CASE REPORT

Lymphocytic Mastitis with Florid Follicular Hyperplasia Mimicking a Lymphoproliferative Disorder

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ABSTRACT

Lymphocytic mastitis is a rare benign fibroinflammatory breast condition that can clinically and histologically mimic malignancy. Differentiating between reactive and neoplastic lymphoid infiltrates can be challenging in cases exhibiting dense lymphocytic infiltration. An accurate diagnosis relies on careful evaluation of clinical, histomorphological and immunohistochemical features, with molecular studies such as polymerase chain reaction (PCR) employed in diagnostically ambiguous cases. We present a case of a 54-year-old woman with underlying metabolic syndrome who presented with painless bilateral breast lumps. Histopathological examination following wide local excision confirmed a final diagnosis of bilateral lymphocytic mastitis with florid follicular hyperplasia. This case highlights the histopathological variability of lymphocytic mastitis.
Keyword: Lymphocytic Mastitis, Breast Neoplasms, Lymphoproliferative Disorders, Follicular Hyperplasia, Breast Inflammatory Diseases
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INTRODUCTION

Lymphocytic mastitis, is a benign fibroinflammatory breast disease commonly associated with autoimmune conditions, include thyroiditis and systemic lupus erythematosus (1). Diabetic mastopathy, often considered an overlapping entity, is a term more frequently used to describe similar lesion in patients with long-standing diabetes mellitus (1,2). Lymphocytic mastitis typically affects young to middle-aged women and present as painless, palpable breast lumps, which may be unilateral or bilateral (1,3). The exact prevalence of both lymphocytic mastitis and diabetic mastopathy is unknown (1). The immunopathogenesis of non-diabetic lymphocytic mastitis is postulated to be autoimmune in origin. Notably, the lymphoepithelial lesions observed in Hashimoto thyroiditis and Sjugren syndrome closely resemble those seen in diabetic mastopathy. Based on literature review, the postulated pathogenesis for diabetic mastopathy may be due to the neoantigen formation from chronic hyperglycemic state (1,2). These neoantigens may trigger an autoimmune response that results in B-cells proliferation, autoantibody production, cytokine release and consequent stromal proliferation with extracellular matrix expansion (1,2). Radiologically, the most frequently reported ultrasonographic findings include irregular hypoechoic masses with posterior acoustic shadowing. These features are typically categorized as BI-RADS category 4, indicating a suspicious abnormality, and are often radiographically indistinguishable from breast malignancy (1). Histologically, lymphocytic mastitis is characterised by varying degrees of small lymphocytic infiltrates surrounding ducts, lobules, and blood vessels, set within a background of keloid-like stromal fibrosis, with or without epithelioid fibroblasts (1-3). To our knowledge, florid follicular hyperplasia is not a typical histological feature of lymphocytic mastitis and is more commonly associated with lymphoproliferative disorder such as marginal-zone lymphoma, Castleman disease or IgG4-related diseases of breast (3-5). This case report presents an unusual presentation of florid follicular hyperplasia occurring in lymphocytic mastitis, thereby raising awareness of its histopathological variability and the importance of its distinction from true

lymphoproliferative disorders.

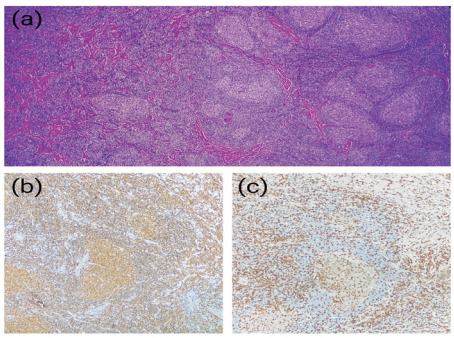

Fig 1: Lymphocytic mastitis. Haematoxylin and eosin (H&E) stain (40×) (a) shows lymphocytic infiltrates with prominent lymphoid follicles and keloid-like stromal fibrosis. Immunohistochemical (IHC) stain for CD20 (100×) (b) and CD3 (100×) (c) show B-cells rich follicles and T-cells zone.

CASE REPORT

A 54-year-old postmenopausal woman, with underlying metabolic syndrome (diabetes mellitus, dyslipidaemia, fatty liver) and cholelithiasis, presented in July 2024 with one month history of bilateral breast swelling. Clinical examination demonstrated two poorly defined breast lumps, one measuring 2×2cm at 12 o'clock region of the right breast and another measuring 1.5×1.5cm at 1 o'clock region of the left breast. Bilateral breast ultrasonography revealed a BI-RADS 4 lesion in the right breast and the lesion in the left breast was suggestive of phyllodes tumour. Fine needle aspiration cytology performed in August 2024 yielded an unsatisfactory sample from the right breast, while the left breast lesion showed scanty epithelial cells. Blood investigation revealed a fasting blood sugar (FBS) level of 8.0 mmol/L, high-density lipoprotein (HDL) of 1.05 mmol/L, low-density lipoprotein (LDL) of 5.5 mmol/L, aspartate aminotransferase (AST) of 61 U/L, alanine aminotransferase (ALT) of 59.2 U/L. Autoimmune screening was not carried out. Subsequently, wide local excision of both breast lumps was performed. Macroscopically, the right and left breast specimens showed well circumscribed, tan-coloured firm masses, measuring (25×13×35) mm and (30×12×10) mm, respectively. On microscopic examination, both breast lesions demonstrated dense, polymorphous lymphoid aggregates with florid follicular hyperplasia, accompanied by prominent keloid-like stromal fibrosis, and scattered residual breast lobules. The germinal centres within the florid follicular hyperplasia were variably enlarged, exhibited BCL6 positivity and BCL2 negativity, and retained an intact follicular dendritic cells meshwork highlighted by CD21 and CD23, all are enclosed by preserved mantle zones. They also exhibited a normal polarization and high proliferative index. These findings are consistent with features of reactive follicular hyperplasia. The variable sized follicles occupied about one-third of the lymphoid tissue, and in some areas, were tightly packed with attenuated interfollicular zones. The interfollicular lymphoid cells were mostly small mature-appearing lymphocytes, composed of B-cells (CD20+, CD5-, LEF1-, CD43-, SOX11-) admixed with T-cells (CD3+ and CD5+) with B-cells slightly predominating. The absence of LEF1 and SOX11 expression aided in excluding small lymphocytic lymphoma and mantle cell lymphoma. The lymphoid infiltrates were seen surrounding the ducts, lobules, and blood vessels. There was no aberrant immunomarker expression on the B-cells. Plasma cells comprised less than 1% of the total nucleated cell population and exhibited no light chain restriction by kappa and lambda in-situ hybridization. IgG4-related disease was excluded due to sparse IgG4-positive plasma cells present. The preserved breast ducts were lined by normal two-tiered epithelium with no evidence of epithelial atypia or malignancy. No apparent feature suggestive of lymphoma was identified. No skin tissue was included. Considering the patient's clinical history of metabolic syndrome, along with the histomorphological and immunohistochemical findings, a final diagnosis of lymphocytic mastitis (diabetic mastopathy) was made. The patient was followed up for two months post operation and no clinical recurrence of breast lumps was detected.

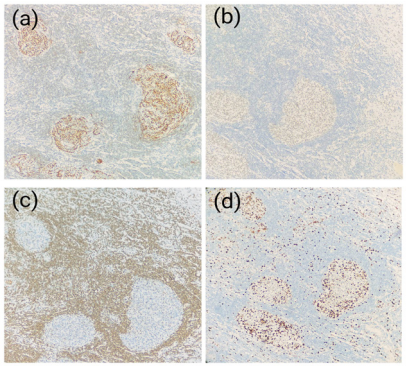

Fig 2: Germinal centres. IHC for CD21 (100×) (a) BCL6 (100×) (b), BCL2 (100×) (c) and Ki67 (100×) (d) show intact follicular dendritic meshwork and features of reactive germinal centres accordingly. Ki67 exhibited a normal polarization.

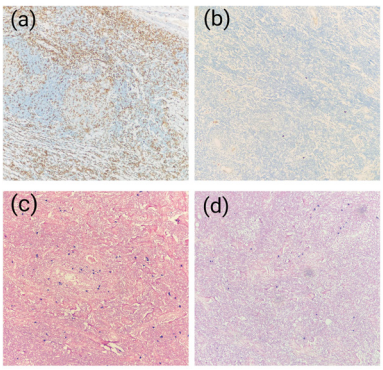

Fig 3: IHC staining for CD43 (100×) (a) showed no aberrant expression by the B-cells. IgG4-positive plasma cells are sparse (100×) (b). Kappa ISH (100×) (c) and Lambda ISH (100Ч) (d) showed occasional scattered plasma cells with absence of light chain restriction.

DISCUSSION

We report a case of lymphocytic mastitis characterised by dense lymphocytic infiltration of breast tissue

accompanied with multiple prominent lymphoid follicles. The histomorphological findings raised suspicious for lymphoma or other lymphoproliferative disorders, warranting detailed morphologic assessment and comprehensive immunohistochemical analysis before the diagnosis of lymphocytic mastitis.

Lymphocytic mastitis, also termed as sclerosing lymphocytic lobulitis or diabetic mastopathy in patients with diabetes, is described as perilobular and perivascular B-cells predominant lymphocytic infiltrates associated with keloidal-like stromal fibrosis, lobular atrophy and the presence of epithelioid fibroblasts (1-3). While epithelioid fibroblasts were previously thought to be related to diabetic condition, a study by Masaru Oba et. al. reported that epithelioid fibroblast is not specific for diabetic mastopathy and our case supports this observation (3). Consistent with previous literatures on lymphocytic mastitis, our case also showed a dominant B-cells lymphocytic infiltrate (2).

Breast lymphoma is a rare but represents the most common haematological malignancy of the breast. The key histological features that help in excluding lymphoma include the absence of aberrant immunomarker expression on the B-cells (3). IgG4-related disease is another benign mass-forming lymphoproliferative disorder of clinical importance due to its responsiveness to steroid therapy. It is characterized histologically by lymphoplasmacytic infiltrates, storiform fibrosis, obliterate phlebitis and increased IgG4+ plasma cells (4). Castleman disease is a benign lymphoproliferative disorder typically originating from lymphoid tissue and its presence in the breast is thought to arise from intramammary or interpectoral lymph nodes (5). The current case lacked key features of Castleman disease, including atrophic germinal centres, interfollicular lymphoplasmacytic infiltrates, onion-skin mantle zone hyperplasia, and hyalinised proliferating blood vessels (5).

Although studies have shown that patients with lymphocytic mastitis are not at higher risk of developing B-cell breast lymphomas (2, 3), the number of patients in the studied population are rather small. Therefore, careful long-term follow-up is recommended to better understand the natural history and progression of this rare entity. Lymphocytic mastitis remains a diagnostic challenge for surgeons, radiologist, and pathologist, as its features may overlap with malignant conditions. An incorrect diagnosis could result in the unwarranted administration of chemotherapy or immunosuppressive agents, exposing the patient to unnecessary adverse effects. A multidisciplinary team approach usually employed in managing breast mass.

The limitations of this case report include a short duration of patient follow-up, which restricts a more comprehensive understanding of the clinical course. Molecular analysis is typically not part of the standard diagnostic workflow, though it may be appropriate in select cases.

CONCLUSION

Lymphocytic mastitis is a rare inflammatory breast disease that can closely mimic lymphoproliferative disorders, particularly in the setting of dense lymphoid infiltrates. Distinguishing between reactive lymphocytic infiltrates and neoplastic infiltrates requires thorough work up including extensive sampling, detailed morphological assessment and broad immunohistochemical profile coupled with strong clinical correlation. Multidisciplinary team approach is often recommended in managing breast mass. As this entity is increasingly recognized, especially in association with diabetes mellitus and autoimmune diseases, further studies are warranted to better understand its aetiology, pathogenesis, pathological features, and clinical management. Continued surveillance may be valuable in characterizing the clinical behavior and its relationship with malignancy.

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