รายงานผู้ป่วย | Case Report

โรคโรไซดอร์ฟแมนของเต้านมที่มีลักษณะคล้ายมะเร็ง : รายงานผู้ป่วย

Rosai–Dorfman Disease of the Breast Mimicking Carcinoma: A Case Report

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บทคัดย่อ

หลักการและเหตุผล : โรคโรไซดอร์ฟแมน (Rosai-Dorfman disease; RDD) เป็นโรคความผิดปกติของฮิสทิโอไซต์ชนิดไม่ใช่แลงเกอร์ฮานส์ที่พบได้ยาก และอาจแสดงลักษณะคล้ายมะเร็งทั้งทางคลินิกและรังสีวิทยา การเกิดที่เต้านมพบได้น้อยมากและอาจทำให้วินิจฉัยผิดพลาด รายงานนี้มีวัตถุประสงค์เพื่อเน้นย้ำความสำคัญของการตรวจทางพยาธิวิทยาในการยืนยันการวินิจฉัยและป้องกันการรักษาที่ไม่จำเป็น

ผู้ป่วยหญิงอายุ 60 ปี มีโรคข้ออักเสบรูมาตอยด์มาพบแพทย์เนื่องจากคลำพบก้อนที่เต้านมขวา แมมโมแกรมและอัลตราซาวด์พบลักษณะสงสัยมะเร็งสูง (BI-RADS 5) การตรวจชิ้นเนื้อด้วยเข็มพบการอักเสบเรื้อรังโดยไม่พบเซลล์มะเร็ง หลังผ่าตัดก้อนออก ผลพยาธิวิทยาพบเซลล์ฮิสทิโอไซต์ขนาดใหญ่ที่มีเอมเพอริโพเลซิสและย้อมติด S100 และ CD68 สรุปวินิจฉัยเป็นโรคโรไซดอร์ฟแมน ผู้ป่วยฟื้นตัวดีและไม่พบการกลับเป็นซ้ำในการติดตามโรค

Rosai-Dorfman ของเต้านมเป็นภาวะที่พบได้ยากแต่สำคัญ เนื่องจากลักษณะทางคลินิกและรังสีวิทยามักคล้ายมะเร็งเต้านม อาจนำไปสู่การวินิจฉัยผิดพลาดและการรักษาที่ไม่จำเป็น การตรวจทางพยาธิวิทยายังคงเป็นมาตรฐานหลักในการยืนยันการวินิจฉัยที่ถูกต้อง

คำสำคัญ : โรคโรไซดอร์ฟแมน ไซนัสฮิสทิโอไซโตซิส เต้านม การแสดงลักษณะคล้ายมะเร็ง

ABSTRACT

Background : Rosai-Dorfman disease (RDD) is a rare non-Langerhans cell histiocytic disorder that can mimic malignancy both clinically and radiologically. Breast involvement is exceptionally uncommon and may lead to diagnostic misinterpretation. We report this case to highlight the importance of histopathology in achieving a definitive diagnosis and avoiding overtreatment.

A 60-year-old woman with underlying rheumatoid arthritis presented with a palpable right breast mass. Mammography and ultrasonography were highly suggestive of malignancy (BI-RADS 5). Core needle biopsy revealed an inflammatory process without definite evidence of malignancy.

A subsequent wide excision demonstrated numerous large histiocytes with emperipolesis, positive for S100 and CD68 on immunohistochemistry, confirming the diagnosis of Rosai–Dorfman disease. The postoperative course was uneventful, and no recurrence was observed on follow-up.

Breast Rosai–Dorfman disease is an uncommon entity that may closely simulate carcinoma on clinical and imaging evaluation. Recognizing this diagnostic pitfall is crucial, as histopathology remains the gold standard for accurate diagnosis and to prevent unnecessary extensive surgery.

Keywords : Rosai-Dorfman disease, Sinus histiocytosis, Breast, Benign mimic of malignancy.

Introduction

Rosai-Dorfman disease (RDD), first described by Rosai and Dorfman in 1969 as sinus histiocytosis with massive lymphadenopathy (SHML), is a histiocytosis characterized by nodal or extranodal accumulation of large, S100-positive histiocytes/macrophages that commonly exhibit emperipolesis[1]. This rare non-Langerhans-cell histiocytic disorder of uncertain biological potential was historically regarded as a benign proliferative process[2,3], but recent molecular studies have identified recurrent somatic mutations involving the MAPK/ERK pathway (such as KRAS, NRAS, MAP2K1, ARAF, and CSF1R), indicating clonality in a subset of cases and suggesting that RDD may represent a histiocytic neoplasm with typically indolent clinical behavior[1,4-6].

Clinically, RDD has a slight male predominance and most commonly presents during the second to fifth decades of life, although it can occur at any age[1,3,7]. The classic form involves massive, painless cervical lymphadenopathy, but extranodal involvement is observed in approximately 40 to 50% of patients, affecting virtually any organ system[1,3,7-9]. The skin, upper respiratory tract, and central nervous system are among the most frequently involved extranodal sites[1,3,7].

Primary breast involvement by RDD is exceedingly rare, with fewer than 50 cases reported in the English-language literature to date[10-14]. Although RDD generally follows an indolent course, it is currently regarded as a histiocytosis of uncertain biological potential rather than a purely benign process[1,4,6]. Breast RDD poses a diagnostic dilemma because its clinical and radiologic findings often mimic carcinoma. Mammographic findings frequently reveal irregular or spiculated high-density masses, whereas ultrasonography shows hypoechoic lesions with indistinct margins, features commonly categorized as BI-RADS 4 or 5, and often leading to surgical excision for definitive diagnosis[10,12-14].

Histopathologically, RDD is characterized by sheets of large histiocytes with abundant pale cytoplasm, round vesicular nuclei, and prominent emperipolesis, which are intact lymphocytes, plasma cells, or neutrophils engulfed within histiocytes without degradation[8,15].

Immunohistochemically, the lesional histiocytes are strongly positive for S100 and CD68 but negative for CD1a, distinguishing RDD from Langerhans cell histiocytosis. Additional markers, including OCT2 and cyclin D1, may aid in diagnosis in limited or challenging biopsy specimens[16-18].

Although most localized cases follow a self-limited course and can be managed conservatively or with local excision, disseminated disease may exhibit aggressive behavior and require systemic therapy such as corticosteroids, IL-6 blockade, radiotherapy, or MEK inhibition. Consensus recommendations have recently been established to guide diagnostic evaluation and management in various clinical settings[5,9,19-21].

According to these guidelines, histopathologic confirmation remains essential, while baseline evaluation should include systemic imaging to assess for multisystem involvement. Management is tailored to the extent and severity[9]. In a published series of breast-limited RDD, most patients underwent simple/local excision, often to secure a definitive diagnosis in lesions categorized as BI-RADS 4 or 5, while observation has also been reported in selected, minimally symptomatic cases. Outcomes have been favorable, with symptom resolution and no documented recurrences or malignant transformation during short- to intermediate-term follow-up[10-14]. Specific management algorithms for breast-limited RDD are not standardized and are individualized according to symptoms, radiologic suspicion, and patient preference[9].

This report aims to highlight the diagnostic challenge of breast Rosai–Dorfman disease, emphasizing its potential to mimic malignancy and the essential role of histopathology in achieving accurate diagnosis and avoiding overtreatment.

Case Report

A 60-year-old Thai female, a housewife, presented with a palpable lump in her right breast for two months, which had gradually increased in size. She denied pain, nipple discharge, trauma, or lactation. There was no family history of breast carcinoma and no constitutional or B symptoms such as fever, night sweats, or weight loss. Her medical history was significant for rheumatoid arthritis, clinically stable on methotrexate 2.5 mg, two tablets weekly (5 mg/week).

On physical examination, an irregular, superficial, firm mass was palpated in the upper outer quadrant of the right breast, measuring approximately 1.5 cm in greatest dimension. The overlying skin showed no erythema, ulceration, or peau d'orange. No palpable axillary lymphadenopathy was detected. The contralateral breast was unremarkable.

Ultrasonography demonstrated a spiculated hypoechoic mass measuring 1.1 × 1.5 × 1.9 cm in the upper outer quadrant of the right breast (Fig. 1). No abnormalities were seen in the left breast or axilla. Digital mammography revealed an indistinct, irregular high-density mass with nipple retraction in the upper part of the right breast (Fig. 2). No suspicious calcification or architectural distortion was noted. The imaging findings were highly suggestive of malignancy (BI-RADS 5).

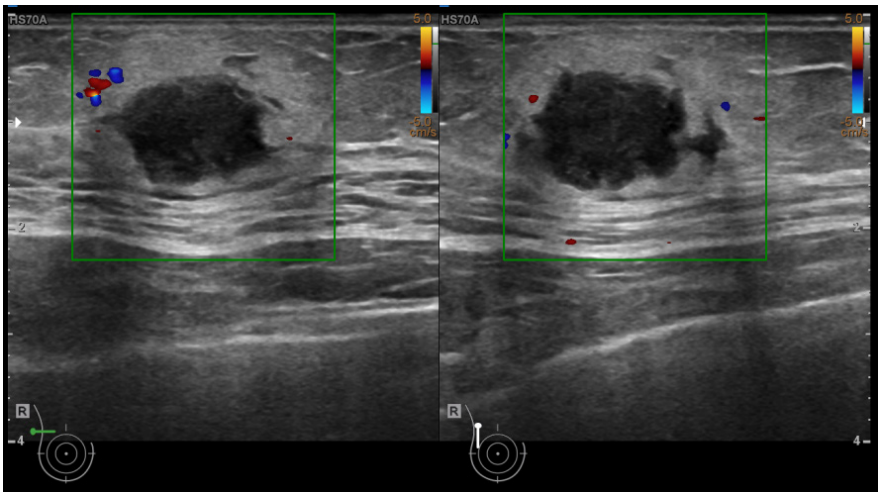

Figure 1. Ultrasonography showed a spiculated hypoechoic mass in the upper outer quadrant of the right breast, about 1.1x1.5x1.9 cm in size.

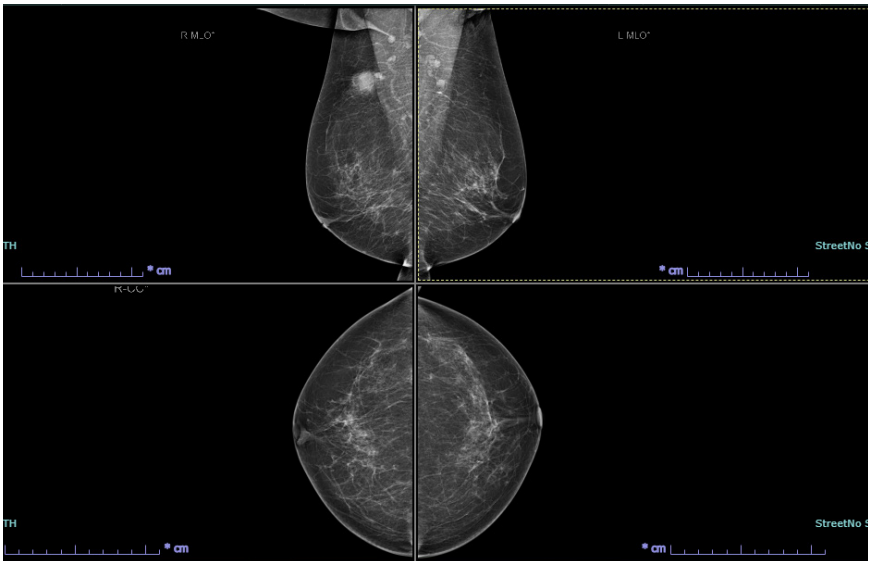

Figure 2. Digital mammography (a). Right mediolateral view and (b). The right craniocaudal view showed an indistinct, irregular, high-density mass without microcalcification at the upper part of the right breast. A skin calcification at the upper outer quadrant of the right breast is noted. Right nipple retraction is observed.

Two separate core needle biopsies, performed at different times during the diagnostic workup, both showed chronic inflammatory infiltrate with histiocytic aggregates but no evidence of malignancy (Fig. 3). Special stains for acid-fast bacilli (AFB) and Gomori methenamine silver (GMS) were negative for microorganisms. Because of discordance between strong clinical-radiologic suspicion and inconclusive biopsy results, a wide excision was performed for definitive diagnosis.

Gross examination showed an ill-defined, firm, gray-white lesion measuring 2.4 × 2.0 × 1.7 cm. Microscopically, the lesion was composed of large pale histiocytes admixed with numerous plasma cells and lymphocytes (Fig. 4a). Many histiocytes demonstrated emperipolesis, characterized by the engulfment of intact lymphocytes and plasma cells within their cytoplasm (Fig. 4b). No epithelial atypia, necrosis, or evidence of malignancy was identified. Immunohistochemical staining showed diffuse strong positivity for S-100 (Fig. 5a) and CD68 (Fig. 5b). Although CD1a was not performed due to the lack of this IHC in our department, the characteristic morphology, together with this immunoprofile, is diagnostic of Rosai–Dorfman disease.

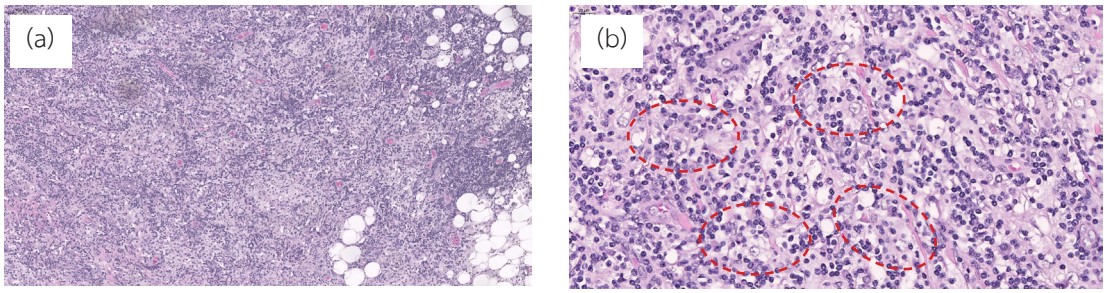

Figure 4. (a) Histology of the excision specimen with H&E stain on low magnification view showed the lesion had a characteristic accumulation of histiocytes with prominent inflammatory infiltrate comprised of plasma cells and lymphocytes (H&E stain, 10X). (b) A high-magnification view showed several histiocytes displaying emperipolesis, engulfing the inflammatory cells (circles) (H&E stain, 40X).

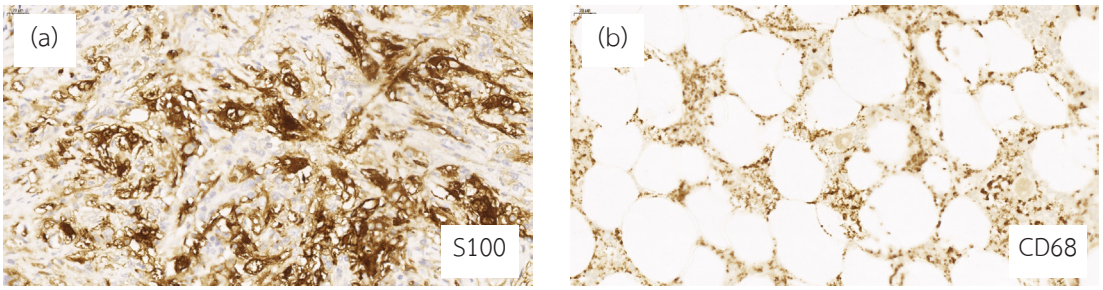

Figure 5. (a) On immunohistochemistry, the histiocytes showed positivity for S-100 (40X) and (b) CD68 (40X), confirming the diagnosis of Rosai-Dorfman disease.

The postoperative recovery was uneventful. The surgical wound healed well without complications. According to the outpatient record, the patient was scheduled for follow-up breast ultrasonography in 6 months; however, no subsequent imaging results were documented. At the time of obtaining informed consent for publication, approximately four years after the initial diagnosis, the patient reported no breast-related symptoms or palpable mass recurrence. She has not returned for further breast evaluation at our institution. Her rheumatoid arthritis remains stable under treatment at a local hospital.

Discussion

This case highlights the diagnostic challenges of breast Rosai-Dorfman disease (RDD), an exceedingly rare manifestation of a histiocytosis of uncertain biological potential[1]. Similar to most reported cases, the lesion in our patient radiologically mimicked breast carcinoma, showing an irregular or spiculated hypoechoic mass on ultrasonography, and a high-density, ill-defined lesion on mammography, which are typically classified as BI-RADS 4 or 5, commonly prompting surgical excision[7,10-14].

The difficulty in preoperative diagnosis is well documented. Core needle biopsy (CNB) may yield non-specific findings when only peripheral inflammatory zones are sampled, often being interpreted as chronic inflammation, lymphoid proliferation, or histiocytic infiltration rather than RDD[13-15]. In our case, two separate CNBs were inconclusive, similar to prior reports emphasizing the limited diagnostic yield of CNB and the importance of repeat biopsy or excision in discordant triple-assessment settings[13-15].

Histologically, the lesion displayed classic extranodal RDD morphology, including large pale histiocytes with emperipolesis and a mixed inflammatory background rich in plasma cells, which is identical to that seen in nodal and other extranodal sites[1,3,7,8].

Immunohistochemically, the tumor cells expressed S100 and CD68, supporting the diagnosis. Although CD1a staining was not performed, the combination of characteristic histiocytic morphology and lack of cytologic atypia was considered diagnostic, in keeping with previous studies describing similar immunophenotypes in limited breast biopsies[7,15,18].

The differential diagnosis includes Langerhans cell histiocytosis (LCH), which shows CD1a and Langerin positivity and features nuclear grooves and eosinophil-rich inflammation, absent in RDD[17,18]. Histiocytic sarcoma demonstrates cytologic atypia, mitoses, and loss of emperipolesis[17,18]. IgG4-related mastitis may resemble RDD due to abundant plasma cells but shows storiform fibrosis, obliterative phlebitis, and an elevated IgG4/IgG ratio (≥ 40%), features not seen in this case[3,7,15,18]. Granulomatous mastitis and malakoplakia can also mimic RDD, but the presence of granulomas or Michaelis–Gutmann bodies distinguishes them[3,7,15]. A concise immunohistochemical panel including S100, CD68 or CD163, CD1a or Langerin, and cytokeratin (± GATA3 or p63) can reliably differentiate these entities in small biopsies [15,17].

From a pathogenetic standpoint, RDD is increasingly recognized as a clonal histiocytic neoplasm in a subset of cases. Earlier studies proposed viral triggers, including HHV-6 and EBV [22,23], whereas contemporary molecular analyses have demonstrated recurrent somatic mutations in KRAS, NRAS, MAP2K1, ARAF, and CSF1R[4,6], implicating MAPK/ERK pathway activation. This finding has therapeutic relevance, as MEK inhibitors have shown efficacy in histiocytic neoplasms harboring these mutations[5]. Most localized or extranodal RDD, however, including breast-limited cases, exhibit indolent behavior and respond well to conservative or surgical management[9, 19-21].

The current case shares the clinicopathologic features of previously published breast RDDs, occurring in a middle-aged woman,

presenting as a localized mass without nodal or systemic disease, and showing typical histology[7,10-14]. A noteworthy aspect is the patient's history of rheumatoid arthritis under low-dose methotrexate therapy, which may have modulated the inflammatory microenvironment, consistent with prior reports suggesting immune dysregulation in the pathogenesis of RDD[4,6,9].

Although this rare case contributes to the understanding of breast-limited RDD, certain limitations exist. The absence of molecular analysis precludes confirmation of potential MAPK/ERK pathway alterations, and long-term follow-up imaging data were unavailable. Nonetheless, clinical follow-up indicated no recurrence or new symptoms, consistent with the typically indolent course of localized RDD. Continued documentation of well-characterized cases, integrating clinical, histopathologic, and molecular data, will be essential to better delineate the biological behavior and guide evidence-based management of this rare entity[1,4-6,9,20,21].

Conclusion

Rosai–Dorfman disease (RDD) of the breast is a rare but important mimic of malignancy. Its clinical and radiologic features often resemble breast carcinoma, which may lead to misdiagnosis and unnecessary aggressive treatment. Accurate diagnosis requires triple assessment, including clinical, radiologic, and pathologic correlation. Histopathological examination remains the gold standard for confirming the diagnosis. Increased awareness of this entity is essential to prevent diagnostic errors and ensure appropriate management.

Ethical Approval

This patient report was approved by the Ethics Committee of Maharat Nakhon Ratchasima Hospital, No.098/2025 and written informed consent was obtained from the patient.

Declaration of Competing Interest

The authors report no conflicts of interest.

References

1. Natkunam Y, Demicco EG, Idbaih A, Rossi S, Wenig BM, Zelger B. Rosai–Dorfman disease. In: WHO Classification of Tumours Editorial Board, Chan J, Coupland SE, volume editors. WHO Classification of Tumours: Haematolymphoid Tumours. Vol. 11. (Part A). 5th. ed. Lyon : International Agency for Research on Cancer ; 2024 : 248-51.
2. Foucar E, Rosai J, Dorfman R. Sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease): review of the entity. Semin Diagn Pathol 1990;7(1):19-73. PMID: 2180012.
3. Gaitonde S. Multifocal, extranodal sinus histiocytosis with massive lymphadenopathy: an overview. Arch Pathol Lab Med 2007; 131(7):1117-21. doi: 10.5858/2007-131-1117-MESHWM.
4. Elbaz Younes I, Sokol L, Zhang L. Rosai-Dorf man Disease between Proliferation and Neoplasia. Cancers (Basel) 2022;14(21):5271. doi: 10.3390/cancers14215271.

5. Diamond EL, Durham BH, Ulaner GA, Drill E, Buthorn J, Ki M, et al. Efficacy of MEK inhibition in patients with histiocytic neoplasms. Nature 2019;567(7749):521-4. doi:10.1038/s41586-019-1012-y.
6. Garces S, Medeiros LJ, Patel KP, Li S, Pina-Oviedo S, Li J, et al. Mutually exclusive recurrent KRAS and MAP2K1 mutations in Rosai-Dorfman disease. Mod Pathol 2017;30(10):1367-77. doi: 10.1038/modpathol.2017.55.
7. Dalia S, Sagatys E, Sokol L, Kubal T. Rosai-Dorfman disease: tumor biology, clinical features, pathology, and treatment. Cancer Control 2014;21(4):322-7. doi: 10.1177/107327481402100408.
8. Rosai J, Dorfman RF. Sinus histiocytosis with massive lymphadenopathy. A newly recognized benign clinicopathological entity. Arch Pathol 1969;87(1):63-70. PMID: 5782438
9. Abla O, Jacobsen E, Picarsic J, Krenova Z, Jaffe R, Emile JF, et al. Consensus recommendations for the diagnosis and clinical management of Rosai-Dorfman-Destombes disease. Blood 2018;131(26):2877-90. doi: 10.1182/blood-2018-03-839753.
10. Iancu G, Gica N, Mustata LM, Panaitescu AM, Vasile D, Peltecu G. Rosai-Dorfman Disease: Breast Involvement-Case Report and Literature Review. Medicina (Kaunas) 2021;57(11):1167. doi: 10.3390/medicina57111167.
11. Wang Q, Bradley K, Zhang M, Li S, Li X. Rosai-Dorfman disease of the breast: a clinicoradiologic and pathologic study. Hum Pathol 2023;141:30-42. doi: 10.1016/j.humpath.2023.08.009.
12. Choo PZQ, Loh AHL, Selvarajan S, Tan PH, Tan VKM, Yong WS, et al. Breast-related extranodal Rosai-Dorfman disease presenting as subcutaneous masses with thick hyperechoic rim, with review of the literature. Breast J 2021;27(12):883-6. doi: 10.1111/tbj.14286.
13. Shin GW, Park YM, Heo YJ, Baek JW, Lee YJ, Han JY, et al. Sonographic features of Rosai-Dorfman disease in the breast: A case report. J Clin Ultrasound 2020;48(2):108-10. doi: 10.1002/jcu.22781.
14. Delaney EE, Larkin A, MacMaster S, Sakhdari A, DeBenedectis CM. Rosai-Dorfman Disease of the Breast. Cureus 2017;9(4):e1153. doi: 10.7759/cureus.1153.
15. Ravindran A, Rech KL. How I Diagnose Rosai-Dorfman Disease. Am J Clin Pathol 2023;160(1):1-10. doi: 10.1093/ajcp/aqad047.
16. Ravindran A, Goyal G, Go RS, Rech KL; Mayo Clinic Histiocytosis Working Group. Rosai-Dorfman Disease Displays a Unique Monocyte-Macrophage Phenotype Characterized by Expression of OCT2. Am J Surg Pathol 2021;45(1):35-44. doi: 10.1097/PAS.0000000000001617
17. Paulli M, Bergamaschi G, Tonon L, Viglio A, Rosso R, Facchetti F, et al. Evidence for a polyclonal nature of the cell infiltrate in sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease). Br J Haematol 1995;91(2):415-8. doi: 10.1111/j.1365-2141.1995.tb05313.x.

18. Brenn T, Calonje E, Granter SR, Leonard N, Grayson W, Fletcher CD, et al. Cutaneous rosai-dorfman disease is a distinct clinical entity. Am J Dermatopathol 2002;24(5):385-91. doi: 10.1097/00000372-200210000-00001.
19. Pulsoni A, Anghel G, Falcucci P, Matera R, Pescarmona E, Ribersani M, et al. Treatment of sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease): report of a case and literature review. Am J Hematol 2002;69(1):67-71. doi: 10.1002/ajh.10008
20. Gonzales MR, White JC, Mangum DS, Powell JL. Sporadic extranodal Rosai-Dorfman-Destombes disease treated with tocilizumab. Pediatr Blood Cancer 2022; 69(12):e29754.doi: 10.1002/pbc.29754.
21. Paryani NN, Daugherty LC, O'Connor MI, Jiang L. Extranodal rosai-dorfman disease of the bone treated with surgery and radiotherapy. Rare Tumors 2014;6(4):5531. doi: 10.4081/rt.2014.5531.
22. Levine PH, Jahan N, Murari P, Manak M, Jaffe ES. Detection of human herpesvirus 6 in tissues involved by sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease). J Infect Dis 1992;166(2):291-5. doi: 10.1093/infdis/166.2.291.
23. Tsang WY, Yip TT, Chan JK. The Rosai-Dorfman disease histiocytes are not infected by Epstein-Barr virus. Histopathology 1994; 25(1):88-90. doi: 10.1111/j.1365-2559.1994.tb00604.x.