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Case report

Diabetic mastopathy: A rare clinicopathologic entity with considerable autoimmune potential

Dhuha N. Boumarah [a,*], Ali S. AlSinan [a], Eman M. AlMaher [b], Miral Mashhour [c], Mohammed AlDuhileb [d]

[a] Department of Surgery, King Fahd University Hospital, Imam Abdulrahman Bin Faisal University, Saudi Arabia
[b] Department of Surgery, Security Forces Hospital, Dammam, Saudi Arabia
[c] Department of Pathology, King Fahad Specialist Hospital, Dammam, Saudi Arabia
[d] Department of Surgery, King Fahad Specialist Hospital, Dammam, Saudi Arabia

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ABSTRACT

Introduction and importance: Diabetic mastopathy is a rare entity affecting diabetic patients. It has been previously linked to type 1 diabetes mellitus; however, due to the several accompanying conditions, a theory of autoimmune factors contributing to the origin of this condition has been on the rise. In this paper, we report a case of diabetic mastopathy associated with several autoimmune diseases to highlight the immunological potential of this condition.

Case presentation: A 25-year-old female, known to have type 1 diabetes mellitus, hypertension, hypothyroidism, adrenal insufficiency, dilated cardiomyopathy and end-stage renal disease, was referred to our clinic for a breast lump. Radiological investigations showed a dense mass with irregular borders in the retroareolar area of the left breast. A core biopsy was obtained which revealed keloid-like fibrosis along with lymphocytes infiltrated, suggestive of lymphocytic mastopathy.

Clinical discussion: Fibrous mastopathy has been merely attributed to a long-standing use of insulin therapy by diabetic patients; recent observations, however, proved the major contribution of immunity to etiopathogenesis. Even though human leukocyte antigen (HLA) association has not been supported in the literature, the histological changes of breast lymphocytic infiltrate are seen in patients who not only have T1DM, but also thyroiditis, systemic lupus erythematosus, Sjogren's syndrome, and Addison's disease. The frequent presence of several possible autoimmune conditions has promoted the theory of an autoimmune process affecting connective tissues, however, these claims are yet to be proven by future studies.

Conclusion: Recent observations have proved the major contribution of immunity to etiopathogenesis of diabetic mastopathy. We shed light on the role of the immune system in triggering the disease process by reporting a case of diabetic mastopathy with a cluster of autoimmune diseases. Future studies should explore the genetic background of the condition as it would potentially have several clinical implications. The discussed pathophysiologic explanations raise the possibility of autoimmunity as a key driver in pathogenesis and indicate the need to change the nomenclature of this condition.

1. Introduction

Diabetic mastopathy, also termed sclerosing lymphocytic mastopathy, fibrous mastopathy or lymphocytic lobulitis of the breast, is a rare benign entity that accounts for less than 1% of all benign breast lesions [1,2]. Despite the benign nature of the condition, it has some clinical and diagnostic features resembling malignancy, thus, it is usually associated with several diagnostic difficulties [3]. Fibrous mastopathy was previously linked to type 1 diabetes mellitus (T1DM), which was considered the sole causative factor, however, further hypotheses then suggested the multifactorial etiology, including the contribution of autoimmunity to the pathogenesis [4,5]. Additionally, the autoimmune phenomena of fibrous mastopathy was greatly supported by the distinctive histopathological findings, which represents an essential tool to establish accurate diagnosis [6]. Herein, we report a case of diabetic mastopathy associated with several autoimmune diseases, along with

* Corresponding author.
E-mail address: Dohanahar@gmail.com (D.N. Boumarah).

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summarizing pertinent literature, to highlight the autoimmune potential of this condition. The case has been written in accordance with the SCARE guidelines [7].

2. Case presentation

A 25-year-old female, known case of T1DM, hypertension (HTN), hypothyroidism, adrenal insufficiency, dilated cardiomyopathy (DCM) with an ejection fraction (EF) of 50% and end stage renal disease (ESRD) on hemodialysis, complicated by hyperparathyroidism, was referred to our breast clinic for an incidental finding of a lump in her left breast during screening prior to renal transplant. Based on patient's observation, the mass was not associated with any nipple discharge, and menstruation had no effect on any of the mass features. The patient did not use any oral contraceptive pills and her family history was negative for breast and other gynecological malignancies. She is nulliparous, divorced and has regular menstrual periods. She was diagnosed to have T1DM when she was 10 years of age and started on insulin therapy since then. Significantly, her diabetes mellitus course was complicated by bilateral retinopathy and retinal detachment, with secondary blindness 3 years prior to presentation. A retroareolar mass was detected on examination measuring around 3 cm, hard, mobile and not attached to surrounding skin or muscular structures as demonstrated in Fig. 1. Bilateral axillary and supraclavicular lymph nodes were all nonpalpable.

All elements of complete blood count were unremarkable apart from anemia, with a hemoglobin of 10.1 g/dL. Renal function parameters revealed the evidence of chronic kidney disease with creatinine exceeding 650 mg/dL and blood urea nitrogen (BUN) of more than 16 mg/dL, along with hyperkalemia. Glycosylated hemoglobin was equal to 7.4%. Parathyroid hormone was elevated with a reading of 1135 pg/mL and thyroid enzymes, on the other hand, demonstrated evidence of hypothyroidism.

Radiological modalities were utilized to obtain mass characteristics and establish a preliminary diagnosis. Bilateral breast mammography showed a dense breast obscuring the accurate visualization of the mass as shown in Fig. 2. However, ultrasound (US) of the breast demonstrated the presence of a retroareolar mass with irregular borders, measuring around 3 cm, as illustrated in Fig. 3. The lesion was labeled as Breast Imaging-Reporting and Data System 4 (BIRADS-4) and an US-guided core tissue biopsy was performed to rule out malignancy. Pathology results illustrated the presence of keloid-like fibrosis along with lymphocytes and plasma cells infiltrating the breast tissue and suggesting the diagnosis of lymphocytic mastopathy (Fig. 4). Immunohistochemical analysis was also done and results were negative for malignancy.

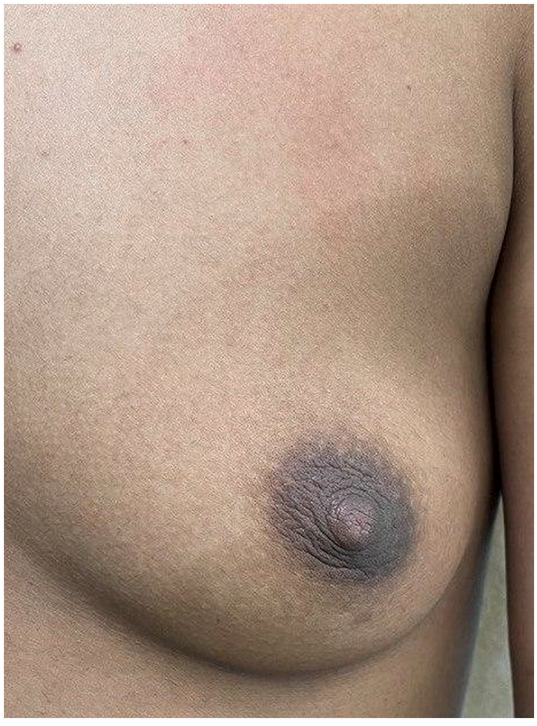

Fig. 1. A retroareolar mass with irregular borders, measuring 3 cm, was evident on examination.

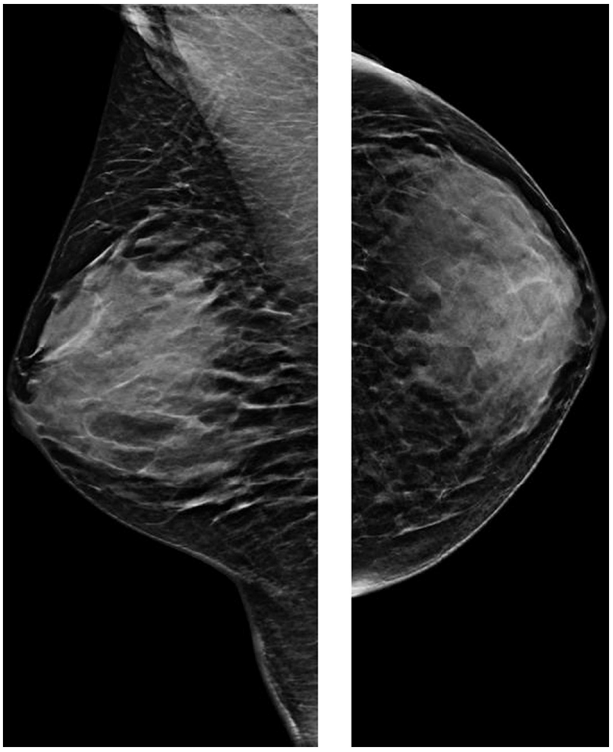

Fig. 2. Bilateral Mammogram of the breast was inconclusive as shown, revealing nonspecific findings due to the markedly dense breast parenchyma.

3. Discussion

Diabetes mellitus is associated with a wide spectrum of complications, classified into acute and chronic subtypes. One of the chronic, poorly studied, complications affecting individuals with diabetes and other autoimmune diseases has been known as “diabetic mastopathy” [1,8,9]. It is recognized as an uncommon, benign, clinicopathologic entity with few hundred cases reported in English literature [10]. The disease affects both young and middle-aged (34–47 years) females, in

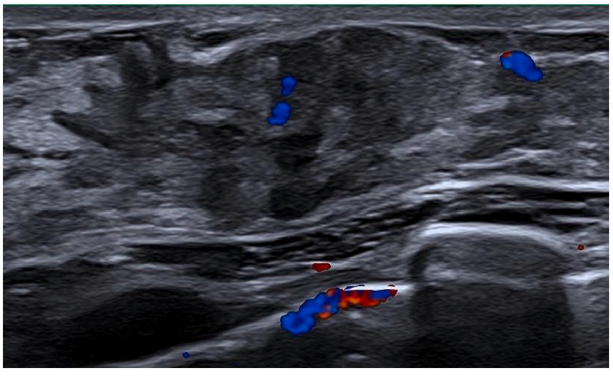

Fig. 3. Ultrasound of left breast illustrating the presence of a hypoechoic mass with characteristics suspicious for malignancy.

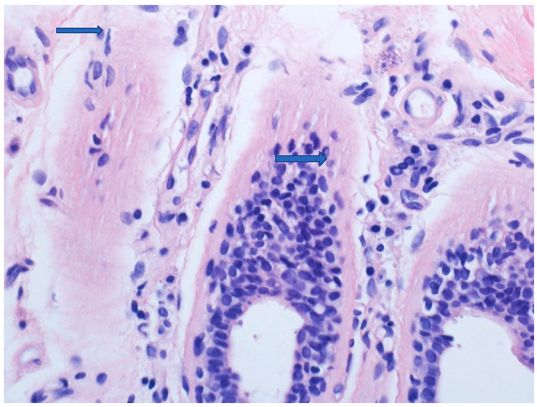

Fig. 4. Chronic inflammatory changes with lymphocytes and plasma cells surrounding breast lobules.

particular, with a small reported number of cases among males [11,12]. It has been first described in 1984 by Soler et al. as a condition merely attributed to long standing insulin-dependent diabetes [8]. Several reports since then showed its association with other autoimmune diseases, such as Hashimoto's thyroiditis and Sjogren's syndrome, suggesting an autoimmune origin. The main clinical manifestation of sclerosing lymphocytic mastopathy is a palpable, painless, mass identified via self-examination, similarly, in our case the mass was incidentally found during screening prior to renal transplant [13].

To date, pathogenesis of lymphocytic mastopathy is still not fully understood. A local autoimmune response toward breast tissue is one of the suggested theories [14,15]. It has been shown that B-cell lymphocytes infiltrating into the breast tissue have human leukocyte antigen-DR isotype (HLA-DR) as an expression on the epithelium surface, namely, HLA-DR 3, 4, and 5 [5,16]. Autoantibody production and B-lymphocytes proliferation can be additionally triggered through the release of cytokines from macrophages and assembly of antigens as products of proteins' non-enzymatic glycosylation [17]. Among patients with diabetes mellitus, two hypotheses were suggested to explain the pathogenesis of the disease. Firstly, anti-insulin antibodies can cross-react with breast ductal epithelium causing inflammation and fibrosis. Moreover, hyperglycemia was found to contribute to the causation by inducing several fibroinflammatory changes, including the expansion of the extracellular matrix, which in turn, increases collagen production and decreases the process of degradation. Interestingly, the same immunological reaction was observed among patients with other autoimmune diseases such as Sjogren's syndrome and Hashimoto's thyroiditis [9]. These pathophysiologic explanations raise the possibility of autoimmunity as a key driver in pathogenesis and indicate the need to change the nomenclature of this condition.

Even though HLA association has not been supported in the literature [13], the histological changes of breast lymphocytic infiltrate are seen in patients that not only have T1DM, but also thyroiditis, systemic lupus erythematosus, Sjogren's syndrome, Addison's and IgG4-related disease [18]. The frequent presence of several possible autoimmune conditions has promoted the theory of an autoimmune process affecting connective tissues, however, these claims are yet to be proven [19].

Mammogram results are usually nonspecific and inconclusive as it cannot provide a detailed illustration of dense, glandular, breast parenchyma [20]. On the other hand, Logan and colleagues conducted a retrospective study to describe possible ultrasonic findings of the condition and they found that breast lesions of diabetic mastopathy usually manifest as hypoechoic masses with slight to marked acoustic shadowing [21]. Breast carcinoma, therefore, remains the main differential diagnosis for diabetic mastopathy and a pathologic specimen is a necessity to differentiate between the two entities and reach a definitive diagnosis [19].

The management of fibrous mastopathy follows the recommended approach of other benign breast lesions. Conservative therapy is usually initiated, after the crucial steps of triple assessment, as experienced with our patient. Risk of cancer among these patients is similar to the general population, as reported by Kudva et al. and, hence, the role of surgery remains very minimal. Surgical intervention is only preferred in cases where malignancy cannot be excluded or when anxiety presents [19].

4. Conclusion

Fibrous mastopathy has been merely attributed to a long-standing use of insulin therapy by diabetic patients; recent observations, however, proved the major contribution of immunity to etiopathogenesis. The benign nature of this condition permits following a conservative approach when managing similar cases. The current paper sheds light on one of the overlooked aspects of this entity and highlights the major role of immune system in triggering the disease process by reporting a case of diabetic mastopathy with a cluster of autoimmune diseases. Future studies should explore the genetic background of the condition as it would potentially have several clinical implications.

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Ethical approval

Not applicable.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Research registration

Not applicable.

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CRediT authorship contribution statement

-DB, study concept and design, data collection, data analysis and interpretation, writing the paper, artwork editing.

-AA, data collection, data analysis and interpretation, writing the paper.

-EM, data collection, data analysis and interpretation, grammar correction.

-MM, data analysis and interpretation, writing the paper, and editing artwork.

-MA, data collection, data analysis and interpretation.

Declaration of competing interest

None declared.

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References

[1] N.B. Agochukwu, L. Wong, Diabetic mastopathy: a systematic review of surgical management of a rare breast disease, Ann. Plast. Surg. 78 (2017) 471–475.
[2] M. Corbetta Machado, G. Regalo, Lymphocytic mastopathy – a rare entity and a diagnostic challenge, Int.J.Surg.Case Rep. (2020) 1–3.
[3] L. Chen, J. Tsang, Y. Ni, S. Chan, K. Chan, S. Zhang, et al., Lymphocyte subsets contribute to the degree of lobulitis and ductitis in sclerosing lymphocytic lobulitis of the breast, J. Clin. Pathol. 69 (6) (2015) 527–532.
[4] J.E. Tomaszewski, J.S.J. Brooks, D. Hicks, et al., Diabetic mastopathy: a distinctive clinicopathologic entity, Hum. Pathol. 23 (1992) 780–786.
[5] J.D. Seidman, L.A. Schnaper, L.E. Phillips, Mastopathy in insulin-requiring diabetes mellitus, Hum. Pathol. 25 (1994) 819–824.
[6] O. Dorokhova, S. Fineberg, T. Koenigsberg, Y. Wang, Diabetic mastopathy, a clinicopathological correlation of 34 cases, Pathol. Int. 62 (10) (2012) 660–664.
[7] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, for the SCARE Group, The SCARE 2020 guideline: updating consensus Surgical CAse REport (SCARE) guidelines, Int. J. Surg. 84 (2020) 226–230.
[8] N.G. Soler, R. Khardori, Fibrous disease of the breast, thyroiditis, and cheiroarthropathy in type 1 diabetes mellitus, Lancet 1 (1984) 193–194.
[9] K.A. Ely, G. Tse, J.F. Simpson, R. Clarfeld, D.L. Page, Diabetic mastopathy: a clinicopathologic review, Am. J. Clin. Pathol. 113 (2000) 541–545.
[10] C.-l.R. Chan, R.S.L. Ho, T.W.H. Shek, A. Kwong, Diabetic mastopathy, Breast J. 19 (2013) 533–538.
[11] A.M. Pluchinotta, E. Talenti, G. Lodovichetti, et al., Diabetic fibrous breast disease: a clinical entity that mimics cancer, Eur. J. Surg. Oncol. 21 (1995) 207–209.
[12] S.P. Weinstein, E.F. Conant, S.G. Orel, et al., Diabetic mastopathy in men: imaging findings in two patients, Radiology 219 (2001) 797–799.
[13] K. Thorncroft, L. Forsyth, S. Desmond, R. Audisio, The diagnosis and management of diabetic mastopathy, Breast J. 13 (6) (2007) 607–613.
[14] P.M. Camuto, E. Zetrenne, T. Ponn, Diabetic mastopathy: a report of 5 cases and a review of literature, Arch. Surg. 135 (2000) 1190–1193.
[15] J. Decraene, C. Van Ongeval, G. Clinckemaillie, H. Wilddiers, Sclerosing lymphocytic lobulitis mimicking a tumor relapse in a young woman with a history of breast cancer, J. Belg. Soc. Radiol. 99 (2015) 72–75.
[16] A. Lee, A. Bateman, S. Turner, J. Theaker, W. Howell, HLA class II DRB1 and DQB1 allelic polymorphism and sclerosing lymphocytic lobulitis of the breast, J. Clin. Pathol. 52 (6) (1999) 445–449.
[17] I.S. Schwartz, J.A. Strauchen, Lymphocytic mastopathy. An autoimmune disease of the breast? Am. J. Clin. Pathol. 93 (1990) 725–730.
[18] R. Goulabchand, A. Hafidi, et al., Mastitis in autoimmune diseases: review of the literature, diagnostic pathway, and pathophysiological key players, J. Clin. Med. 9 (4) (2020) 958, https://doi.org/10.3390/jcm9040958. Published 2020 Mar 30.
[19] Y. Kudva, C. Reynolds, T. O'Brien, C. Powell, A. Oberg, T. Crotty, "Diabetic Mastopathy", or sclerosing lymphocytic lobulitis, is strongly associated with type 1 diabetes, Diabetes Care 25 (1) (2002) 121–126.
[20] E. Wood, P. Propeck, Atypical sonographic presentation of diabetic mastopathy: a case report and literature review, J.Clin.Imaging Sci. 11 (2021) 60.
[21] W.W. Logan, N.Y. Hoffman, Diabetic fibrous breast disease, Radiology 172 (1989) 667–670.