

## Case report

# Rosai-Dorfman disease of the breast: A case report

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A case report of Rosai-Dorfman disease (sinus histiocytosis with massive lymphadenopathy) of the breast is one of the rare diseases, characterized by benign proliferative disorder of histiocyte. Most of them occur within lymph nodes whereas the rest involve extranodal sites. Breast involvement is considered extremely rare but considerable because of radiological findings simulating breast cancer. We hereby report a case of a 59-year-old Thai woman who underwent screening mammography. Her biopsy resulted in abnormal histiocytes with S-100 protein expression, some of them with emperipolesis (lymphophagocytosis). Recognition of Rosai-Dorfman disease leads to correct diagnosis and further appropriate proper treatment strategy.

**Keywords:** Breast, Rosai-Dorfman disease.

Rosai-Dorfman disease (RDD) is a benign proliferative non-Langerhans cell histiocytosis, typically affects lymph nodes, especially cervical regions. Extranodal involvement alone occurs about 23.0% and commonly affects the skin, soft tissue, upper respiratory tract, eyes, and bone. The breast is an unusual site ( $< 1.0\%$ )<sup>(1)</sup> and less than 40 cases have been reported in literatures.<sup>(2)</sup> Our case seems to be the first in Thailand with breast involvement. Patients are primarily childhood and early adulthood with female predilection<sup>(3)</sup> but less common in Asians.<sup>(1)</sup> Treatment options can vary according to the severity or vital organ involvement.<sup>(4)</sup> Most RDD is spontaneous regression or response well to therapy. Few cases of death have been reported, particularly those with multiorgan involvement.<sup>(5)</sup>

## Case presentation

A 59-year-old Thai woman underwent routine screening mammography. She had no clinical history of Rosai-Dorfman disease or radiographic evidence of extramammary involvement. Her first mammogram was performed two years earlier with negative

findings. Her second study revealed a 0.7-cm new isoechoic mass with circumscribed margin in subcutaneous layer at the lower inner quadrant of the left breast on ultrasonography (**Figure 1**) whereas mammography shows no demonstrable abnormality. Her first biopsy showed chronic inflammation, no immunohistochemical evidence of carcinoma, plasma cell neoplasm, or IgG4-related disease. Owing to benign pathology and concordant with imaging, the management was observation. Follow-up mammography the next 14 months found developing asymmetry without associated calcification at the lower inner quadrant of the left breast (**Figure 2**) and ultrasound showed increasing size of the irregular heterogeneous echoic mass with echogenic rim and developing internal vascularity (**Figure 3**).

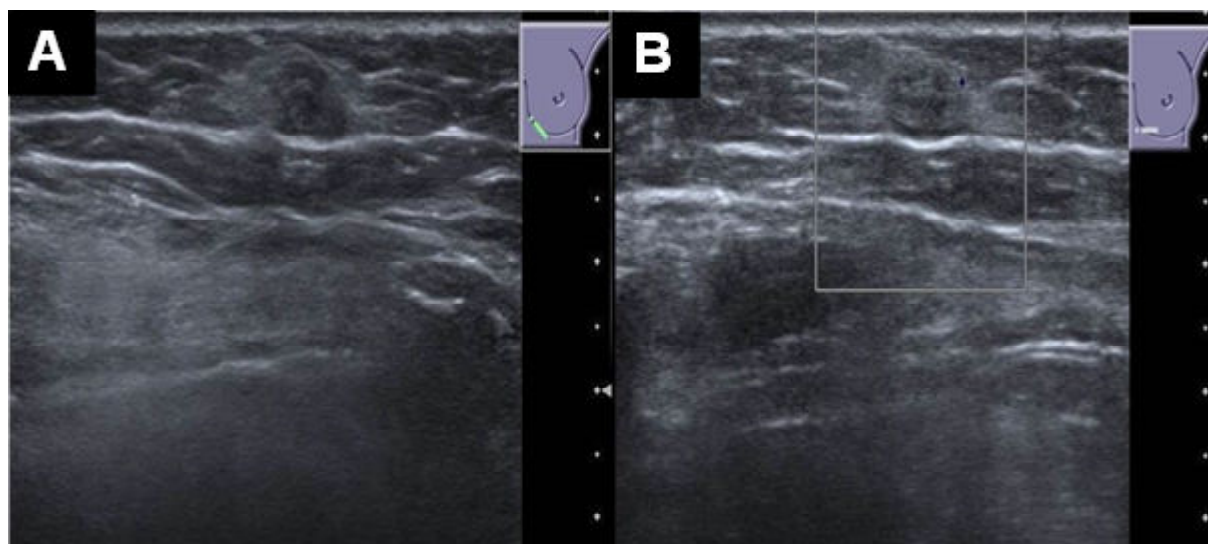
Then core needle biopsy was repeated, yielding chronic mastitis, suspicious for extranodal Rosai-Dorfman disease. Her second biopsy resulted in a number of abnormal histiocytes with S-100 protein expression in nucleus and cytoplasmic staining, some of them with emperipolesis (histiocytes that engulfed intact lymphocytes and/or plasma cells). CD68 was positive and CD1a was negative. IgG4 plasma cells are less than 10.0% of the total IgG<sup>+</sup> plasma cell, thus IgG4-related disease was excluded. Excision of the whole breast mass was recommended for a complete pathological examination. Afterwards, our patient underwent wide excision with needle-guided wire localization under ultrasound guidance.

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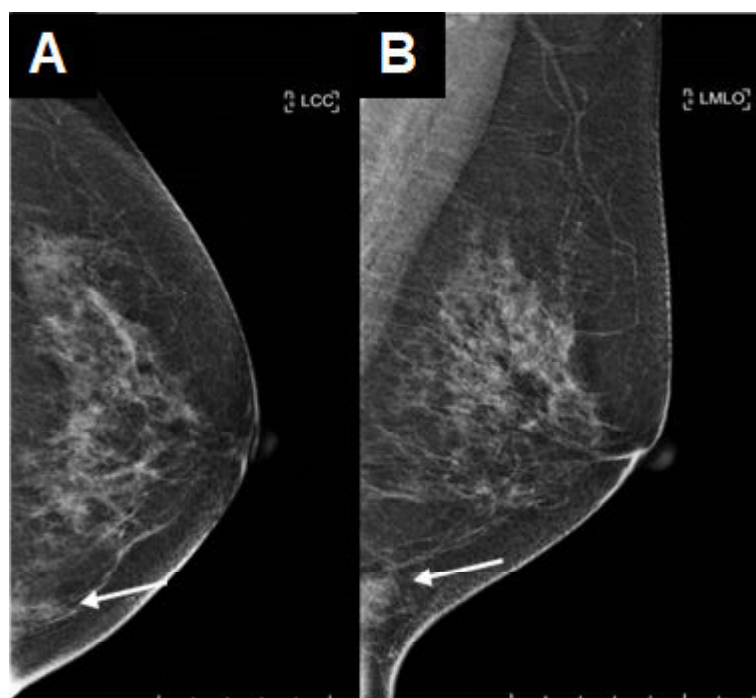
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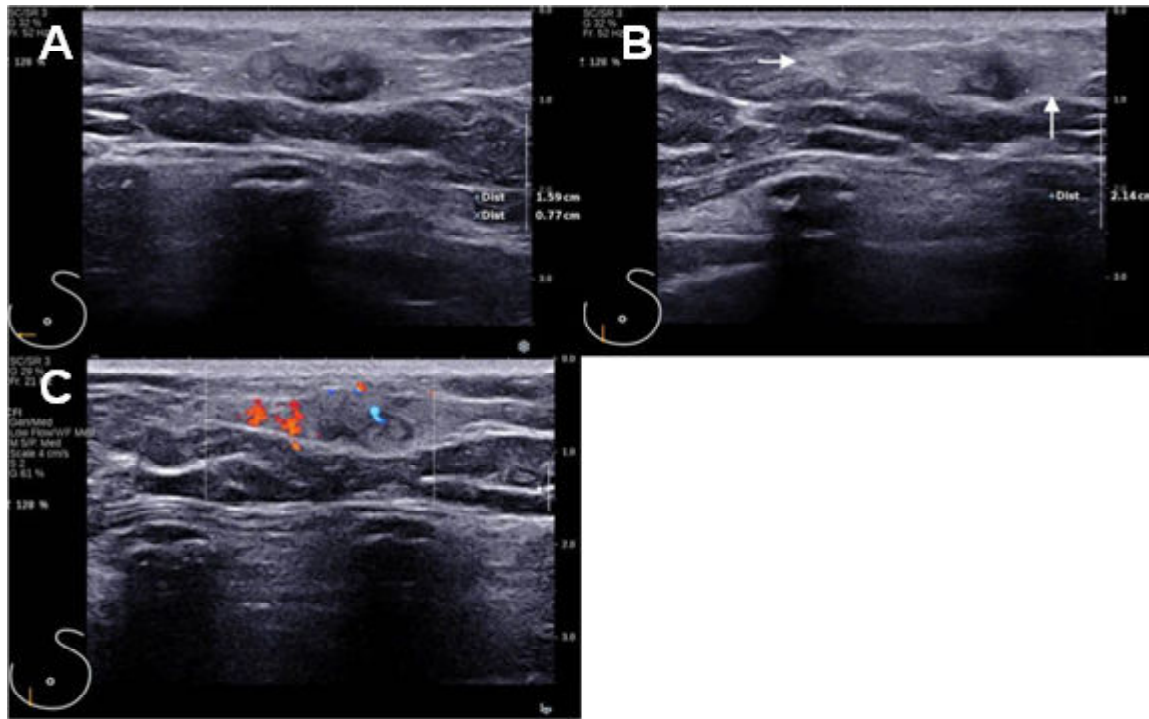
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**Figure 1.** Grayscale (A) and color Doppler ultrasound (B) images demonstrated a 0.7-cm circumscribed isoechoic mass without vascularity in subcutaneous layer at the lower inner quadrant of the left breast.



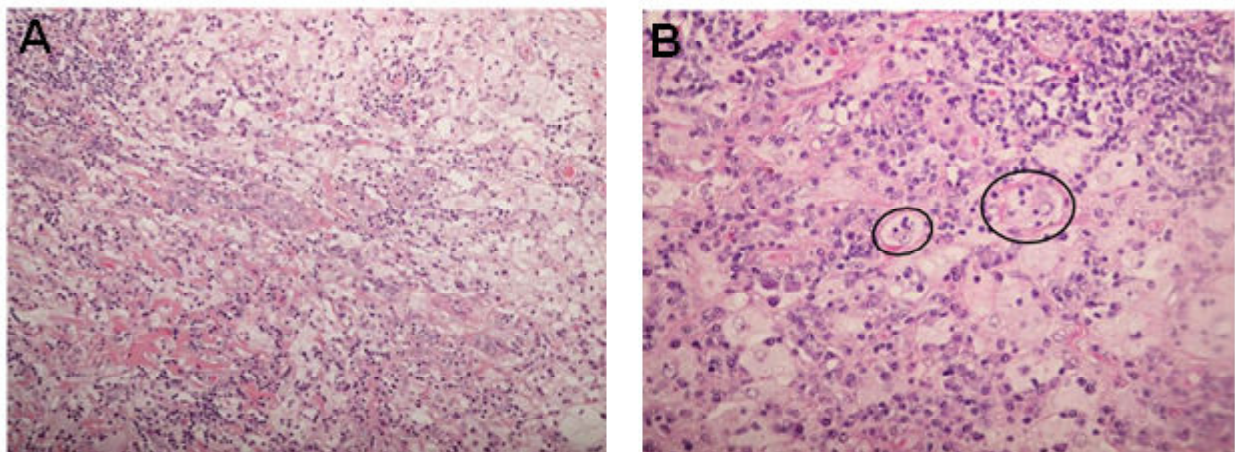
**Figure 2.** Full-field digital diagnostic mammograms (A) craniocaudal view (B) mediolateral oblique view showed a focal asymmetry without calcifications at the lower inner quadrant of the left breast (arrows).



**Figure 3.** Grayscale (A) transverse view (B) longitudinal view and (C) color Doppler ultrasound follow-up images showed increasing size of the irregular heterogeneous echoic mass with echogenic rim (arrows in B) and developing internal vascularity, measuring 0.8 x 1.6 x 2.1 cm.

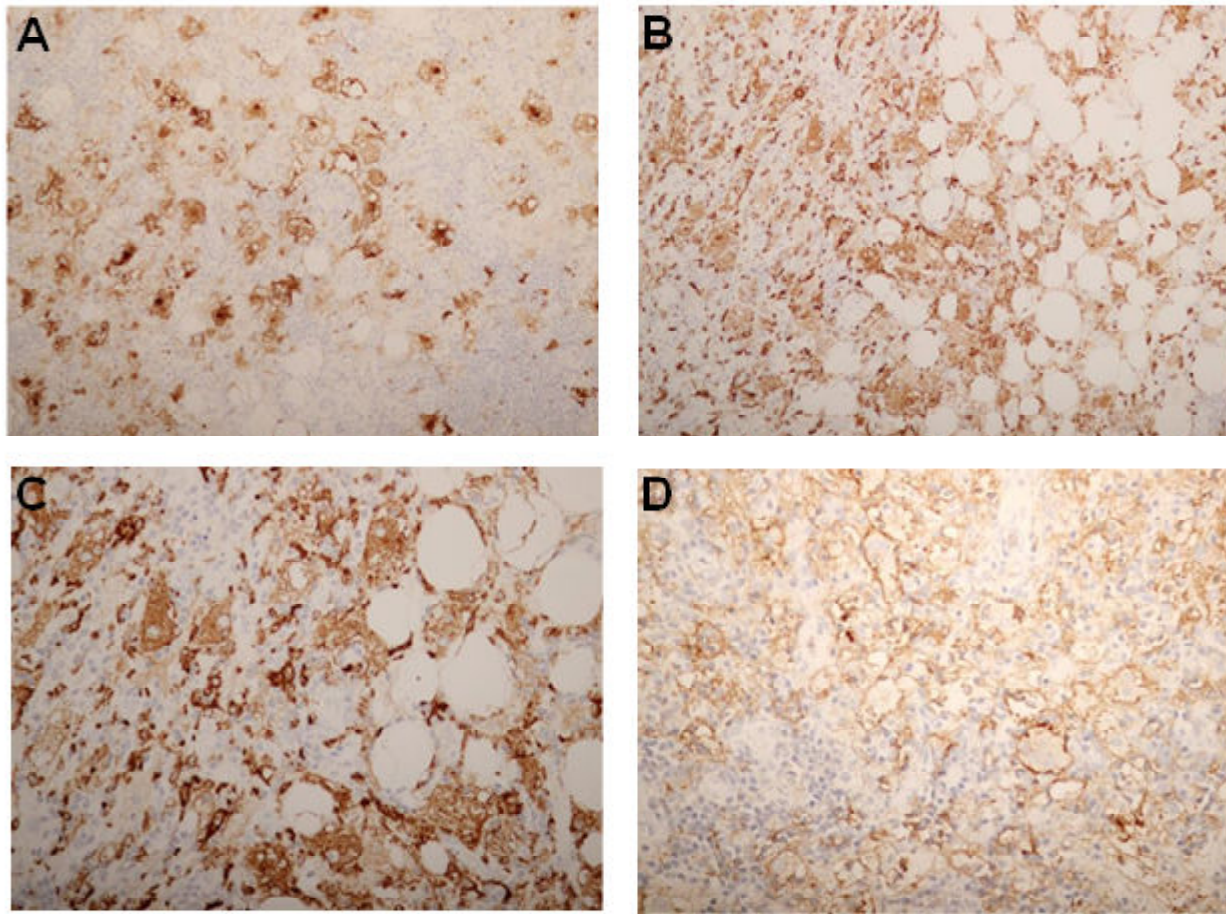
The final pathological report confirmed the diagnosis of RDD with negative all surgical margins. The specimen showed mixed inflammatory cell infiltration, involving breast stroma and glandular component. Multinodular aggregates of typical large histiocytes in a background of lymphocytes and plasma cells are noted (**Figure 4A**). The lesion contained numerous characteristic, large histiocytes with round vesicular nuclei and abundant pale eosinophilic

cytoplasm. High power view of typical histiocyte revealed emperipolesis (phagocytosis of intact lymphocytes and plasma cells) as shown in **Figure 4B**. Microscopic examination also showed positive for S-100 (**Figure 5A**), CD68 (**Figure 5B**), CD 163 (**Figure 5C**), and CD14 (**Figure 5D**). She had no complications after surgery and was discharged the next day after hospitalization.



**Figure 4.** Microscopic examination showed mixed inflammatory cell infiltration, involving breast stroma and glandular component. (A) Multinodular aggregates of typical large histiocytes in a background of lymphocytes and plasma cells are noted, (H and E stain, 20X). (B) The lesion contained numerous characteristics, large histiocytes with round vesicular nuclei and abundant pale eosinophilic cytoplasm. Some typical histiocytes also showed emperipolesis (circles), (H&E stain, 40X). H&E - Hematoxylin and Eosin





**Figure 5.** (A) Specimen revealed large histiocytic cells, staining in nucleus and cytoplasm with S100 protein (20X), (B) lesional histiocytes staining with CD68 (20X), (C) lesional histiocytes staining with CD163 (40X) and (D) lesional histiocytes staining with CD14 (40X).

## Discussion

Clinical presentations of most breast RDD are painless palpable mass with a mean age of 53.2 years.<sup>(3)</sup> However, in many cases, asymptomatic women are incidentally found on imaging. Mammographic findings usually show as masses without calcifications<sup>(6)</sup> but there was a prior reported case presenting with focal asymmetry<sup>(7)</sup> similar to our case. Ultrasound usually reveals as hypoechoic masses<sup>(6)</sup>, unlike heterogeneous echoic mass found in our report. The other ultrasound findings in our case were similar to prior reports including mass with irregular shape, ill-defined margin and echogenic rim.<sup>(3, 6, 8, 9)</sup> These findings were indistinguishable from breast carcinoma, then tissue diagnosis usually required consequently to differentiate between benign and malignant entity. Echogenic rim in breast RDD may represent inflammatory process of disease which corresponding to inflammatory cells infiltration in breast stroma as seen in pathology. Among the previous largest review literature<sup>(3)</sup>, breast

RDD primarily involved breast parenchyma, skin and subcutaneous tissues, and intramammary lymph nodes in descending order. Histologically, histiocytes that express S-100 are considered diagnostic of RDD.<sup>(4)</sup> Immunohistochemical stains of RDD cells are also positive for hemoglobin scavenger receptor and acute phase-regulated transmembrane protein (CD163) and pan-macrophage antigens (CD68, CD14) while CD1a is typically negative.<sup>(1)</sup> Besides, emperipolesis is considered a useful feature, but not specific and often hard to find in extranodal lesions.<sup>(10)</sup> The differential diagnosis of IgG4-related disease should be considered because of similar histopathologic features including prominent lymphoplasmacytic infiltration and fibrosis. But the criteria for IgG4-related disease is an IgG4-positive/IgG-positive cell ratio > 40.0%.<sup>(11)</sup> The clinical course of RDD is variable with episodes of exacerbation and remission.<sup>(6)</sup> Appropriate multidisciplinary workup

to determine other organ involvement, systemic disease, or underlying hematologic malignancies should be performed.<sup>(12)</sup> There are no current guidelines for treating breast RDD. Surgical excision is recommended if the mass has inconclusive histopathologic findings, tumor recurrence<sup>(13)</sup> or increasing size of the lesion during the follow-up.

## Conclusion

RDD of the breast is a rare benign proliferative disorder that radiological imaging can mimic breast malignancy. Histopathology plays an important role in accurate diagnosis of histiocytes with characteristic S-100 expression. There are no current standardized guidelines on treatment or follow-up of patients with disease confined to the breast. Due to the limited number of cases, further studies are needed to determine the best treatment strategy.

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## Conflicts of interest statement

Each of the authors has completed an ICMJE disclosure form. None of the authors declare any potential or actual relationship, activity, or interest related to the content of this article.

## Data sharing statement

Data generated or analyzed for the present report are included in this published article. Further details are available from the corresponding author on reasonable request after deidentification of the patient whose data are included in the report.

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