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Lupus mastitis with predominant kappa-restricted plasma cell infiltration: report of a rare case

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Abstract

Lupus mastitis (LM) is a rare complication of systemic lupus erythematosus (SLE) or discoid lupus erythematosus (DLE). The clinical presentations of LM may mimic breast malignancy, and biopsy or excision is usually performed. Histologically, LM is featured by lymphoplasmacytic inflammation involving breast ducts, lobules, blood vessels and adipose tissue. Characteristic hyaline fat necrosis can be noted in most cases. Here, we reported a case of LM in an elderly female patient who presented with bilateral breast lesions. Histologically, the breast lesions showed prominent hyaline fat necrosis and predominantly plasmacytic inflammation involving breast ducts, vessels and fat lobules. Fibrinoid necrosis of vessels was also noted. The infiltrated plasma cells were Kappa light chain-restricted, but did not show the immunophenotypes for a plasma cell neoplasm. In addition, the patient developed Kappa-restricted plasma cell myeloma 2 years later. The patient was followed up for 8 years, and her breast lesion did not show recurrence. The patient's unique clinicopathological presentations indicated a potential correlation between her LM and subsequently developed myeloma. It also indicated that the immunophenotypical characterization of infiltrated plasma cells in LM patients with predominant plasma cell infiltration may be important to rule out potential plasma cell neoplasms.

Keywords: Lupus, Mastitis, Plasma cell, Kappa-restricted, Myeloma

Introduction

Lupus mastitis (LM), which refers to panniculitis involving subcutaneous or parenchymal adipose tissue of the breast, is a rare finding in patients with systemic lupus erythematosus (SLE) or discoid lupus erythematosus (DLE). LM can sometimes be the initial presentation of systemic symptoms for SLE (Voizard et al. 2017), making the diagnosis challenging. The etiology of LM is unclear, and surgical treatment should be avoided since physical trauma is associated with progression or relapse of the disease (Bayar et al. 2007). Histologically, most LM cases show lymphocyte-predominant inflammation involving breast ducts, lobules, vessels and adipose tissue, with hyaline fat necrosis being the most characteristic finding. Here, we reported 1 case of LM which showed very distinctive histologic findings from the usual LM. Besides, the patient developed plasma cell myeloma 2 years after the LM diagnosis. Myeloma has been known to be a rare association with lupus (Castro et al. 2018; Maamar et al. 2008), though concurrence of LM and myeloma in SLE patient has never been reported. The unique clinical and pathological manifestations of this patient indicated a potential etiological correlation between LM and plasma cell myeloma.

Case presentations

A 77-year-old female patient with 15 years history of SLE, who was complicated by end-stage renal disease, peripheral neuropathy, seizure and chronic anemia, presented with palpable bilateral breast lesions. Ultrasound

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examination revealed a 2.0 cm ill-defined mass in the right breast, and two additional ill-defined masses of 1.1 cm and 0.9 cm in the left breast. Radiologically, all the masses showed diffuse surrounding edema and increased surrounding stiffness, which were worrisome features for malignancy. Ultrasound-guided core biopsies of the masses were performed. Microscopically, the most prominent finding was lobular panniculitis diffusely involving the masses. Large areas of hyaline fat necrosis were also seen together with panniculitis (Fig. 1a), which were the typical finding for LM (Rosa and Mohammadi 2013). Perivascular inflammation with prominent fibrinoid necrosis of the vascular wall was noted (Fig. 1b). The inflammation was also seen around the breast ducts (Fig. 1c). On high magnification, the periductal space showed a band of dense inflammatory infiltration predominantly composed of plasma cells, with scattered lymphocytes intermixed in between (Fig. 1d). The panniculitis also revealed similar plasma cell-predominant infiltration (Fig. 1e). The morphologic findings and the patient's SLE history supported the diagnosis of LM.

Two years after the diagnosis of LM, the patient was found to have diffuse lytic bone lesions throughout the calvarium. Bone survey revealed additional lytic lesions involving bilateral humerus and femur. Serum protein electrophoresis and immunofixation identified monoclonal IgA Kappa at a concentration of 4.0 g/dL. Bone marrow core biopsy revealed hypercellular marrow with a dense population of plasma cells, which were highlighted by CD138 immunostain (Fig. 1f). A diagnosis of plasma cell myeloma was made based on the morphologic and immunohistochemical findings.

As compared to usual LM cases that showed a lymphocyte-predominant inflammation, this case was distinctive by predominantly plasmacytic infiltration and the subsequently developed plasma cell myeloma. Therefore, immunostains were retrospectively performed to characterize the immunophenotypes of inflammatory cells in the LM. As a result, CD138 stain confirmed the plasma cell-predominant infiltration (Fig. 2a), which comprised more than half of the periductal inflammatory cell population. CD20-positive B cells (Fig. 2b) were

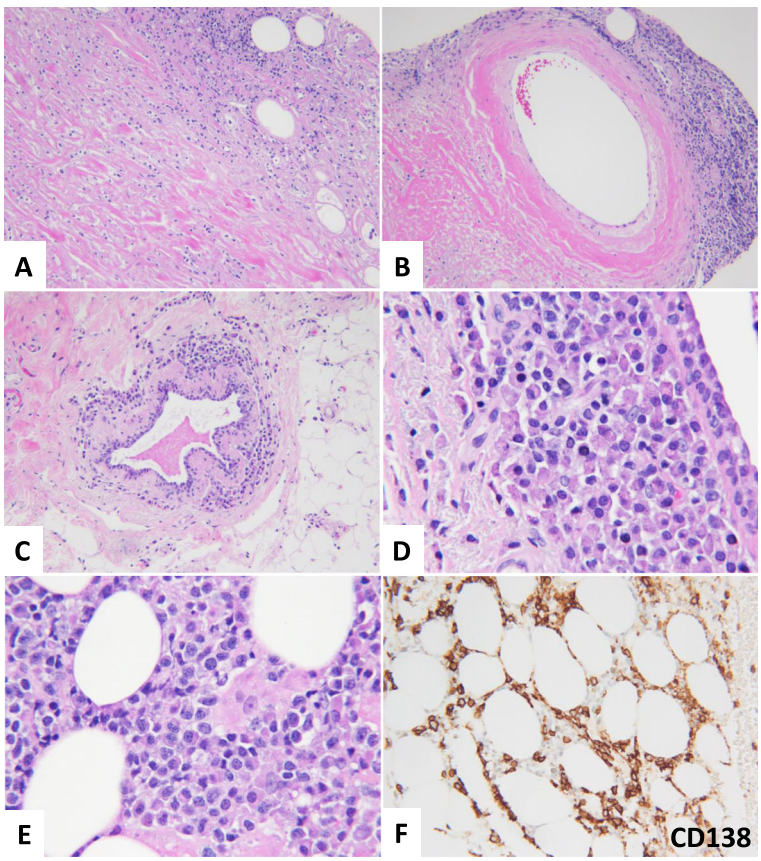

Fig. 1 Histological manifestations of lupus mastitis. **a** Panniculitis (upper right) with adjacent hyaline fat necrosis (lower left). **b** Perivascular inflammation with fibrinoid necrosis of the vascular wall. **c** Periductal inflammation. **d** High magnification of periductal inflammation and **e** panniculitis showing plasmacytic predominant infiltration. **f** CD138 immunostain of bone marrow biopsy revealed dense plasma cell population. (H&E, original magnification, × 100 [**a, b, c**], × 200 [**f**], × 400 [**d, e**])

noted mostly at the periphery of the periductal inflammation. In comparison, CD3-positive T cells (Fig. 2c) were situated more towards the duct lumen, with some infiltrating into the ductal epithelium. Immunostains for immunoglobulin Lambda (Fig. 2d) and Kappa (Fig. 2e) light chains showed that the plasma cells were kappa-restricted, indicating the monoclonality of the plasma cells. However, the plasma cells in this case were positive for CD19 (Fig. 2f) and were negative for CD117 (Fig. 2g) and CD56 (Fig. 2h), which were consistent with the immunophenotypes for benign plasma cells. Therefore, despite that the plasma cells were light chain-restricted, their immunophenotypes were not consistent with a plasma cell neoplasm.

Discussion

LM is an uncommon complication of SLE or DLE. The etiology is unclear and is most likely due to immunologic causes. Typical pathologic findings for LM include lobular fat necrosis with hyalinization, perivascular, periductal, and/or perilobular inflammation. The inflammatory infiltration in LM is a mixture of different

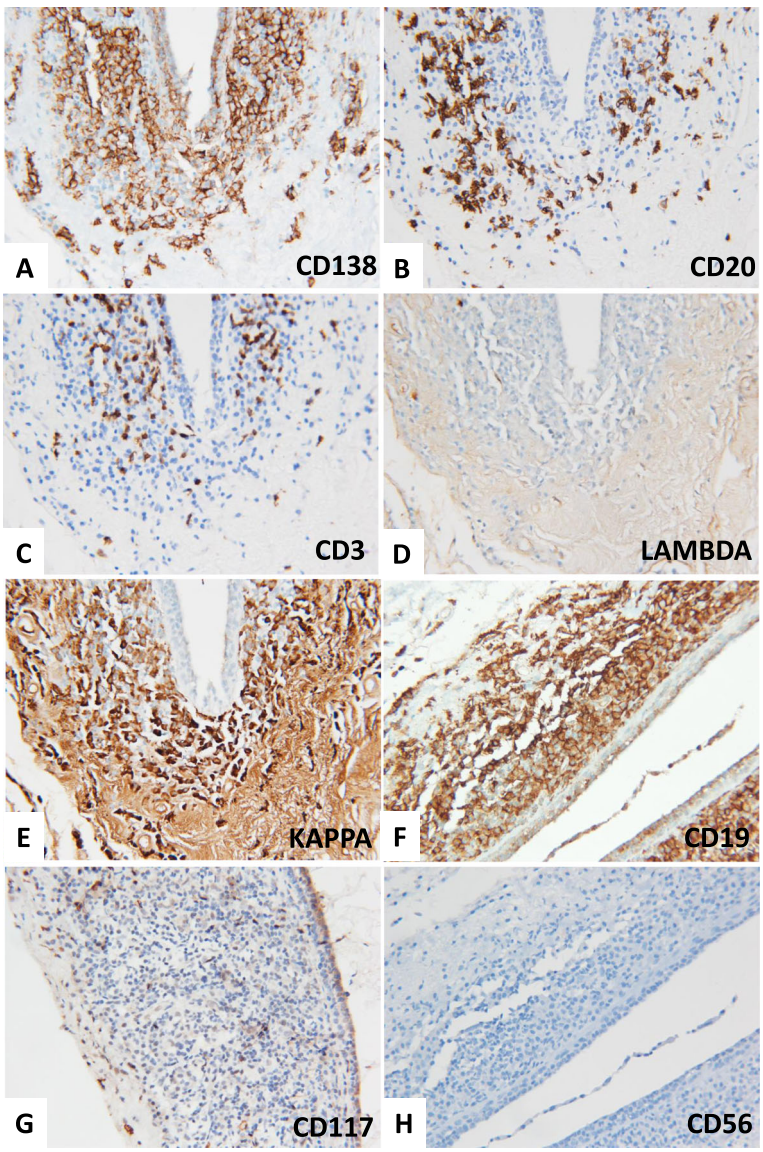

Fig. 2 Immunostains to characterize periductal inflammatory cells in lupus mastitis. **a** CD138 highlighting plasma cells in over half of the inflammatory cells. **b** CD20 and **c** CD3 immunostains highlight smaller populations of both B lymphocytes and T lymphocytes. **d** Lambda and **e** Kappa light chain immunostain showed the Kappa-restriction of plasma cells. Immunostains for **f** CD19, **g** CD117 and **h** CD56 indicated the non-neoplastic nature of the plasma cells. (Immunohistochemistry, original magnification, × 200 [**a-h**])

inflammatory cells, with lymphocytes being the predominant type in most cases (Warne et al. 2011). LM is mostly presented in females, with only four cases being reported in male patients (Thapa et al. 2016; Crevits et al. 2009; Martella et al. 2008; Fernandez-Flores et al. 2006). LM frequently presents as a firm breast mass, with concerning imaging findings, like irregular borders, nipple retraction, or breast skin changes. Therapeutic strategies for LM is similar to SLE, which include hydroxychloroquine or chloroquine with or without corticosteroids or steroid-sparing immunosuppressive agent, like methotrexate or azathioprine (Belmont 2013).

Plasma cell myeloma is a very rare complication of SLE, with only 18 cases reported so far (Castro et al. 2018; Maamar et al. 2008; Okoli et al. 2009; Choi et al. 2010). The mean interval between the diagnosis of SLE and myeloma was 7 years, and the vast majority of patients (92.3%) were female (Okoli et al. 2009). The association between SLE and myeloma is possibly immunological; however, the exact etiology is not well understood. In addition, the concurrence of LM and multiple myeloma in SLE or DLE patients has never been reported before.

Compared to most cases of LM, this patient showed unique plasma cell-predominant inflammation diffusely involving breast ducts, vessels and adipose tissue. Prominent hyaline fat necrosis and fibrinoid necrosis of vessels were also noted. In addition, the patient developed plasma cell myeloma 2 years after the LM diagnosis, which raised the differential diagnosis of the breast lesions with plasmacytoma. By immunostains, the infiltrated plasma cells were found to be light chain-restricted, but their immunophenotypes were consistent with non-neoplastic plasma cells. Besides, instead of forming discrete mass lesions, the infiltrated plasma cells were restricted to the periductal and perivascular spaces and the interstitium of adipose tissue with a mixture of both B- and T-lymphocytes. No recurrence was found for the breast lesions after local excision. In addition, the typical panniculitis with hyaline fat necrosis for LM were also readily identified. Altogether, these features favor the diagnosis of LM with light-chain restricted plasmacytic infiltration instead of plasmacytoma.

The light chain restriction for plasma cells in this case also raised the possibility that the patient's breast lesion could be a B cell lymphoma with plasmacytic differentiation. However, no systematic symptom or evidence of lymphoma was identified in this patient. Besides, the inflammatory infiltration of the breast lesion showed a dual population of both T and B cells in addition to plasma cells. Importantly, the patient was followed up for 8 years, and no systematic comorbidity or recurrence of the breast lesion was found. Therefore, it was unlikely that the breast lesion represented a type of B cell lymphoma with prominent plasma cell differentiation.

Light chain restriction has been reported in several types of autoimmune diseases, for example, Russel body gastritis/duodenitis (Zhang et al. 2014), Sjogren syndrome (Jasani 1988), myasthenia gravis (Knight et al. 1986), and cold agglutinins hemolytic anemia (Harboe and Lind 1966), etc. Light chain-restricted plasma cell response likely plays a central role in the production of autoimmune antibodies and the pathogenesis of autoimmune diseases. The kappa-restricted plasma cells in this report may also represent a similar autoimmune response, which was not necessarily associated with an underlying hematopoietic neoplasm. However, associations between autoimmune diseases and plasma cell dyscrasias have been demonstrated in large scale meta-analysis (McShane et al. 2014). Therefore, the light chain-restricted plasma cells in this case may be etiologically correlated with the subsequent development of myeloma. However, no causal evidence of such association can be provided from this single case study. More mechanistic investigations about the etiology of plasma cell myeloma in patients with autoimmune diseases may be helpful to address the question.

In summary, we reported an unusual case of LM in an elderly female patient with long-standing SLE. The patient presented with bilateral breast lesions. Histologically, plasma cell-predominant inflammation involving fat lobules, breast ducts, and vessels were noted. Characteristic hyaline fat necrosis for LM was also identified. Besides, the infiltrated plasma cells were kappa-restricted, but did not show an immunophenotype characteristic for plasma cell neoplasm. Intriguingly, 2 years after the LM diagnosis, the patient developed plasma cell myeloma, which was also Kappa-restricted. Although the occurrence of LM and the subsequently developed myeloma in this case could be incidental, we could not completely exclude the etiological correlation between the two. This case indicated potential necessity to investigate immunophenotypes of the infiltrated plasma cells and to rule out underlying plasma cell neoplasm for LM patients with similar histologic presentations.

Abbreviations

LM: Lupus mastitis; SLE: Dystemic lupus erythematosus; DLE: Discoid lupus erythematosus

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Authors' contributions

Dr. Harbhajanka designed the study and revised the manuscript. Dr. Yan conducted data gathering and manuscript writing. Dr. Oduro, Dr. Gilmore and Dr. Bomeisl provided valuable guidance in study design and manuscript writing. The authors' read and approved the final manuscript.

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References

Bayar S, Dusunceli E, Ceyhan K, Unal E, Turgay M (2007) Lupus mastitis is not a surgical disease. Breast J 13(2):187–188
Belmont HM (2013) Treatment of systemic lupus erythematosus - 2013 update. Bull Hosp Jt Dis (2013) 71(3):208–213
Castro I, Arroyo SC, Yanez V, Cabezas C (2018) Multiple myeloma in systemic lupus erythematosus. Report of two cases. Rev Med Chil 146(5):670–674
Choi JW, Han SW, Kwon KT, Kim GW (2010) Early onset multiple myeloma in a patient with systemic lupus erythematosus: a case report and literature review. Clin Rheumatol 29(11):1323–1326
Crevits J, Van Steen A, Van Ongeval C, Marchal G (2009) Unilateral calcifying lupus mastitis in a male breast. Breast J 15(3):307–308
Kinonen C, Gattuso P, Reddy VB (2010) Lupus mastitis: an uncommon complication of systemic or discoid lupus. Am J Surg Pathol. 34(6):901-6. https://doi.org/10.1097/PAS.0b013e3181da00fb. PMID: 20410809.
Harboe M, Lind K (1966) Light chain types of transiently occurring cold haemagglutinins. Scand J Haematol 3(4):269–276
Jasani B (1988) Immunohistologically definable light chain restriction in autoimmune disease. J Pathol 154(1):1–5
Knight JG, Laing P, Adams DD, Bray JJ, Ling NR (1986) Autoantibodies to acetylcholine receptor in myasthenia gravis: light chains. Neurology 36(11):1531–1533
Maamar M, Tazi Mezalek Z, Harmouche H, Adnaoui M, Aouni M, Maaouni A (2008) Systemic lupus erythematosus and multiple myeloma: an uncommon association. Two cases and literature review. Clin Exp Rheumatol 26(4):667–670
Martella S, Matthes AG, Bassi F, Fasani R, De Lorenzi F, Gatti G, Luini A (2008) Lupus mastitis in male mimicking a breast lump. Int J Surg 6(6):e67–e69
McShane CM, Murray LJ, Landgren O, O'Rorke MA, Korde N, Kunzmann AT, Ismail MR, Anderson LA (2014) Prior autoimmune disease and risk of monoclonal gammopathy of undetermined significance and multiple myeloma: a systematic review. Cancer Epidemiol Biomark Prev 23(2):332–342
Okoli K, Irani F, Horvath W (2009) Multiple myeloma and systemic lupus erythematosus in a young woman. J Clin Rheumatol 15(6):292–294
Rosa M, Mohammadi A (2013) Lupus mastitis: a review. Ann Diagn Pathol 17(2):230–233
Thapa A, Parakh A, Arora J, Goel RK (2016) Lupus mastitis of the male breast. BJR Case Rep 2(2):20150290
Voizard B, Lalonde L, Sanchez LM, Richard-Chesnay J, David J, Labelle M, El Khoury M, Trop I (2017) Lupus mastitis as a first manifestation of systemic disease: about two cases with a review of the literature. Eur J Radiol 92:124–131
Warne RR, Taylor D, Segal A, Irish A (2011) Lupus mastitis: a mimicker of breast carcinoma. BMJ Case Rep 2011
Zhang H, Jin Z, Cui R (2014) Russell body gastritis/duodenitis: a case series and description of immunoglobulin light chain restriction. Clin Res Hepatol Gastroenterol 38(5):e89–e97

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