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CASE REPORT

Imaging Findings of Progressing Rosai–Dorfman Disease of the Breast: a Case Report and Literature Review

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INTRODUCTION

Rosai–Dorfman disease (RDD) or sinus histiocytosis with massive lymphadenopathy is a rare benign proliferative disease of histiocytes with unclear aetiology. Destombes first described the histological findings in 1965, and Rosai and Dorfman described the entity as sinus histiocytosis with massive lymphadenopathy in 1969.[1,2] Its classic manifestation is painless massive cervical lymphadenopathy in young patients although involvement of other nodal groups has also been described. Extranodal involvement is common and present in up to 43% of cases.[3] Exclusive extranodal disease is less common, present in up to 23%.[3] Breast parenchymal involvement is extremely rare with about 40 cases reported.[4,5] RDD of the breast can mimic breast cancer radiologically. To the best of our knowledge, RDD of the breast with progressing radiological features in addition to increase in number or size of masses has not been described in the literature in the context of suspected malignancy. We present such a case and review the radiological and pathological features. It is important to raise awareness of this rare but important breast cancer mimicker.

CASE PRESENTATION

A 56-year-old lady with good past health and no family history of breast cancer, presented with a 1-month history of palpable right breast mass at the upper inner quadrant. Mammogram (MMG) with craniocaudal and mediolateral oblique views demonstrated focal asymmetry at the upper inner quadrant of the right breast (Figure 1). Ultrasound (USG) revealed a 1.4 cm × 0.8 cm circumscribed parallel oval hypoechoic mass with posterior acoustic enhancement at 1 o'clock, 8 cm from the nipple, corresponding to the focal asymmetry seen on MMG and the palpable mass (Figure 2). According to the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) 5th edition the mass was classified as category 3: probably benign (>0% but ≤2% likelihood of malignancy). The patient was subsequently referred to breast surgery team for management of palpable breast mass.

Bedside USG 6 months later demonstrated interval enlargement of the mass (2.2 cm × 0.9 cm × 2.6 cm) and right axillary lymphadenopathy. Bedside USG-guided core biopsy of the mass and fine needle aspiration of right

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Ethics Approval: This case report was conducted in accordance with the Declaration of Helsinki. The patient provided consent for all tests and procedures.

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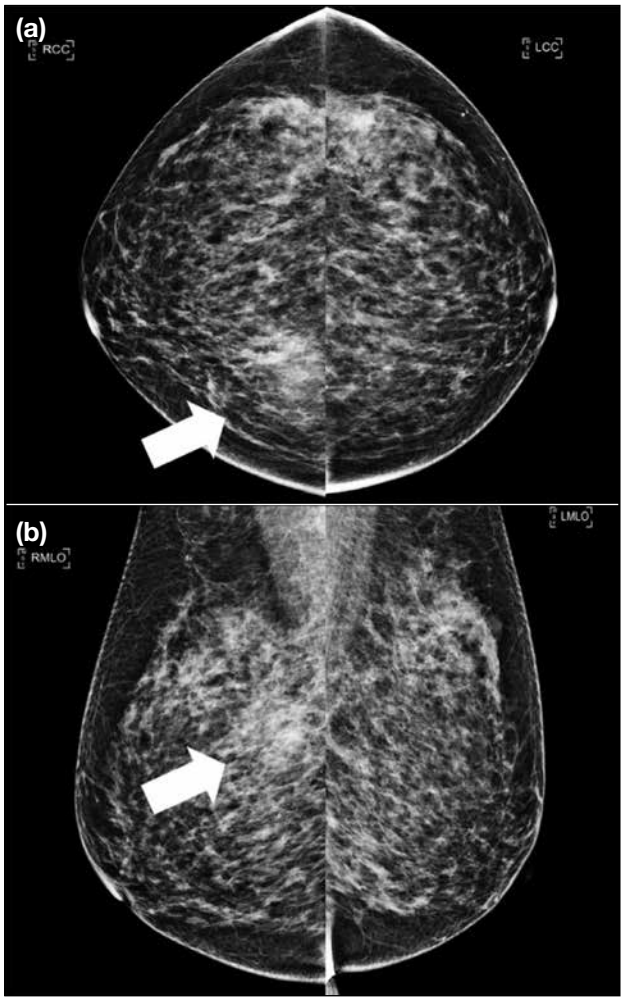

Figure 1. Bilateral mammogram with (a) craniocaudal and (b) mediolateral oblique views. Focal asymmetry at upper inner quadrant of right breast (arrows). No lymphadenopathy is evident.

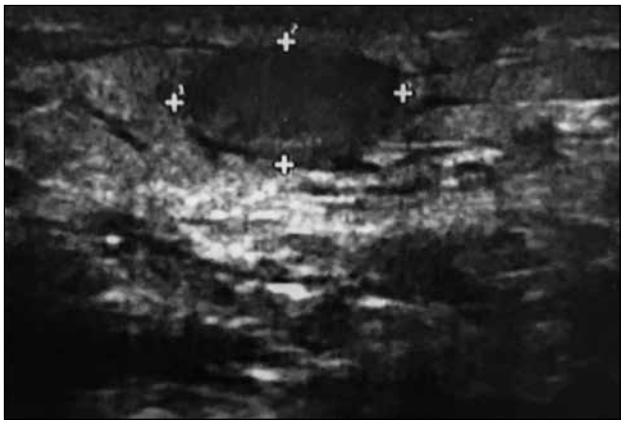

Figure 2. Selected image of ultrasound right breast mass. A 1.4 cm × 0.8 cm circumscribed parallel oval hypoechoic mass with posterior acoustic enhancement at 1 o'clock, 8 cm from the nipple, corresponding to the focal asymmetry and the palpable mass.

axillary lymphadenopathy was performed. Pathology results showed features of RDD for both the right breast mass and right axillary lymph node with no evidence of malignancy (Figures 3 and 4). The patient opted for conservative treatment with clinical and imaging follow-up.

Follow-up MMG performed 2 years after the initial presentation showed further interval increase in size of the focal asymmetry and development of associated overlying skin thickening. Right axillary lymphadenopathy was also noted in the mediolateral oblique view (Figure 5). USG showed interval increase in size of the mass (2.6 cm × 1.5 cm × 3.0 cm) with indistinct margin. Associated subcutaneous oedema and overlying skin thickening was demonstrated. Doppler USG showed increased vascularity adjacent to the mass (Figure 6a to c). Right level I axillary lymphadenopathy with cortical thickening up to 0.4 cm was noted (Figure 6d).

In view of the interval enlargement of the mass as well as development of indistinct margin and skin changes the mass was re-classified as BI-RADS assessment category 4A: low suspicion for malignancy (>2% but ≤10% likelihood of malignancy). Tissue diagnosis was suggested despite prior pathology showing RDD. Repeat USG-guided core biopsy of the mass and fine needle aspiration of right axillary lymphadenopathy were performed. Pathology again showed features of RDD with no evidence of malignancy.

The patient opted for conservative treatment. There were no clinical signs or symptoms to suggest associated or underlying conditions. No further investigations including blood tests for inflammatory or autoimmune markers were performed. She remains healthy 3 years after the initial presentation.

DISCUSSION

The precise pathophysiology of RDD remains unknown. It has been proposed to be related to inherited conditions such as histiocytosis-lymphadenopathy plus syndrome, neoplastic conditions such as lymphoma and myelodysplastic syndrome, immune-related diseases such as systemic lupus erythematosus, immunoglobulin G4–related disease, and infection such as herpes simplex virus 6.[5,6]

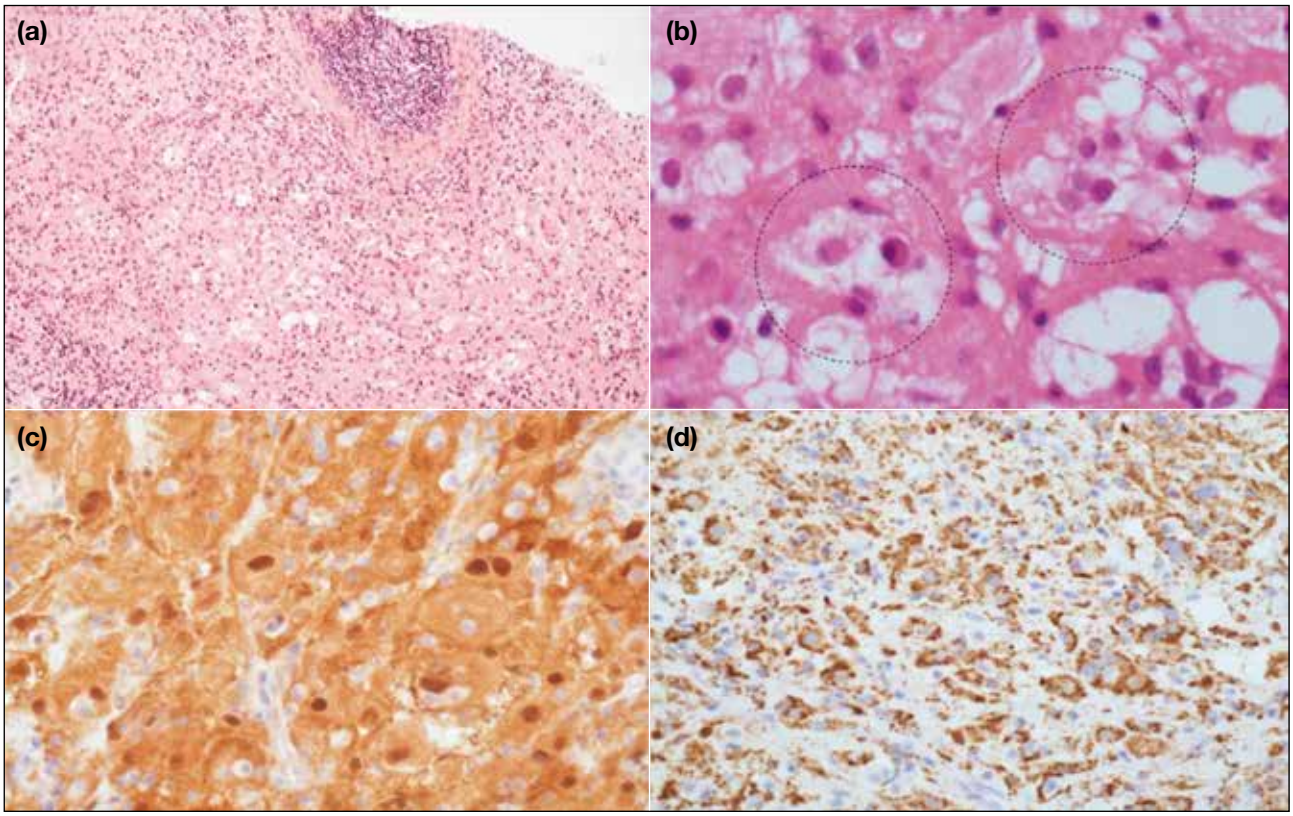

Figure 3. Histopathology findings of core biopsy of right breast mass. (a) Lower-power view (×4): section showed cores of tissue with lymphocytes, plasma cells and histiocytes infiltration. (b) High-power view (×40): presence of emperipolesis: enlarged histiocytes engulfing lymphocytes and plasma cells (circles). (c) Immunostaining showing S-100 protein positive histiocytes (brown). (d) Immunostaining showing CD68 positive histiocytes (brown).

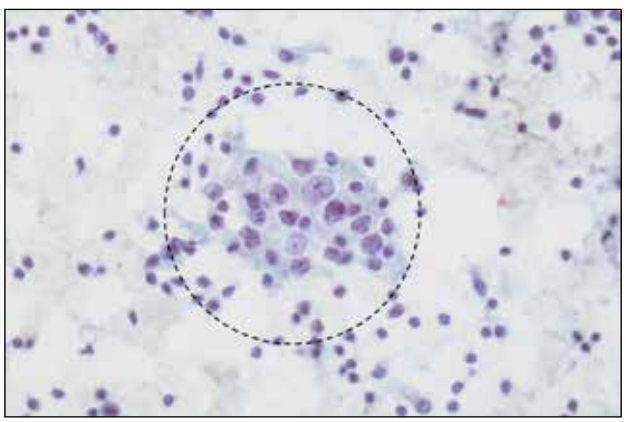

Figure 4. Fine-needle aspiration cytology of right axillary lymph node (×40). Presence of emperipolesis: enlarged histiocytes engulfing lymphocytes and plasma cells (circle).

RDD can manifest with a wide range of phenotypes. The classic presentation is painless massive cervical lymphadenopathy in children or young adult males.[4] Other symptoms may include fever, night sweats, weight loss, and organ-specific symptoms depending on the site of involvement.[7] Extranodal disease is not uncommon, present in up to 43% of cases; the most commonly involved sites are skin and subcutaneous tissue, upper respiratory tract, skeletal system and salivary glands.[3,8] Breast parenchymal involvement is extremely rare, reported in only about 40 cases.[4] Cases with exclusive breast involvement are mostly women aged >50 years who present with single or multiple palpable lesions or an abnormal screening MMG.[9,10] Male breast involvement has also been described.[7]

The imaging findings of RDD of the breast overlap those of malignant lesions and occasionally mimic other typically benign lesions. On MMG, RDD of the breast can manifest as an irregular mass with indistinct margins, a circumscribed mass or asymmetry. Associated architectural distortion has also been described.[3,5,11] On USG, it usually manifests as a hypoechoic mass with indistinct or angulated margins.

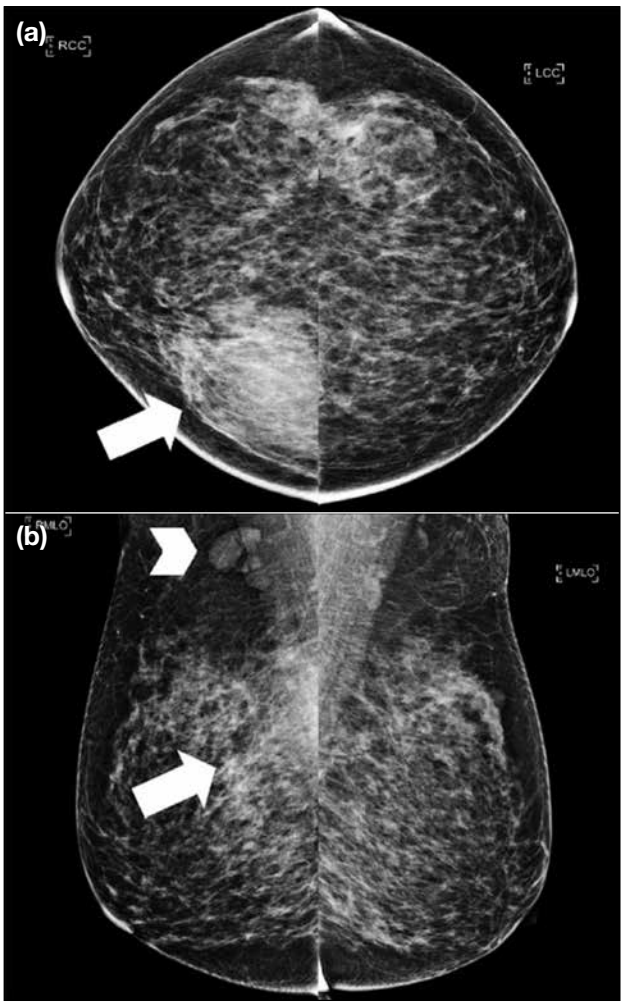

Figure 5. Follow-up bilateral mammogram with (a) craniocaudal and (b) mediolateral oblique (MLO) views. Known focal asymmetry at upper inner quadrant of right breast shows interval increase in size (arrows), with overlying skin thickening. Right axillary lymphadenopathy was shown in MLO view (arrowhead).

Increased intralesional vascularity on Doppler USG is also a reported feature.[5] Cases with sonographic features mimicking cyst and fibroadenoma have been described as well.[9] Mammographic and sonographic findings of RDD of the breast are usually indistinguishable from those of malignant lesions. They are usually classified as BI-RADS category 4 or 5 and warrant tissue diagnosis. Associated axillary lymphadenopathy is not uncommon and present in up to 38% of cases.[5] In our patient, the imaging features progressed at follow-up examination, with interval increase in size of the mass, development of indistinct margins, and skin changes, hence BI-RADS assessment category was upgraded from 3 to 4A. To the best of our knowledge, such progression has not been described in the literature.

Laboratory findings of RDD are non-specific and include elevated erythrocyte sedimentation rate, anaemia, leucocytosis, and polyclonal hypergammaglobulinaemia.[3]

Definitive diagnosis relies on cytological evaluation of fine needle aspiration, histopathological analysis of core needle biopsy or surgical excision.[12,13] Regardless of the presence of nodal or extranodal disease, or the site of involvement, RDD is characterised by aggregation of large polygonal histiocytes. Pathological hallmark features of this disease include emperipolesis (passage of intact lymphocytes within intracytoplasmic vesicles of histiocytes), S-100 protein and CD68 positivity, and CD1a negativity.[12,13]

It remains controversial whether patients with proven RDD should be investigated for other sites of involvement, including those with breast involvement. Some authors suggest further evaluation with ^{18}F-fluoro-2-deoxyglucosepositron emission tomography/computed tomography, whole-body computed tomography, whole-body magnetic resonance imaging, or selected imaging based on symptoms of organ involvement, but no consensus has been established.[5,6] Others suggest that systemic investigation is not necessary in patients with unifocal RDD of the breast who are otherwise asymptomatic.[14]

The clinical course of RDD varies from spontaneous regression, stable persistent disease, disease progression, to fatality.[3,8,15] Risk factors associated with a poor prognosis include involvement of larger number of nodal groups, more extranodal system involvement, involvement of the lower respiratory tract, liver or kidneys, and immunological abnormalities.[3,5,6] The clinical course of RDD of the breast remains uncertain due to the limited number of reported cases.[11]

Treatment for RDD includes observation, corticosteroids, immunomodulatory drugs, surgery, chemotherapy, and radiotherapy.[6] However, there is no consensus on the optimal management. In 2018, the Rare Histiocytoses Steering Committee and Working Group of the Histiocyte Society approved a management algorithm for RDD. For asymptomatic extranodal disease, observation was suggested since 20% to 50% of patients with nodal or cutaneous disease will have spontaneous remission. This is suitable for patients with uncomplicated lymphadenopathy or asymptomatic cutaneous RDD and potentially for those with asymptomatic disease at other sites.[6] For symptomatic extranodal disease, resection of single-site disease, which could be curative,

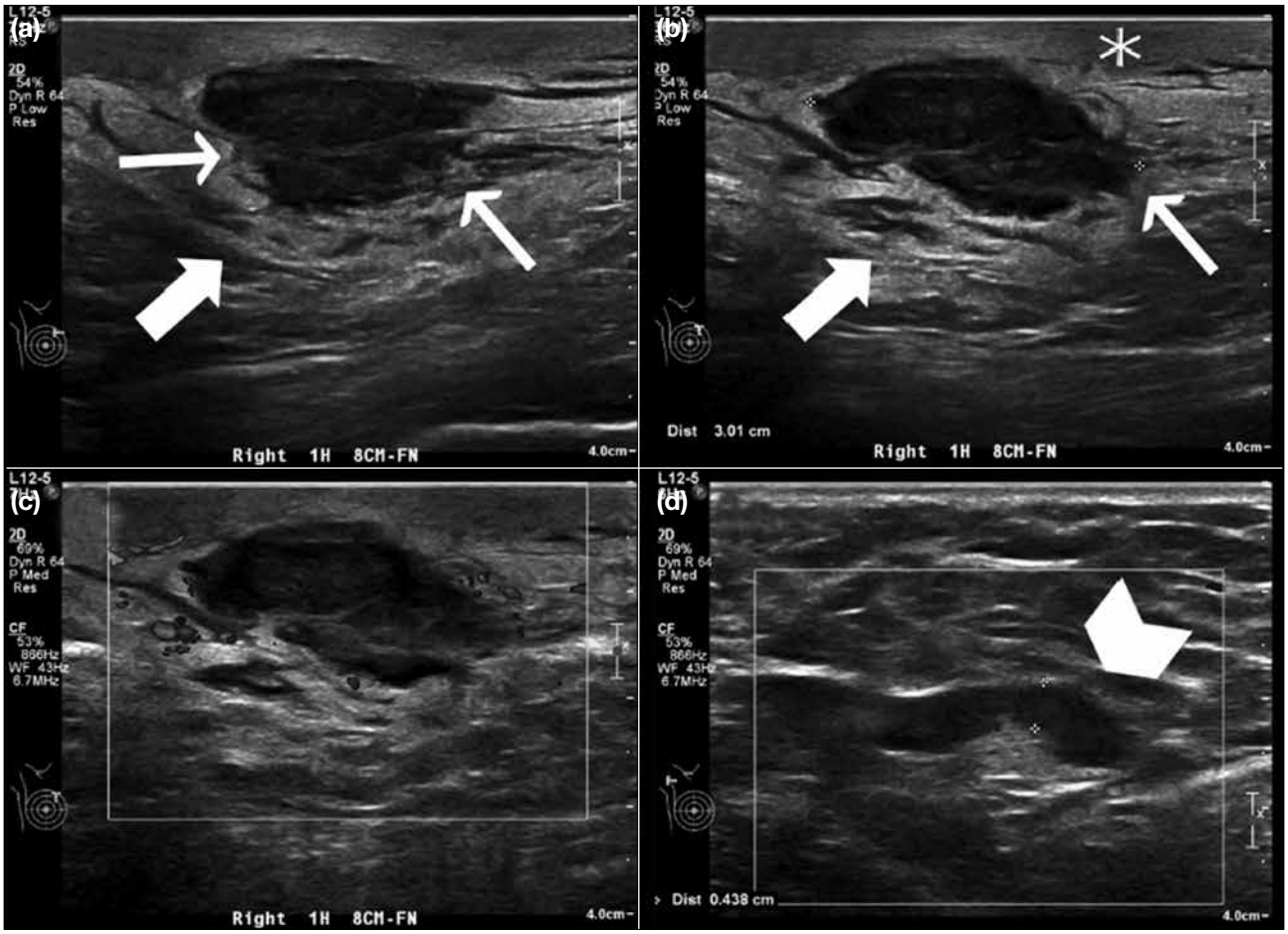

Figure 6. Selected images of ultrasound of right breast mass and axillary lymph nodes. (a to c) Interval increase in size of the 1 o'clock mass, with partial indistinct margin (thin arrows). Associated subcutaneous oedema (thick arrows) and overlying skin thickening (asterisk) was also noted. Increased vascularity adjacent to the mass is demonstrated. (d) Right level I axillary lymphadenopathy with cortical thickening (arrowhead).

systemic therapy for unresectable or multifocal disease and resection/debulking of sites causing neurologic or end-organ dysfunction are proposed.[6] However, the proposed management algorithm does not specifically address RDD of the breast: there is no proposed follow-up schedule, and no comments about the need for re-biopsy or subsequent management when there is progression in size or radiological features of the breast lesion in an otherwise asymptomatic patient, as in our case. To the best of our knowledge, no reported cases with a preoperative diagnosis of RDD of the breast was subsequently upgraded after surgical excision. Whether there is a need to re-biopsy and what is the appropriate management when there is progression in size and radiological features of a known breast RDD lesion requires further study.[10,14]

CONCLUSION

We report a case of RDD of the breast with progressing radiological features. We describe the radiological and pathological features and review this entity. It is important to raise awareness of this rare but important breast cancer mimicker.

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