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Case Report

Breast involvement in mixed connective tissue disease

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ABSTRACT

To date, mammographic involvement in mixed connective tissue disease has not been described in the literature to the authors' knowledge. In addition, only 2 case reports have described panniculitis in mixed connective tissue disease. We present a patient with mixed connective tissue disease with coarse sheet-like calcifications on mammography bilaterally, which increased over time corresponding to rise in levels of anti-dsDNA. Biopsy showed fat necrosis with calcifications, chronic inflammation and fibrosis, vasculitis, as well as CD3, CD4, and CD8+ T cells and CD20+ B cells. These findings are similar histologically and mammographically to "lupus mastitis."

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Clinical case

A 44-year-old African-American female with family history of premenopausal breast cancer and past medical history of mixed connective tissue disease (MCTD), characterized by overlap of systemic lupus erythematosus (SLE), scleroderma, and Raynaud's phenomenon, antibodies positive for dsDNA, RNP, SS-A, Smith, histone, and SCL-70, presented for diagnostic mammography for skin thickening in both breasts. Bilateral large confluent groups of sheet-like coarse calcifications in the left upper-inner, left lower-inner, right upper-inner, and right lower-inner breast were seen (Fig. 1A). The largest of these

groups spanned 6 cm. Bilateral skin thickening was noted, left greater than right. All 4 quadrants were scanned by ultrasound. No discrete masses or nodules were identified. The findings were assessed as BI-RADS Category 4. The decision was made to proceed with stereotactic core biopsy of the left lower inner calcifications.

Multiple tissue samples were obtained of the calcifications in the lower inner quadrant of the left breast. Specimen radiographs confirmed the presence of the calcifications. Pathology showed fat necrosis with calcifications (Fig. 2A), and adjacent breast tissue with chronic inflammation and fibrosis (Fig. 2B). Cytokeratin stain was negative in the area of fat necrosis. Vasculitis was seen within the left breast (Fig. 2C), without lymphangectasia. Lymphocytes stained positive for CD3, CD4, and

Conflicts of interest: None

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E-mail address: Ross.Varma@mountsinai.org (R. Varma).<https://doi.org/10.1016/j.radcr.2019.01.001>1930-0433/© 2019 The Authors. Published by Elsevier Inc. on behalf of University of Washington. This is an open access article under the CC BY-NC-ND license. (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

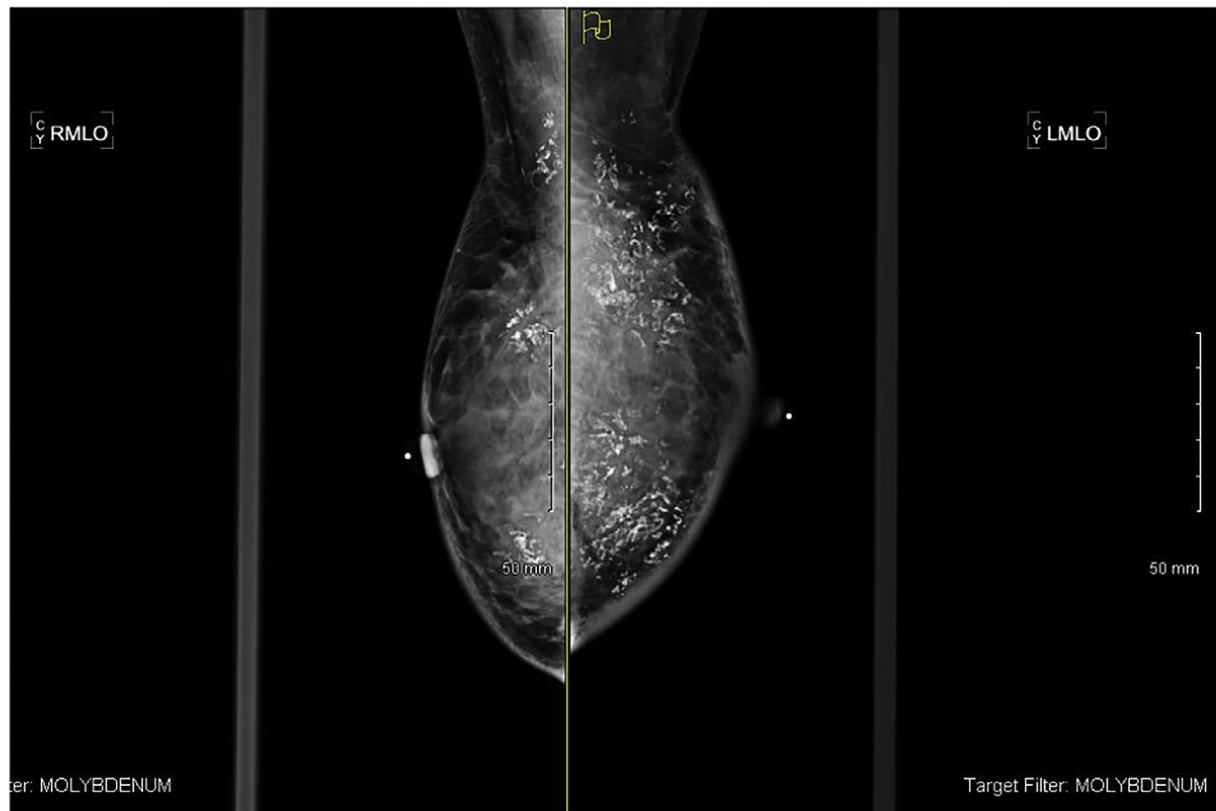
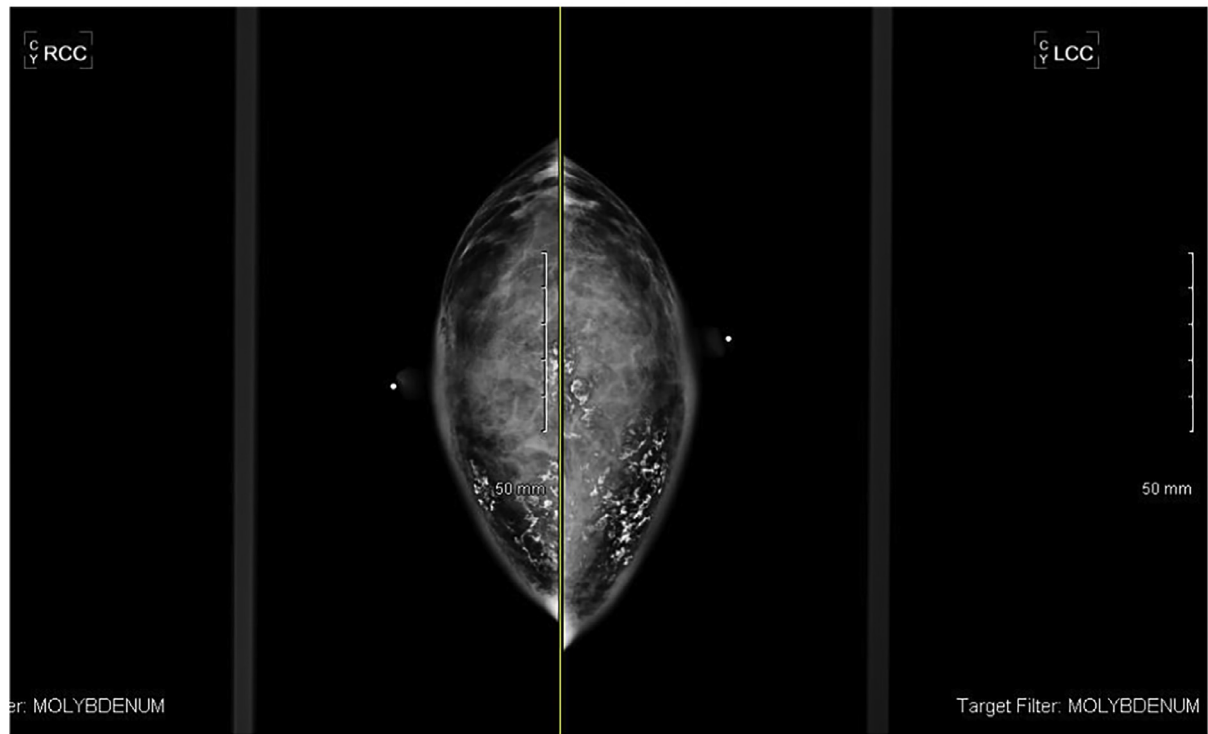
A

Fig. 1 – (A) Mammogram from November 2015, CC and MLO views. (B) Mammogram from November 2016, CC and MLO views.

B

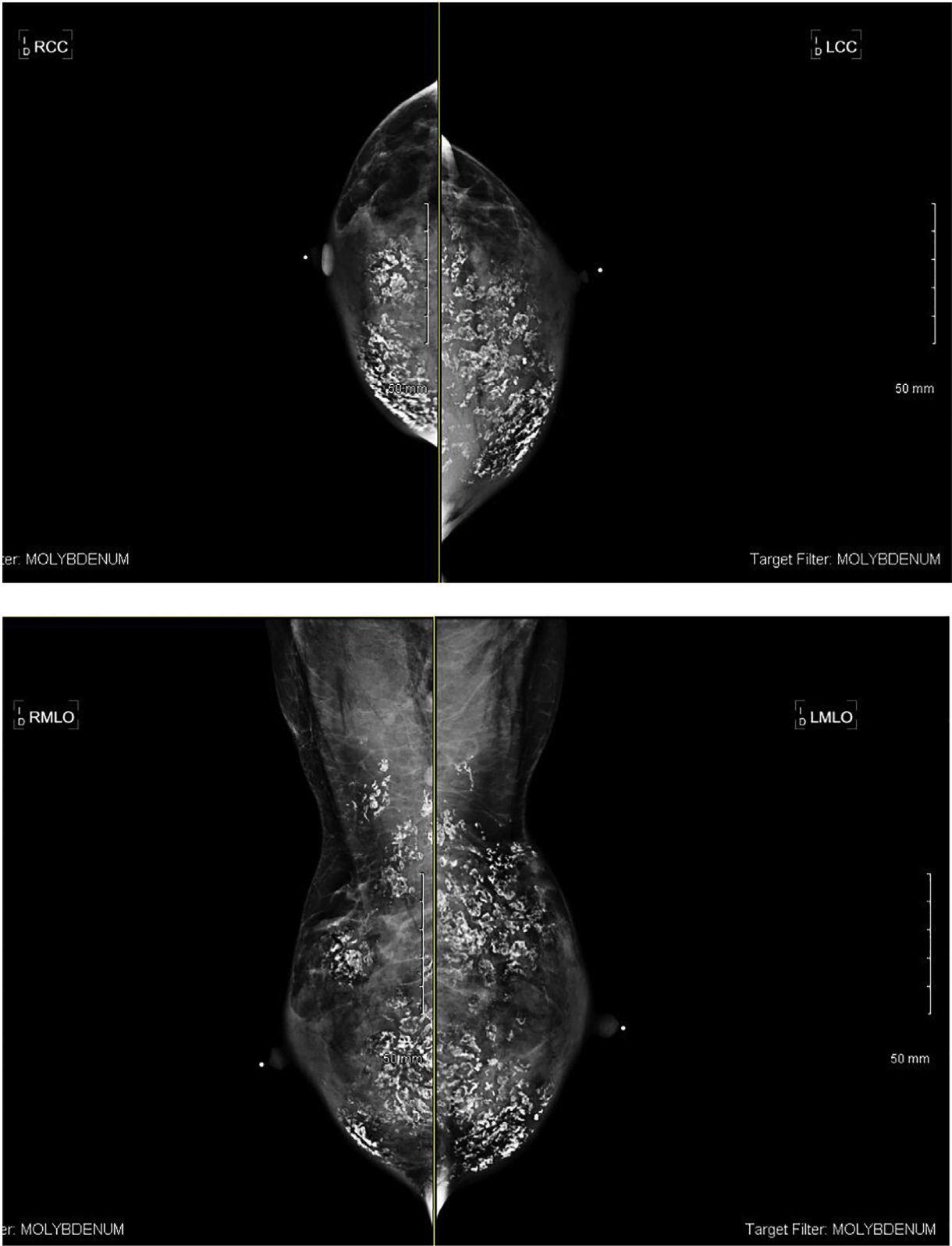


Fig. 1 – Continued

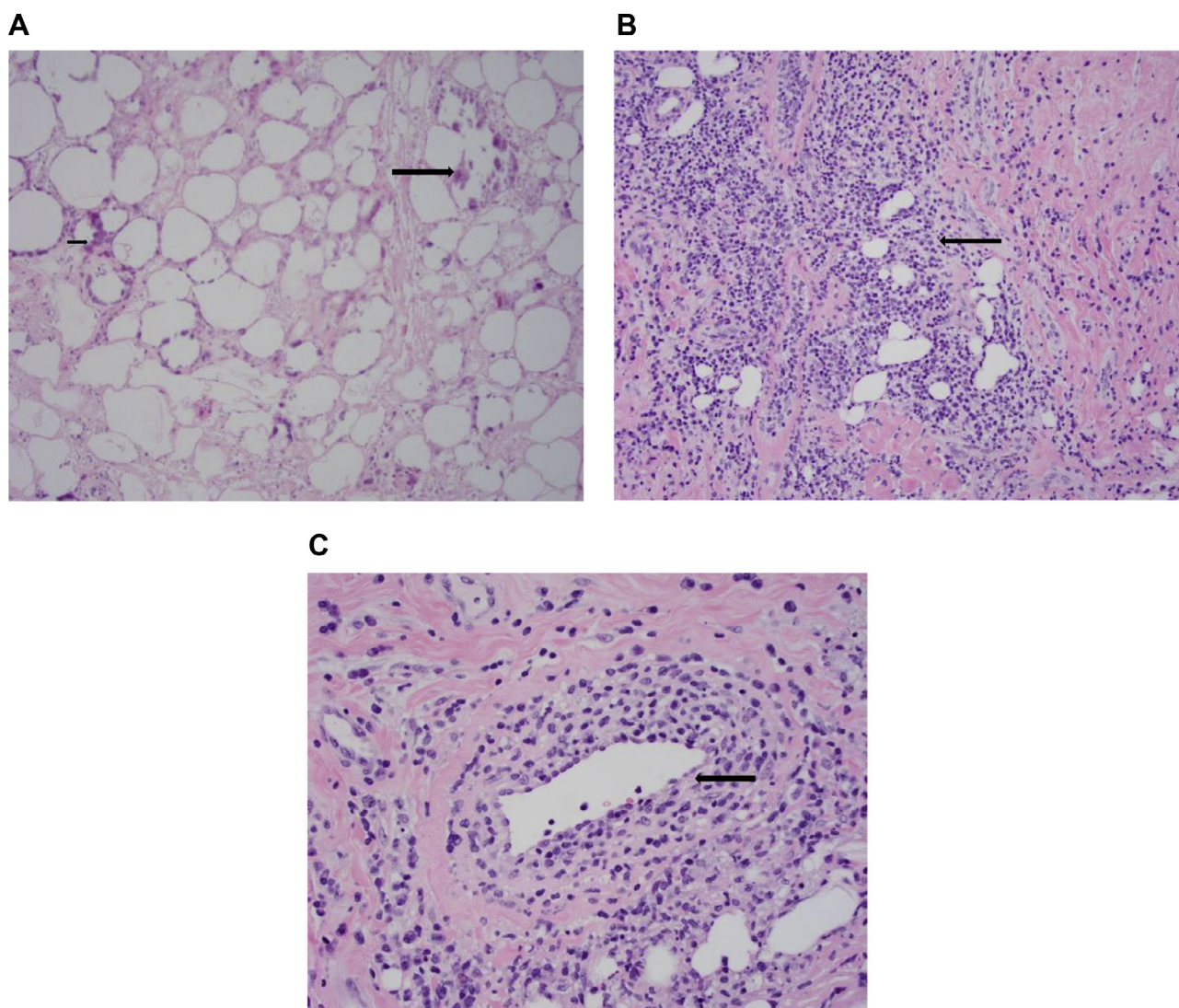


Fig. 2 – (A) H&E stain at 20x magnification. Left breast biopsy shows fat necrosis with calcifications (arrow). (B) H&E stain of left breast biopsy at 20x magnification. Inflammatory infiltrate (arrow) and adjacent fibrosis is consistent with chronic mastitis. (C) H&E stain of left breast biopsy at 40x magnification shows vasculitis.

CD8+ T cells, and CD20+ B cells (Fig. 3), supporting a reactive process. An hourglass tissue marker was placed at the site of biopsy.

Three years prior, the patient had presented with subcutaneous nodularities in the submentum, neck, and bilateral upper thigh, for which she underwent biopsy of a submental mass. This biopsy showed fibroadipose tissue with crushed lymphocytes consistent with panniculitis (Fig. 4). One month later the patient underwent biopsy for a left back mass, which showed panniculitis with necrosis. The lymphocytic infiltrate showed a mixed population of T cells positive for CD2, CD3, CD4, CD5, CD7, and CD8, and CD20+ B cells. Vasculitis and lymphangectasia were not seen in this sample.

The patient was instructed to follow up in 6 months for bilateral mammography, but returned 1 year later. On examination, sheet-like calcifications in both breasts had increased in the areas noted previously (Fig. 1B), corresponding to an

increase in quantitative dsDNA antibody levels in the interim (Fig. 5). These findings were given BI-RADS Category 3. Given the family history of premenopausal breast cancer, the patient's heterogeneously dense breast tissue, and the limited visualization of breast tissue by ultrasound, the patient was given the recommendation to follow up with mammography in 6 months and consider MRI for possible additional screening. The patient was lost to follow-up.

Discussion

This case report is the first to describe the mammographic appearance of MCTD within the breast. It also describes the third case report of panniculitis in MCTD, and describes its histologic appearance.

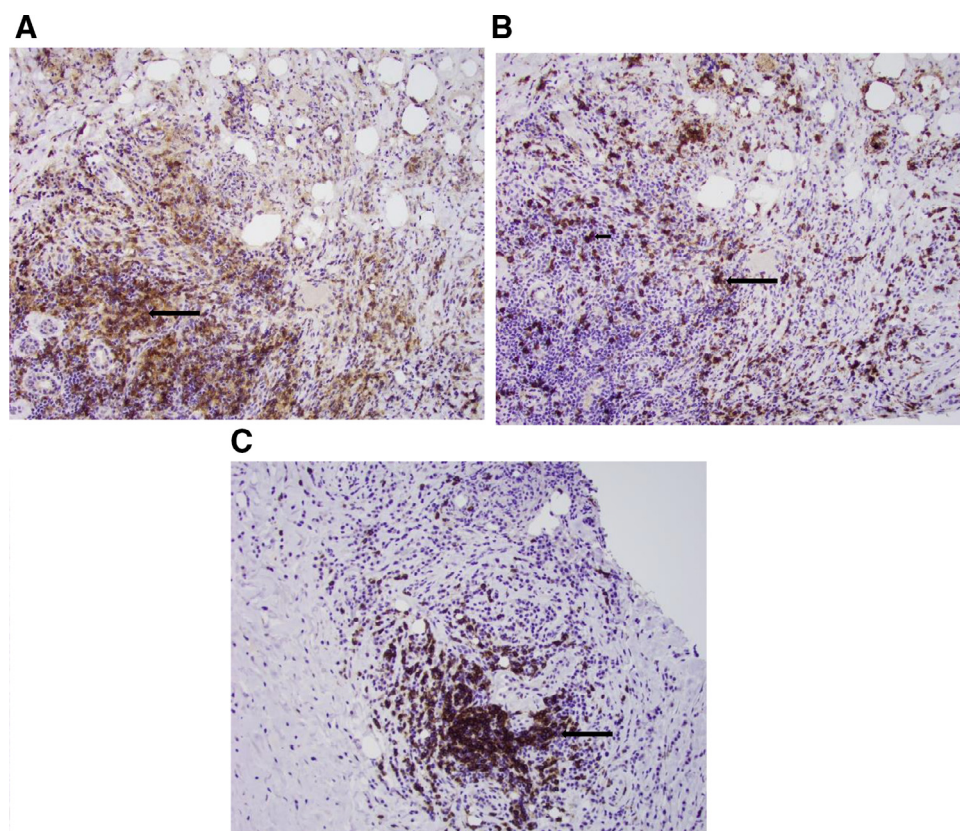


Fig. 3 – 20× magnification of left breast biopsy after horseradish peroxidase stain (brown) for CD4 (A) CD8 (B), and CD20 (C).

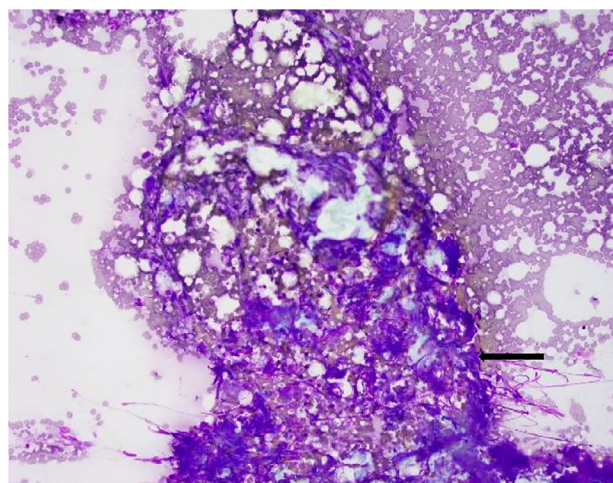


Fig. 4 – Diff-Quick stain at 20× magnification. Submental mass biopsy shows fibroadipose tissue with crushed lymphocytes, consistent with panniculitis.

Breast involvement in MCTD was first reported in 1994 when a patient presented with a 3 month history of bilateral breast enlargement [1], where histology showed edematous and fibroadenotic breast tissue, a T-cell infiltrate, lymphang-

iectasia, and a non-necrotizing vasculitis. The patient was treated with prednisolone until symptoms resolved 4 months later. Of the histologic features described, our patient's biopsy results show in common fibrosis, a non-necrotizing vasculitis, and T-cell infiltrate.

Panniculitis is a very rare entity in MCTD, with only 2 case reports described in the literature [2,3]. Of these reports, MCTD panniculitis has never been described to affect the breasts. In the first case report, a skin biopsy from an affected patient's leg showed septal panniculitis with lymphocytic infiltrate and fat necrosis, multiple dermal lymphangiectasis, and dilation of venules between fat lobules [2]. In the second case report, a skin biopsy from a patient's abdomen revealed septal fibrosis and lipomembranous changes [3]. In common with these described findings, panniculitis with fat necrosis and fibrosis were seen in our patient, however lymphangiectasis was not seen.

A subset of SLE, lupus panniculitis, results in inflammation of the subcutaneous adipose tissues. When SLE affects the breasts, this is known as lupus mastitis [4]. Lupus mastitis, typically but not always, presents as a single tender mass on clinical exam [4], and may show similar appearing calcifications on mammography as our patient [5]. Our patient did not present with breast tenderness, perhaps because it was relatively early in the disease process. Features of lupus mastitis include masses in the breast, axillary lymphadenopathy, fat necrosis, fibrosis, and calcifications. The mean age of presen-

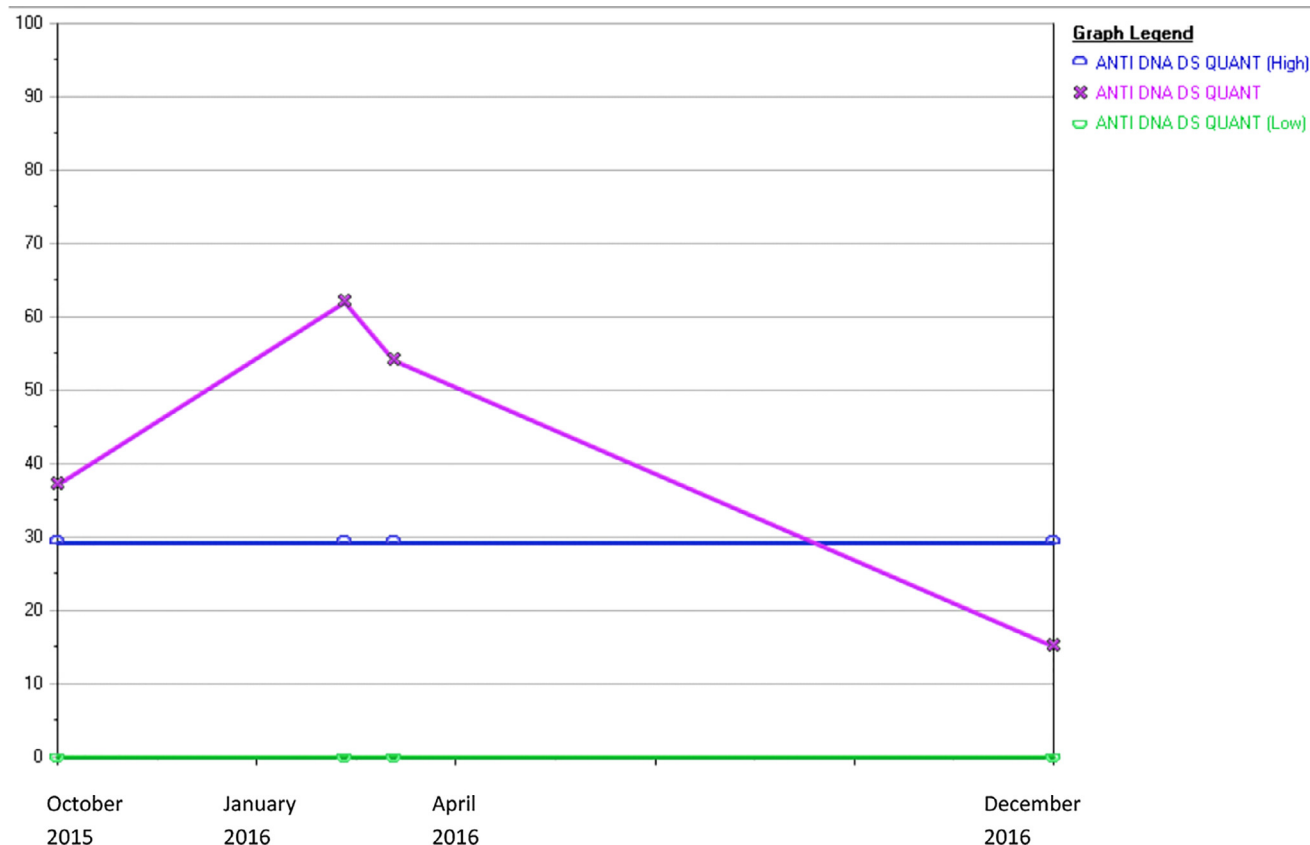


Fig. 5 – Quantitative anti-dsDNA levels are shown by the magenta line over time. The horizontal blue and green lines represent the bounds of normal values for the test. Levels were initially elevated and increased between the patient's mammograms in November 2015 and 2016. The patient's values returned to normal limits in December 2016.

tation is 37 years old, and predominantly women are affected, fitting the demographic profile of our patient [4]. Pathology pathognomonic for lupus mastitis includes lymphocytic infiltration, occasional germinal centers, and marked hyaline fat necrosis with sclerosis. The inflammatory infiltrate in lupus mastitis is described as a mixed T and B-cell population, with predominantly CD3+, CD4+ T cells intermixed with CD20-positive B cells and polyclonal plasma cells [6]. This infiltrate is similar to that seen in our patient. Lymphocytic vasculitis is also common in lupus mastitis [6], and was also seen in our patient.

Given the similar histological and mammographic presentation of “lupus mastitis” and our patient with MCTD, more research is needed to determine if there is a common pathologic mechanism. Additionally, MCTD mastitis may manifest along a continuum of inflammatory changes. More radiologic, pathologic, and clinical research is needed to further understand MCTD manifestations within the breast.

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