International Invention of Scientific Journal
Online ISSN: 2457-0958
Available Online at https://iisj.in **Volume 9, Issue 01 (January-February-March)|2025**|Page: 40-43
Case Report-Medical Sciences

Rosai-Dorfman disease: A rare presentation as an isolated axillary lymphadenopathy, a case report and literature review

Corresponding Author:
Reza Yusofvand
Department of Exceptional Talents, Faculty of Medicine Sciences, Lorestan University of Medical Sciences, Khorramabad, Iran

Article Received: 01- January-2025, Revised: 18-January-2025, Accepted: 08-February-2025

ABSTRACT:

Back Ground: Rosai-Dorfman Disease (RDD) is a rare benign histiocytic disorder characterized by the proliferation of non-Langerhans cell histiocytes, primarily affecting young adults. The etiology remains unclear, although infectious and autoimmune factors have been suggested. Recent advancements have revealed significant genetic factors, particularly involving the MAPK/ERK pathway.

Case Presentation: A 30-year-old female presented with a six-month history of progressive swelling in the left axilla, fatigue, intermittent fevers, and significant weight loss. Examination revealed firm, non-tender left axillary lymphadenopathy and erythematous papular skin lesions. Laboratory tests indicated mild inflammation, and imaging confirmed isolated left axillary lymphadenopathy. An excisional biopsy demonstrated histiocytic proliferation with emperipolesis and immunohistochemistry of the histiocytes was positive for S100, CD68, but negative for CD1a, confirming the diagnosis of RDD. The patient responded well to corticosteroid treatment, showing significant clinical improvement within four weeks.

Discussion: Isolated axillary lymph node involvement in RDD is rare, with only a few cases reported. The etiology remains enigmatic, with theories suggesting a dysregulated immune response potentially triggered by infectious agents. Recent molecular studies have identified mutations in the MAPK pathway, including ARAF, MAP2K1, NRAS, and KRAS, linking RDD to neoplastic myeloproliferative conditions. The diagnosis relies on histopathological examination and immunohistochemistry, highlighting the importance of recognizing RDD in young adults with unexplained lymphadenopathy.

Conclusion: This article presents a case of Rosai-Dorfman Disease (RDD) in a 30-year-old female patient who exhibited an unusual presentation with isolated left axillary lymphadenopathy and skin lesions. It emphasizes the importance for clinicians to consider RDD in younger patients with unexplained lymphadenopathy and systemic symptoms. The article highlights that timely diagnosis and appropriate treatment can result in positive outcomes, and it calls for further research to improve understanding and management of RDD.

Keywords: Rosai-Dorfman disease , isolated axillary lymphadenopathy , case report

INTRODUCTION:

Rosai-Dorfman Disease (RDD) is a rare histiocytic disorder(1) .Rosai-Dorfman Disease is a benign histiocytic disorder first described in 1969, characterized by the proliferation of non-Langerhans cell histiocytes(2). It predominantly affects young adults, with a male predominance(3). The etiology remains unclear, although infectious and autoimmune factors have been proposed (4). Significant advancements have been made in understanding its genetic factors particularly involving the MAPK/ERK pathway(5). Classic manifestations include bilateral cervical lymphadenopathy, with variable systemic symptoms such as fever, weight loss, and night sweats(6). Although most cases are self-limiting, atypical presentations, particularly with isolated axillary lymphadenopathy and extranodal involvement , have been reported. This case report aims to highlight a rare presentation of RDD.

Case Presentation:

A 30-year-old female presented to the outpatient clinic with a six-month history of progressive swelling of the left axilla, accompanied by fatigue and intermittent fevers. Initially, she attributed the symptoms to seasonal allergies, but they persisted and worsened over time. The patient reported significant weight loss of approximately 6 kg during this period.

On examination, there were noticeable left axillary lymphadenopathy, with multiple palpable lymph nodes ranging from 2 to 5 cm in diameter, which were firm and non-tender and No hepatosplenomegaly and petechiae and ecchymosis was noted. Additionally, the patient presented with erythematous papular skin lesions across her left arm , resembling an allergic reaction. There was no history of tuberculosis exposure or consumption of unpasteurized dairy products and

the patient did not have high risk sex and did not mention the history of drug , cigar and alcohol consumption .There was no significant past medical history, no known allergies, and no recent travel or infectious disease exposure and family history was negative for hematologic and oncologic disease.

Laboratory investigations showed a mild elevation in erythrocyte sedimentation rate (ESR) at 40 mm/hr and C-reactive protein (CRP) at 15 mg/L and normal antinuclear antibodies and normal rheumatoid factor. Complete blood count, liver function tests, and renal function tests were within normal limits. Serological tests for HIV, EBV, and CMV were negative
A axillary ultrasound confirmed enlarged lymph nodes , prompting further imaging studies through chest ,abdomen , and pelvis CT scan with contrast, which revealed isolated left axillary lymphadenopathy measuring 2.2 * 2cm along with skin lesions suspicious for involvement(figure 1) but cervical ct scan was normal and diagnostic mammogram of left breast was unremarkable with no evidence of malignancy in craniocaudal and medial lateral oblique projection(figure 2).

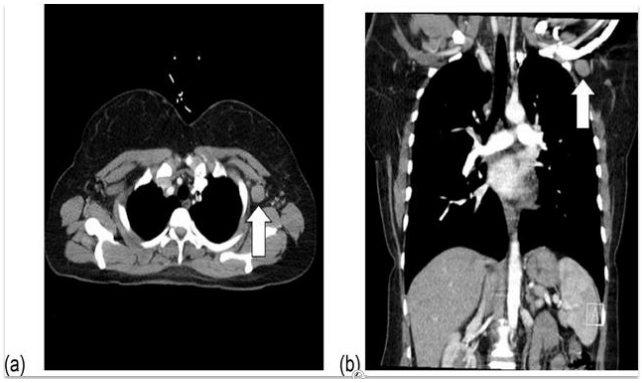

*Figure 1:contrast – enhanced computer tomography(CT) imaging of the chest , abdomen , and pelvis demonsrate an large left axillary lymphnode (arrow)measuring 2.2 * 2cm on axial(a) and coronal planes(b).*

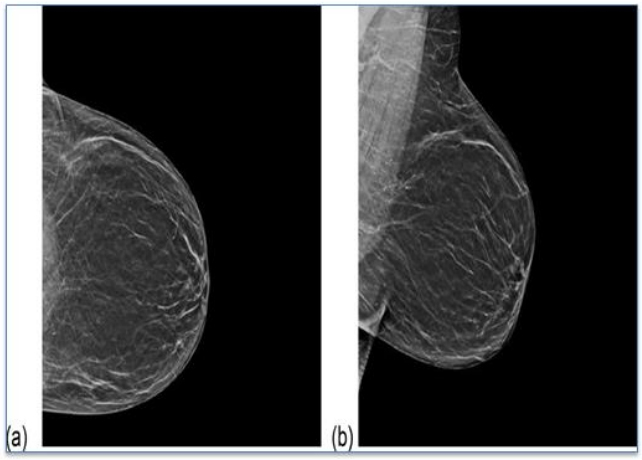

Figure 2 :diagnostic mammogram of left breast was unremarkable with no evidence of malignancy in craniocaudal and medial lateral oblique projection

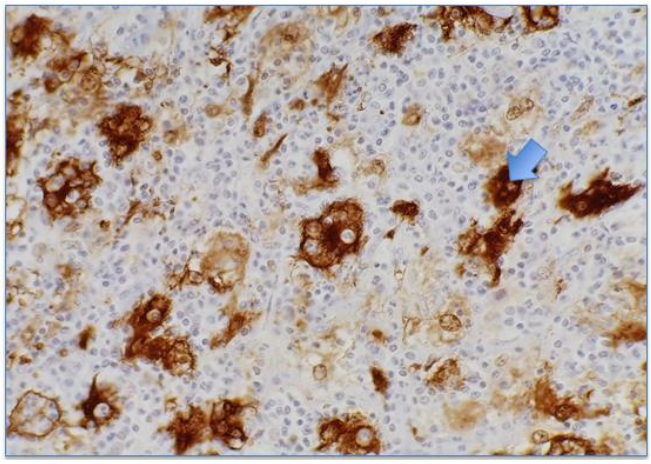

Figure 3: mass involved by histiocytic infiltrate showing emperipolesis highlighted by positive staining for S100(arrow)

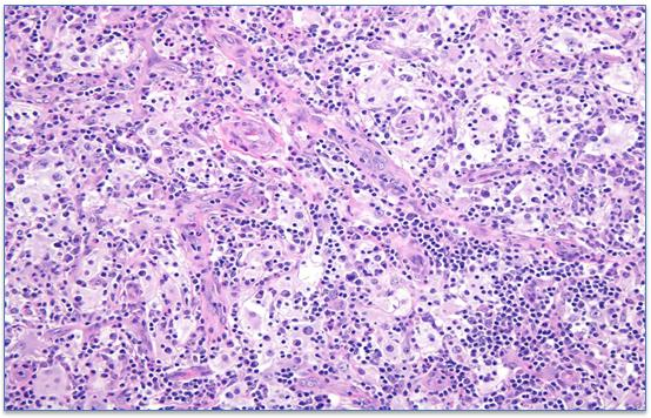

Figure 4: Rosai-Dorfman disease showing a prominent histiocytic infiltrate in a background of inflammatory cells, predominantly comprised of lymphocytes and plasma cells.

An excisional biopsy of a lymph nodes was performed, and histopathological analysis showed sheets of large histiocytic cells with evidence of emperipolesis, confirmed by immunohistochemical staining positive for S-100 protein and CD68 and negative CD1afigure 3,4). These findings confirmed the diagnosis of Rosai-Dorfman Disease.

The patient was treated with corticosteroids, starting with prednisone at 40 mg daily. Within four weeks, she reported significant clinical improvement, including reduced lymph node size and resolution of fevers and skin lesions. A follow-up examination at three months revealed sustained improvement, with no recurrence of symptoms.

DISCUSSION:

Rosai-Dorfman Disease remains an enigmatic condition primarily presenting as cervical lymphadenopathy, and an isolated axillary lymph node involvement, as observed in our patient, is a rere presentation of nodal RDD. To our knowledge, only three cases have been reported in the literature (Table 1). systemic and extranodal involvement can complicate the clinical picture. This case emphasizes the importance of considering RDD as a differential

diagnosis in young adults with unexplained lymphadenopathy, particularly when accompanied by systemic symptoms and skin lesions.

The etiology of RDD is not well understood, but several theories suggest a dysregulated immune response, possibly triggered by infectious agents such as viruses or bacteria (
7). Some studies have suggested a link with viral infections, particularly human herpesvirus (HHV-6) and Epstein-Barr virus (EBV) (8). However, in our case, serological tests for common viruses were negative, aligning with the inconsistent findings in the literature regarding viral associations.Management of RDD is challenging due to its rarity and the lack of standardized treatment protocols.
recent molecular and genetic studies have established that RDD is a neoplastic myeloproliferative condition, with mutations in the MAPK pathway identified in some cases(5) . Kinase mutations in ARAF,MAP2K1, NRAS, and KRAS are present in nodal and extranodal RDD according to recent investigations(9,10). RDD has also been studied for BRAF V600E mutations, which have been connected to histiocytic neoplasms such as Erdheim Chaster disease(11).

In this case, the patient's systemic symptoms, including fever and weight loss, align with those typically reported in RDD, underscoring its systemic nature and the diverse presentations of RDD in adults (12).
The diagnosis of RDD relies heavily on histopathological examination and immunohistochemistry . Histologically, the classical finding of emperipolesis—intact lymphocytes within the cytoplasm of histiocytes—is a key diagnostic criterion that can help distinguish RDD from other lymphoproliferative disorders such as lymphoma or reactive lymphadenopathy and in immunohistochemistry the histiocytes are positive for S100, CD68, andCD163, but negative for CD1a and langerin (CD207) which excludes Langerhans cellhistiocytosis (LCH). The S100 stain often highlights the emperipolesis(1) (13).The initial misdiagnosis can delay appropriate treatment, as observed in this case.

The rapid resolution of symptoms with corticosteroids demonstrates their effectiveness in managing RDD, similar to findings in previous studies (14).

Nodal RDD generally has a favorable prognosis. Spontaneous remission has been reported inup to 50% of sporadic RDD cases ,However, up to 10% of patients may die from the disease due to complications, infections, or amyloidosis (15).

In summary, this case highlights the necessity for clinicians to consider Rosai-Dorfman Disease in the differential diagnosis for patients presenting with persistent left axillary lymphadenopathy and systemic signs, particularly when extralymphatic features are present. Awareness of RDD and its atypical manifestations can facilitate timely diagnosis and effective management.

CONCLUSION:

This case report illustrates an atypical presentation of Rosai-Dorfman Disease in a 30-year-old female patient with isolated left axillart lymphadenopathy and skin involvement. Clinicians must maintain a high index of suspicion for RDD, particularly in younger patients exhibiting unexplained lymphadenopathy and systemic symptoms. Timely diagnosis and appropriate treatment can lead to favorable outcomes. Further research into the pathogenesis and optimal management of RDD is warranted to enhance understanding and improve patient care.

Table1 **:** Reported cases of Rosai-Dorfman disease presenting with an isolated axillary lymphadenopathy

Case	Author, year	Age	Sex	Location	Size	Specimen type	IHC	Reference
	Shetty et al. 2020	33	f	Left axillary lymphadenopathy	3.5 cm	Lymph node excision	S100(+), CD31(+), CD68(+),Cd1a(-), CD3(-), CD20(-)	16
	Shetty et al. 2020	88	f	Right axillary lymphadenopathy	2.7 cm	Lymph node excision	S100(+), CD138(+), CD79a(+), CD3(-), CD20(-), kappa(-), lambda(-), PAX5(-), MUM1(+)	16
	Banga et al. 2022	23	f	Right axillary lymphadenopathy	1.5 cm	Fine needle aspiration cytology	No data	17

Declarations:

Acknowledgments: We would like to thank the patient and their family for
their cooperation.
Funding: None to declare.
Conflict of interest: The authors declare that they have no conflict of interest.
Ethical approval: Written informed consent was obtained from the patient for publication of this case report.
Data availability: The data shown in this report are available from the corresponding author on reasonable request

REFERENCES:

1.C. Bruce-Brand, J. W. Schneider, et P. Schubert, « Rosai-Dorfman disease: an overview », J. Clin. Pathol., vol. 73, no 11, p. 697-705, nov. 2020, doi: 10.1136/jclinpath-2020-206733.
2.Rosai J, Dorfman RF. Sinus histiocytosis with massive lymphadenopathy: a newly recognized benign clinicopathological entity. Arch Pathol. 1969;87:63-70.
3. I. Elbaz Younes, L. Sokol, et L. Zhang, « Rosai–Dorfman Disease between Proliferation and Neoplasia », Cancers, vol. 14, no 21, Art. no 21, janv. 2022, doi:10.3390/cancers14215271.
4.Dalia S, Sagatys E, Sokol L, Kubal T. Rosai-Dorfman disease: tumor biology, clinical features, pathology, and treatment. Cancer Control. 2014;21(4):322-327
5.O. Abla et al., « Consensus recommendations for the diagnosis and clinical
management of Rosai-Dorfman-Destombes disease », Blood, vol. 131, no 26, p.2877-2890, juin 2018, doi: 10.1182/blood-2018-03-839753.
6. S. R. Vaiselbuh, Y. T. Bryceson, C. E. Allen, J. A. Whitlock, et O. Abla, « Updates on histiocytic disorders », Pediatr. Blood Cancer, vol. 61, no 7, p. 1329-1335, juill. 2014, doi: 10.1002/pbc.25017.
7. Kahn J, et al. Clinical features and treatment of Rosai-Dorfman disease: A review. Hematol Oncol Clin North Am. 2012;26(5):1045–1069.
8.Lu D, Estalilla OC, Manning JT Jr, Medeiros LJ. Sinus histiocytosis with massive lymphadenopathy and malignant lymphoma involving the same lymph node: a report of four cases and review of the literature. Mod Pathol. 2000;13(4):414-419
9. E. L. Diamond et al., « Diverse and Targetable Kinase Alterations Drive Histiocytic Neoplasms », Cancer Discov., vol. 6, no 2, p. 154-165, févr. 2016, doi: 10.1158/2159-8290.CD-15-0913.
10. S. Garces et al., « Mutually exclusive recurrent KRAS and MAP2K1 mutations in Rosai–Dorfman disease », Mod. Pathol., vol. 30, no 10, p. 1367-1377, oct. 2017, doi:10.1038/modpathol.2017.55.
11. J. Haroche et al., « High prevalence of BRAF V600E mutations in Erdheim-Chester disease but not in other non-Langerhans cell histiocytoses », Blood, vol. 120, no 13, p.
2700-2703, sept. 2012, doi: 10.1182/blood-2012-05-430140.
12. Karamchandani JR, et al. Rosai-Dorfman disease with renal involvement: A case report. Clin Case Rep. 2019;7(2):356–360.
13. Ahn JH, et al. Systemic involvement in Rosai-Dorfman disease: A report of five cases. Pathol Int. 2010;60(9):575–579.
14. Dufour J, et al. Extranodal Rosai-Dorfman disease: A comprehensive review. Cancer Treat Rev. 2017;60:25–35.
15. A. Pulsoni et al., « Treatment of sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease): report of a case and literature review », Am. J. Hematol., vol.
69, no 1, p. 67-71, janv. 2002, doi: 10.1002/ajh.10008.
16. S. Shetty et al., « Mammary Extranodal Rosai-Dorfman Disease With and Without Associated Axillary Lymphadenopathy: Insights for Practitioners of Breast Pathology », Int. J. Surg. Pathol., vol. 28, no 5, p. 541-548, août 2020, doi: 10.1177/1066896920901770.
17. V. Banga, « Sinus histiocytosis with massive lymphadenopathy (Rosai Dorfman Disease)- A rare case of isolated axillary lympadenopathy diagnosed on FNAC », IP J. Diagn.Pathol. Oncol., vol. 7, no 3, p. 191-193, doi: 10.18231/j.jdpo.2022.045.