unmovable and not painful; one was located approximately at the 12 o’clock position on the anterior third of the right breast, and the other was located at the 3 o’clock position on the anterior third of the left breast. After performing a bilateral mammography the area of interest was compressed, which revealed heterogeneous fibroglandular tissue without evidence of masses, architectural distortion or suspicion of calcifications (Figure 1). However, ultrasound (US) showed hypoechoic, solid and irregular nodular lesions with spiculated edges in the region of the palpable mass and posterior acoustic shadowing; at the sites of clinical findings. The masses measured 3.75 x 2.75 cm (right breast) and 3.35 x 1.74 cm (left breast) (Figure 2). Lesions were characterized as Bi-Rads 4C (according to the classification system of the American College of Radiology) and an excisional biopsy was performed. The definite diagnosis was Lymphocytic Mastitis (LM), without evidence of malignancy (Figure 3). Until today (7 years after the initial diagnosis) there are no signs of recurrence.

The second case was a 30-year-old patient with Type 1 diabetes, diagnosed in childhood with no known chronic complications. The patient made a consultation because she had a palpable nodule in the right breast, which was unmovable, hard and not painful, located at the 9 o’clock position, 2 cm from the nipple. Bilateral mammography and localized compression was performed showing heterogeneous fibro-glandular tissue without evidence of focal lesion, architectural distortion or suspicion of calcifications (Figure 4). Ultrasound results in this case also coincided with clinical findings; there was a hypoechoic, solid and irregular nodular lesion with undefined edges and with posterior acoustic shadowing. The mass measured 3 x 2.5 cm (Figure 5). It was characterized as Bi-Rads 4C and an excisional biopsy was performed. The definite diagnosis was LM. Three years after the initial diagnosis and treatment there are no signs of recurrence.

The third case was a 63-year-old woman with Type 2 diabetes and hypothyroidism of autoimmune origin, treated with oral hypoglycemic drugs and levothyroxine. She made a consultation because she had a palpable nodule in the subareolar region of the left breast, associated with inverted nipple. It was hard, unmovable and slightly painful. A bilateral mammography was performed followed by localized compression, which showed predominantly fat tissue, silicone gel prosthesis without signs of extracapsular implant rupture and an irregular mass with undefined edges in the retroalveolar region associated with inverted nipple (Figure 6). Ultrasound revealed the same as the bilateral mammography: a hypoechoic, solid, irregular nodule with acoustic shadowing in the clinically nodule-positive region, measuring around 2.8 x 1.2 cm (Figure 6). Lesions were characterized as Bi-Rads 4C and an excisional biopsy was performed. The definite diagnosis was LM, without evidence of malignancy.

Discussion
LM, also known as diabetic mastopathy or sclerosing lymphocytic lobulitis (1), is a fibrotic inflammation of the breast as a complication of long-lasting insulin-dependent diabetes; however, it can also be associated with autoimmune diseases, endocrine diseases and it can even be found in patients without such conditions, which is the case of our first patient.

It was described for the first time by Soler and Khardori in 1984, but it was not given a name until 1987 by Byrd et al. (2). The etiology of this disease is unknown (1, 2). There are different theories proposed, including the possibility of being an inflammatory or immune reaction to exogenous insulin administration (2). Another theory includes an altered extracellular matrix, produced by hyperglycemia. High levels of glycemia, through a process of glycosylation, will stimulate growth factors, which will induce the production of collagen resistant to degradation. This collagen works as an antigen stimulating a secondary immune response with proliferation of B-lymphocytes and a production of antibodies. The presence of macrophages would generate an increase in the quantity of growth factors, with a subsequent greater production of collagen (3). This explains the histologic findings of this pathology, characterized by variable degrees of
**Figure 1. Digital Mammography.**

A) Craniocaudal view (CC). B) Mediolateral oblique view (MLO): heterogeneous fibroglandular tissue, without evidence of masses, architectural distortion or calcifications. The triangle shows the palpable region of the right breast, which is seen better in MLO view. The triangle of the left breast is not present in this image. C) Focalized compression: compression of the area without evidence of malignancy.

**Figure 2. Gray-scale bilateral ultrasound.**

A) Right breast. B) Left breast: Over the clinically node-positive region, there are hypoechoic, irregular, solid nodules with posterior acoustic shadowing.
Figure 3. Anatomical pathology.
A) Hematoxylin and eosin stain (H&E), 100x: perilobular lymphocytic infiltrate with extensive fibrosis (arrow). B) H&E, 100x: periductal lymphocytic infiltration with keloid fibrosis (arrow). C) H&E, 100x: perivascular lymphocytic infiltrate with the presence of epithelioid and keloid fibrosis (arrow).

Figure 4. Digital Mammography.
Craniocaudal view (CC): heterogeneous fibroglandular tissue, without evidence of masses, architectural distortion or calcifications.

Figure 5. Gray-scale bilateral ultrasound of the right breast.
Over the clinically node-positive region, there are hypoechoic, irregular, solid nodules with posterior acoustic shadowing.
of Type B lymphocytic infiltration at the perilobular level (lobulitis), at the periductal level (ductitis) and at the perivascular level (vasculitis), associated with a great amount of keloid fibrous tissue (2-4). There is also a presence of epithelioid histiocytes, mainly in diabetic patients (4, 5).

Even though we have reported a case of a postmenopausal woman, this condition is more common in premenopausal women (1, 3) and the mean age of appearance is 46.6 ± 15.6 years, according to the paper published by Pereira MA et al. in which 31 patients were studied (4). There are also reports of some cases in men (2, 4).

Clinical findings of these patients are characterized by hard and firm nodules when palpated, generally not painful and of variable sizes. They can be unique or multiple, uni or bilateral, they can appear synchronically or metacronically and they may simulate carcinomas (2-4). They are located anywhere in the breast, but there is predominance in the subareolar region (4,5). These nodules are not accompanied by inflammatory signs, as it occurs in other pathologies of the breasts (4).

Imaging characteristics are not specific (4). In most publications, a frequent finding is the asymmetry. They also describe nodular opacities and even the mammogram can be normal, as was the case in two of our patients. Generally, ultrasound shows a hypoechoic, irregular, solid nodule with significant posterior acoustic shadowing due to the fibrosis that characterizes this pathology (1, 2, 4). Some reports indicate that both bilateral mammography and ultrasound are normal. Even though we do not have breast Magnetic Resonance Imaging (MRI), some research works mention that these lesions can have intense enhancement with gadolinium and non-conclusive captation kinetics, velocity and wash-out curves; therefore, this method does not help to characterize these lesions as benign in all cases (1, 2, 4).

Clinical and imaging findings can simulate a malignant breast pathology and, therefore, most cases need histopathologic confirmation to reach a definite diagnosis. Generally, the steps to take with these patients depend on the amount of lesions. If there is a unique lesion, an excisional biopsy could be an option. In patients with multiple or recurrent lesions,
ultrasound-guided biopsies could be an option and once a diagnosis of benignity is reached, a follow-up examination can be established (3-4).

It is estimated that there is a high degree of recurrence (approximately 32%) and there is no evidence to support that LM predisposes breast cancer development (5).

Several differential diagnoses are proposed, mainly with breast carcinoma. They also include plasma cell mastitis, granulomatous mastitis, non-Hodgkin lymphoma, fibrotic tissue, trauma-type lesions, fibrocystic alterations, polyarteritis nodosa, Rosai-Dorfman disease, and in the case of men, simple gynecomastia (4, 5).

**Conclusion**

LM is a benign disease of the breast occurring most frequently in premenopausal women, generally as a complication of long-standing insulin-dependent diabetes, as well as autoimmune, endocrine diseases and healthy subjects. Its etiology is still unknown; however, the theory of an autoimmune origin is well supported. Clinically, it appears as palpable nodules, which are often firm and slightly painful. The most frequent mammographic finding is asymmetry; however, some nodular opacities can be found and in some cases, the mammography can have negative results. Ultrasound is the most useful imaging technique for this pathology, since it reveals the presence of solid, irregular nodules with posterior acoustic shadowing, similar to malignant lesions. Based on ultrasound findings, it will be necessary to perform a biopsy for a definite diagnosis, which could be an excisional biopsy or an ultrasound-guided biopsy.

**Bibliography**