ORIGINAL REPORT

Diabetic mastopathy: Clinical presentation, imaging and histologic findings, and treatment

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KEYWORDS
Diabetic mastopathy; Clinical presentation; Imaging; Histology; Treatment

Abstract
Objective: Diabetic mastopathy is an uncommon complication of longstanding diabetes mellitus that must be considered in the differential diagnosis with breast cancer. We report the clinical presentation and course, the imaging and histologic findings, and the treatment of the patients diagnosed with diabetic mastopathy at our hospital.

Material and methods: In an 11-year period, we studied six insulin-dependent diabetic patients (five women and one man) with diabetic mastopathy. Imaging studies included mammography, ultrasonography, and magnetic resonance imaging. A definitive histologic diagnosis was reached after core needle or surgical biopsy in all cases. Fine-needle aspiration cytology was not used in any of the cases. The mean follow-up period was 7 years.

Results: The most common clinical presentation was a palpable nodule (67%). The imaging findings were (a) at mammography: asymmetrical density (50%), (b) at ultrasonography: a solid, hypoechoic nodule measuring between 1 cm and 5 cm in diameter, with ill-defined margins, acoustic shadowing, and no Doppler signal (50%), and (c) at MRI: enhancement after the administration of contrast media (66%). The most common histologic finding was lymphocytic mastitis in the initial stages (83%). All patients underwent surgical treatment (100%).

Conclusions: Diabetic mastopathy is an uncommon disease that should be included in the differential diagnosis with breast cancer in diabetic patients. The diagnosis is complex because it requires knowledge of the patient’s history, clinical presentation, and the imaging and histologic findings; conservative surgery is the treatment of choice because the condition does not respond to medical treatment.

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Mastopatía diabética: clínica, hallazgos radiológicos y anatomopatológicos y tratamiento

Resumen
Objetivo: La mastopatía diabética (MD) es una complicación infrecuente de la diabetes mellitus de larga evolución, que plantea el diagnóstico diferencial con el cáncer de mama. Se estudian la presentación clínica y evolución de la MD, los hallazgos radiológicos, la histología y el tratamiento en los pacientes diagnosticados en nuestro hospital.

Material y métodos: Se incluyen 6 pacientes diabéticos insulinodependientes con MD, 5 mujeres y un varón, diagnosticados en un periodo de 11 años. El estudio radiológico se realiza con mamografía, ecografía y resonancia magnética (RM). Se obtiene en todos los casos un diagnóstico anatomopatológico definitivo con biopsia con aguja gruesa o quirúrgica. No se recurre en ningún caso a punción-aspiración con aguja fina. Se lleva a cabo un seguimiento clínico en un periodo medio de 7 años.

Resultados: La presentación clínica más frecuente es el nódulo palpable (67%). Los hallazgos radiológicos son: en la mamografía, la asimetría de densidad (50%), en la ecografía un nódulo/masa sólida, hipoecoico, de 1-5 cm, mal definido, con sombra acústica y sin señal Doppler (50%) y en la RM el realce tras la administración de contraste (66%). El hallazgo anatomopatológico más frecuente es la mastitis linfocítica en estadios iniciales (83%). Se realiza un tratamiento quirúrgico en todos los pacientes (100%).

Conclusiones: La MD es una enfermedad poco frecuente que plantea el diagnóstico diferencial con el cáncer de mama. Su diagnóstico es complejo, pues requiere el conocimiento de los antecedentes personales del paciente, la clínica, la exploración física y los hallazgos radiológicos e histológicos. El tratamiento quirúrgico conservador es de elección, porque no se obtiene respuesta con el tratamiento médico.

Introduction
Diabetic mastopathy (DM) is an uncommon complication of longstanding insulin-dependent diabetes mellitus (IDDM). Its etiology is unknown, though the most accepted theory is that this condition results from an immune reaction. The clinical presentation and the imaging findings suggest that DM must be considered in the differential diagnosis with breast cancer. For this reason, thorough understanding of the condition is essential.

This paper discusses the clinical presentation, imaging findings, histopathologic findings, and treatment of patients who were diagnosed with DM in our hospital.

Materials and methods
Six patients were diagnosed with DM, and treated in our hospital over an 11-year period (from January 1999 to December 2009).

For the study, all patients underwent mammography; in one patient, the mammography was performed in other institution. The mammography unit in our hospital is an Alpha RT Instrumentarium Imaging (Helsinki, Finland).

All patients underwent breast ultrasound, except for one patient, who was incidentally diagnosed with DM after undergoing plastic surgery. The ultrasound system used was an ESAOTE Technos MPX (Genoa, Italy) with a 7.5–10 MHz linear probe.

Magnetic resonance imaging (MRI) was performed on three patients with a Philips Achieva Intera 1.5 T scanner (Best, Holland). The study protocol included two T2-weighted sequences (coronal and axial planes) and one volumetric T1-weighted gradient-echo sequence with 0.8 mm × 0.8 mm × 2 mm spatial resolution with the acquisition of one sequence with no contrast agent and five sequences after contrast administration (Gd-DTPA, 1 mmol/kg at 3 ml/s) followed by a saline solution bolus (15 ml). Image post-processing involved image parametric analysis, multiplanar reconstructions (MPR), and maximum intensity projections (MIP).

Histopathologic diagnosis of all patients was obtained. Three of them underwent ultrasound-guided core needle (14G) biopsy (UGCB) because of a suspected malignant lesion. The remaining three patients underwent surgical biopsy because of lack of clinical–radiological correlation (in one female patient), breast reduction mammoplasty, and suspicion of a breast abscess (in the only male patient).

Hematoxylin–eosin stain was used for the histologic diagnosis (Fig. 1).

The surgical treatment was performed under general anesthesia.

Results
Six patients with IDDM (five females and one male) were diagnosed with DM, and treated in our hospital from January 1999 to December 2009. Table 1 shows the clinical imaging findings in these patients. Mean age at DM diagnosis was 38 years (age range: 28–58 years), and mean time for the development of diabetes was 10 years and 8 months.
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Figure 1  Histological analysis of DM using hematoxylin-eosin stain. (A) Early stage of the disease with significant lobule infiltration by polyclonal mature B lymphocytes, which tend to penetrate the epithelium. (B) Advanced stage of the disease with sclerosis and involution of lobules, as well as reduction of the lymphocyte infiltrate. The lobules become surrounded by a dense collagenous stroma.

(range of diabetes development: 2–21 years). Four patients presented with complications associated with diabetes: retinopathy (two patients), nephropathy (one patient), and cerebral infarction (one patient). A female patient suffered from hyperosmolar coma and multiple organ failure, which finally led her to death.

The most common clinical presentation is a palpable, painful, hard nodule (67%). The only male patient in our series also presented with inflammatory signs and purulent nipple discharge.

The most relevant imaging findings in these patients are shown in Figs. 2–5, which correspond to patients 1, 3, 4, and 6 in Table 1, respectively.

The most common mammographic finding is density asymmetry (50%) (Fig. 3A). Mammographies in the other three patients were normal, though the youngest female patient presented with a high-density pattern.

The most common US finding (50%) is a hypoechoic solid nodule-mass that is variable in size (1–5 cm), with ill-defined margins, posterior acoustic shadowing, and no color Doppler signal inside (Fig. 2B). The only male patient in the study presented with a complex cystic lesion in the retroareolar region (17%) (Fig. 4).

MRI findings are available in three of the patients (50%). These examinations were performed in those patients who, based on the clinical and imaging findings, were diagnosed with a probably malignant lesion although this was not histologically confirmed by percutaneous biopsy. In these three patients, the DM diagnosis was obtained after the surgical procedure. The most common MRI finding is multifocal ring enhancement in the symptomatic region (66%) (Figs. 3B and 5C). However, patient 1 in Table 1, who underwent two breast MRI within a period of 18 months, showed multicentric foci in both breasts corresponding to more compact glandular tissue areas, with no significant enhancement after contrast administration (34%) (Fig. 2C). Ultrasound-guided core needle biopsy with a 14-gauge needle was performed in three patients (50%) for histopathological diagnosis. The other three patients underwent surgical biopsy.

Five patients were diagnosed with lymphocytic mastitis in its initial stage (83%) (Fig. 1A). The youngest female patient was diagnosed with three multicentric lesions (two in her left breast and one in her right breast) in advanced stage (Fig. 1B).

All the patients underwent surgical treatment. Four patients underwent tumorectomy (66%) either to establish a definitive diagnosis through surgical biopsy or for treatment. No recurrence was observed during a mean follow-up time of 7 years. In one female patient (patient 5 in Table 1), the surgical treatment was performed during the mammoplasty (17%). Because of the lack of response to medical treatment and presence of multiple symptomatic foci in both breasts, the remaining female patient (patient 1 in Table 1) underwent bilateral subcutaneous mastectomy and immediate breast reconstruction with implants (17%).

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age *</th>
<th>IDDM duration</th>
<th>No. of lesions</th>
<th>Mammography</th>
<th>Ultrasound</th>
<th>MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Female</td>
<td>28</td>
<td>20</td>
<td>3 (1 in RB and 2 in LB)</td>
<td>Normal (dense)</td>
<td>Hypoechoic solid nodules</td>
<td>Normal</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>40</td>
<td>21</td>
<td>1 in LB</td>
<td>Normal</td>
<td>Normal</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>Female</td>
<td>58</td>
<td>4</td>
<td>Multiple in RB</td>
<td>Asymmetric density</td>
<td>Hypoechoic solid nodules</td>
<td>Contrast-enhancement</td>
</tr>
<tr>
<td>4</td>
<td>Male</td>
<td>33</td>
<td>13</td>
<td>1 in RB</td>
<td>Asymmetric density</td>
<td>Complex cystic lesion</td>
<td>–</td>
</tr>
<tr>
<td>5</td>
<td>Female</td>
<td>34</td>
<td>5</td>
<td>1 in LB</td>
<td>Normal</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>6</td>
<td>Female</td>
<td>37</td>
<td>2</td>
<td>1 in LB</td>
<td>Asymmetric density</td>
<td>Hypoechoic solid nodule</td>
<td>Contrast-enhancement</td>
</tr>
</tbody>
</table>

IDDM, insulin-dependent diabetes mellitus; LB, left breast; MRI, magnetic resonance imaging; RB, right breast.

* Years.
Figure 2  Images of radiological examinations on patient 1. (A) Oblique mammographic projections show dense breasts, with no dominant nodules or microcalcifications. (B) Ultrasound shows that the palpable nodule-mass corresponds to a solid nodule several centimeters in size with microlobulated margins, mild posterior acoustic shadowing, and no color Doppler signal. (C) Symptomatic nodules appear as more compact and homogeneous areas of glandular tissue (arrows) on T2-weighted MRI images (no enhancement in sequences with IV contrast).

Figure 3  Images of radiological examinations on patient 3. (A) Breasts with a predominance of fat and asymmetric density in the upper quadrants of the right breast, corresponding to an area of DM. (B) MRI volumetric reconstruction shows a multinodular contrast-enhanced area with ill-defined borders in the outer quadrants of the right breast with unspecific enhancement (C) and velocity (D) curves corresponding to multifocal DM in the histopathological analysis.

Discussion

DM is a breast condition described along with other breast conditions generally known as ‘granulomatous mastitis’. DM is an uncommon complication of longstanding IDDM. It was first described by Soler and Khardori in 1984, but it was named diabetic mastopathy by Byrd et al. in 1987. The basic histopathological criteria to describe this condition were established in 1992, and are keloid-like fibrosis, lobulitis, ductitis, and lymphocytic vasculitis.

The exact incidence of DM is still unknown, and sometimes, differential diagnosis with breast cancer is complex; thus, clinicians should know about its existence.

The etiology of DM is also unknown. One of the several hypothesis proposed suggests that DM is an inflammatory or immune response resulting from patients’ dependency on exogenous insulin administration.

DM mostly affects 30- to 50-year-old women with longstanding IDDM. It has also been reported in males, though it is often misdiagnosed as gynecomastia. Our study includes

Figure 4  Breast US of patient 4. The palpable nodule-mass in the insulin-dependent diabetic man in our study corresponds to a complex cystic lesion that since it has an inflammatory clinical presentation, it is diagnosed as a retroareolar abscess. The histological study revealed that it is a DM lesion.
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Figure 5 Images of two breast MRI examinations performed on patient 6 during a 3-month time span. (A) Coronal T2-weighted sequence from the first study shows a lesion of DM with compact and homogeneous glandular tissue of several centimeters in size in the upper inner quadrant of the right breast. (B) After 3 months, the symptoms worsen and new imaging examinations are performed. MR image shows a multinodular structure with cystic areas inside that shows ring enhancement after contrast administration (C), and unspecific enhancement (D) and velocity (E) curves.

five women and one man with IDDM who were treated in our hospital over 11 years.

DM should be considered a chronic complication of diabetes, as are diabetic nephropathy and retinopathy. In our study, four patients presented with other complications associated with diabetes including retinopathy, nephropathy, and cerebral infarction.

The most common clinical presentation is the presence of one or more symptomatic or asymptomatic uni- or bilateral breast nodules that are variable in size. These nodules have an almost stone-hard consistency, with well-defined, though irregular, margins. Four out of the six patients in our study consulted us because of this symptom. Accordingly, the recommended imaging techniques are mammography, ultrasound, and MRI.

Mammograms show dense breast tissue with no dominant nodules nor microcalcifications, as well as asymmetric density. Mammographic findings are therefore unspecific. The most common mammographic finding in our study was asymmetric density.

US show the palpable nodules as solid, hypoechoic lesions, with ill-defined margins, posterior acoustic shadowing, and absence of color or pulsed Doppler signal. This was the most common US finding in our study. Not only does this technique help us to identify these lesions, but also is used to guide the core needle biopsy for the histologic diagnosis.

Most references consulted dealing with DM report MR imaging findings from one single case, which supports the rareness of this condition. Only the article by Wong et al. reports MRI findings in three patients. MRI offers a wide variety of possibilities, ranging from the absence of enhancement after contrast administration to intense enhancement of the lesion(s) under examination. Wong et al. argues that contrast enhancement is slightly greater in the palpable lesions than in healthy tissue, in all his cases. A lesion is likely to be benign when there is no enhancement after contrast administration, as is the case of DM. MRI is part of the study protocol on breast disease in our hospital since 2002. The most common finding in female patients with DM who underwent breast MRI was multifocal nodular enhancement after contrast administration on the areas affected by DM, with enhancement and velocity curves that are inconclusive for malignancy.

A histopathological examination is necessary to obtain a definitive diagnosis for DM. Morphologically, DM cannot be distinguished from lymphocytic mastopathies associated with other autoimmune conditions. For this reason, DM is also known as ‘lymphocytic mastopathy’. On a macroscopic level, lesions caused by DM appear as areas of indurated fibrous tissue, with ill-defined margins, and unlike fibrocystic mastopathy, with no cysts. The size of the lesions may vary considerably, from 1 to 6 cm. On a microscopic level, DM is associated with sclerosing lymphocytic lobulitis.

DM is an evolving condition initially characterised by a significant infiltration of the lobules by polyclonal mature B lymphocytes, which tend to penetrate the epithelium. Sclerosis and involution of lobules occur gradually. As the lymphocytic infiltrate diminishes, the lobules become...
surrounded by a dense collagenous stroma, which is the main component of advanced lesions. At diagnosis, most cases in our study were at an early stage.

FNAB is not considered an appropriate technique for histopathological diagnosis due to the low cellularity of these lesions, whereas core needle biopsy is considered the technique of choice.

Surgical biopsy is not indicated for DM diagnosis, except for lesions highly suspicious for malignancy and is not recommended as initial treatment as it is associated with a high rate of recurrences. However, all our patients underwent surgery for different reasons. The male patient underwent surgery because of suspected breast abscess; the asymptomatic female patient because she underwent breast reduction mammoplasty, and the other four female patients underwent surgery because of lack of response to anti-inflammatory therapy—the youngest patient was even administered corticosteroids; trouble with imaging follow-up of probably malignant lesions.

DM recurrence has not been reported over a mean follow-up time of 7 years, which contrasts with results reported in the literature. Based on all this information, we should consider DM to be included in the diagnosis of lesions with clinical and imaging findings suggestive of malignancy in patients with IDDM. Management of these patients involves imaging diagnosis based on mammography, ultrasonography, and MRI, and definitive diagnosis based on core needle biopsy. If DM is confirmed, conserving surgery with tumorectomy is the treatment of choice because the symptoms do not respond to medical treatment and imaging follow-up for this type of lesions is complex.

Authorship

Responsible for the integrity of the study: VRS.
Conception of the study: VRS, JCH.
Design: VRS, JCH, CMR.
Acquisition of data: VRS, RCM.
Analysis and interpretation of data: VRS, JCH, MFN.
Statistical analysis: VRS.
Bibliographic search: VRS, JCH.
Drafting of the manuscript: VRS, CMR, JCH.
Critical review with intellectually relevant contributions: JCH, CMR, RCM, PJGN, MFN, JCG.
Approval of the final version: VRS, JCH, CMR, RCM, PJGN, MFN, JCG.

Conflict of interest

The authors declare no conflict of interest.

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