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CASE REPORT

Fine-Needle Aspiration as a Key Diagnostic Tool in Pediatric Rosai-Dorfman Disease: A Case Report of a 12-Year-Old Male

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Background: Rosai-Dorfman Disease (RDD) is a rare, benign, non-Langerhans cell histiocytosis characterized primarily by massive, painless cervical lymphadenopathy. Its low prevalence (~ 1:200,000) and clinical similarity to endemic conditions like tuberculosis and lymphoma make the diagnosis challenging, particularly in resource-limited settings. Definitive diagnosis hinges on identifying S100-positive histiocytes exhibiting the pathognomonic feature of emperipolesis.

Case Presentation: A previously healthy 12-year-old male from Uganda presented with a one-month history of progressive, asymptomatic, bilateral cervical lymphadenopathy. Systemic symptoms were absent. A provisional diagnosis of RDD was established rapidly via Fine Needle Aspiration Cytology (FNAC). Cytological smears showed abundant histiocytes demonstrating clear emperipolesis, confirming the classic cytological diagnosis. Despite the recommendation for a confirmatory excisional biopsy and further subtyping, the patient was lost to follow-up.

Conclusion: This case demonstrates that high-quality FNAC can reliably establish the diagnosis of RDD in environments where advanced diagnostic tools are scarce, but also underscores the critical need to strengthen patient follow-up systems to ensure complete evaluation and long-term monitoring of rare histiocytic disorders.

Keywords: Rosai-Dorfman Disease, Fine Needle Aspiration Cytology, Emperipolesis, Cervical Lymphadenopathy, Uganda

Introduction

Rosai-Dorfman Disease (RDD), also known historically as Sinus Histiocytosis with Massive Lymphadenopathy, is a rare, non-Langerhans cell histiocytic disorder characterized by the accumulation of large, activated histiocytes in various tissues, most commonly the lymph nodes.[1,2] First comprehensively described by Rosai and Dorfman in 1969, the disease is estimated to have a low prevalence of approximately 1:200,000 and an annual incidence of about 100 cases in the United States, highlighting its rarity.[1,3]

Clinical Presentation and Demographics

Classic RDD typically presents in children and young adults, with a mean age of onset around 20 years, and exhibits a slight male predominance.[2,4] The hallmark clinical feature is massive, bilateral, painless cervical lymphadenopathy, which is observed in approximately 80–90% of patients with the nodal form of the disease.[2,5] While the disease is often self-limiting, constitutional symptoms such as fever, night sweats, and weight loss (B-symptoms) can occur in up to 20% of cases, necessitating a differential diagnosis that includes infectious etiologies, lymphomas, and other lymphoproliferative disorders.[2,6] Furthermore, RDD is known to affect individuals of African descent more frequently in its nodal form.[5] RDD

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can also involve extranodal sites in approximately 40% of patients, with the most common sites being the skin, soft tissues, bone, and central nervous system, which can complicate the diagnosis and dictate the treatment strategy.[5,7]

Pathological Features and Diagnostic Challenge

The definitive diagnosis of RDD relies on histopathological and immunohistochemical analysis of the affected tissue.[7] Pathologically, the lymph nodes show expansion of the sinuses by a proliferation of large, pale histiocytes. The pathognomonic feature is emperipolesis-the presence of intact lymphocytes, plasma cells, or erythrocytes within the cytoplasm of the histiocytes, without evidence of degradation (distinguishing it from phagocytosis).[2,7] Immunohistochemically, these histiocytes are characteristically positive for S100 and CD68, and negative for CD1a, thus differentiating RDD from other histiocytoses, particularly Langerhans cell histiocytosis.[8,9] Given the clinical overlap with more common or aggressive conditions, such as lymphoma or tuberculosis (especially in regions where infectious lymphadenitis is endemic), reliance on accurate pathological features like emperipolesis is critical for initiating appropriate patient management.[10,11]

This case report highlights the diagnostic value of Fine-Needle Aspiration (FNAC) in identifying RDD through emperipolesis, even in the absence of immunohistochemistry, and illustrates the challenges of continuity of care in low-resource settings.

Case Presentation

In September 2025, a previously healthy 12-year-old male Munyankole presented to Kampala International University Teaching Hospital, Western Uganda, with a one-month history of progressive, painless neck swelling. The patient reported no associated B-symptoms (fever, night sweats, or unexplained weight loss). A thorough history revealed no personal or familial history of chronic illnesses, immunodeficiency, or malignancy.

Clinical and Radiographic Findings

On physical examination, multiple, firm, non-tender, bilateral cervical lymph nodes were palpable: 6.0×5.0 cm in aggregate on the right side and a smaller nodule measuring 2.5×2.0 cm on the left side. A subsequent neck ultrasound scan demonstrated multiple enlarged lymph nodes, predominantly involving the base of the right infra-auricular region and the anterior triangle, with minor extension into the apex of the ipsilateral posterior triangle. Similar, though fewer, enlarged nodes were noted at the base of the left anterior triangle. The largest nodes measured 2.5×1.9 cm on the right and 2.5×2.0 cm on the left. The constellation of massive, multifocal lymphadenopathy in an otherwise asymptomatic child raised a high index of suspicion for a lymphoproliferative disorder or malignancy.

Pathological Diagnosis

FNAC was performed on the largest palpable right-sided node. Cytological smears stained with Hematoxylin and Eosin (H&E) and Giemsa revealed a striking and highly characteristic morphology. The background demonstrated a heterogeneous lymphoid population. Crucially, there were numerous histiocytes with abundant pale cytoplasm engulfing intact lymphocytes within their cytoplasm-a pathognomonic finding known as emperipolesis (Figure 1). These distinct cytological features were definitive for RDD.

Outcome

Following the initial cytological diagnosis, a confirmatory excisional biopsy was recommended to further characterize the disease and rule out concurrent pathology. However, the patient was lost to follow-up and did not return for the planned surgical procedure or subsequent clinical review.

Discussion

This report details a classic, albeit rare, presentation of RDD, in a 12-year-old male presenting with massive, painless, bilateral cervical lymphadenopathy. This case offers important insights into the diagnostic challenges of RDD in pediatric populations and underscores the critical role of FNAC in achieving a timely, specific diagnosis.

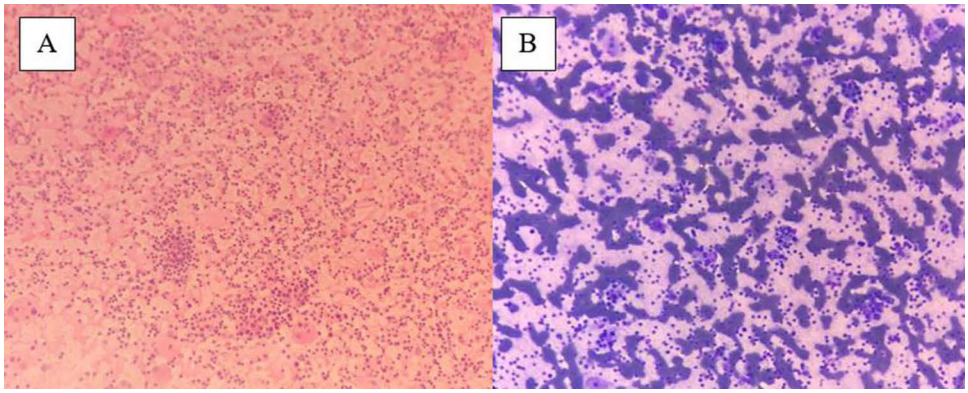

Figure 1 H&E (**A**: x200) and Giemsa (**B**: x200) stained smears show numerous histiocytes with abundant pale cytoplasm containing intact lymphocytes, within a background of lymphoid population.

Clinical Correlation and Differential Diagnosis

The patient's clinical presentation aligns closely with the typical nodal form of RDD: an asymptomatic, prepubertal male (12 years old) presenting with massive cervical lymphadenopathy in the absence of B-symptoms.[2,4] While RDD usually presents around the second decade of life, presentation in younger children is well-documented.[11] The large, firm, non-tender nodes measuring up to 6.0×5.0 cm are the defining physical finding, present in 80–90% of nodal RDD cases.[8] In a young patient with such extensive lymphadenopathy, the initial differential diagnosis must be broad, particularly in endemic regions where Tuberculosis and non-Hodgkin lymphoma are prevalent.[12] Other differential considerations include Castleman disease, Kikuchi-Fujimoto disease, and metastatic carcinoma. The absence of systemic symptoms (B-symptoms) and the normal appearance of surrounding structures on ultrasound, including the thyroid and carotid sheath, helped narrow the focus away from aggressive malignancies, though a definitive diagnosis remained imperative. This scenario highlights the diagnostic challenge RDD poses, as its rarity necessitates a high index of suspicion. Furthermore, studies have noted a higher frequency of nodal RDD among individuals of African descent, which is consistent with the patient's tribal origin in this report.[4,8]

The Definitive Role of Fine Needle Aspiration Cytology

The definitive diagnosis of RDD was achieved by FNAC, demonstrating its utility as a rapid, low-cost, and minimally invasive first-line diagnostic modality.[5,7] The finding of emperipolesis-intact lymphocytes and other hematopoietic cells residing within the cytoplasm of large, pale histiocytes-is the pathognomonic cytological hallmark of RDD.[2,7] While definitive diagnosis often relies on excisional biopsy with immunohistochemistry (S100-positive, CD1a-negative histiocytes),[2,7,8] this case illustrates that the distinctive nature of emperipolesis, when clearly visualized on high-quality smears (H&E and Giemsa), is often sufficient to establish a presumptive diagnosis, guiding initial clinical management while awaiting confirmatory testing. The accuracy of FNAC in diagnosing RDD, particularly when coupled with careful morphological analysis, has been well-established in the literature, often preventing more extensive surgical procedures.[13,14] This is particularly valuable in resource-limited settings or where immediate access to specialized pathology services for full biopsy and immunostaining is constrained. This applies to our setting that lacks immunohistochemistry.

Molecular Insights and Treatment Implications

Recent advancements in understanding RDD have shifted the focus toward its molecular pathogenesis. RDD is now classified as a neoplastic histiocytic proliferation, frequently exhibiting mutations in the RAS-ERK signaling pathway, particularly MAP2K1 and KRAS mutations, linking it to the broader spectrum of other histiocytic disorders.[6,12] These molecular insights are increasingly influencing treatment. While RDD is often self-limiting, therapeutic interventions for refractory or vital organ-threatening disease have expanded to include targeted therapies like MEK inhibitors (cobimetinib) or BRAF inhibitors, depending on the identified mutation, offering highly effective, non-chemotherapeutic

options.[12,15] This molecular understanding is critical, as it underscores the necessity for comprehensive pathological workup beyond morphology, even in classic presentations. The failure to obtain a confirmatory biopsy in this case means that the potential for associated molecular mutations, which could dictate therapy should the disease progress, remains unknown.

Clinical Management and Significance of Follow-Up

RDD is typically a benign, self-limiting disorder that often resolves spontaneously, requiring only observation in many nodal cases.[2] However, the disease can be progressive, persistent, or even life-threatening depending on the site of involvement (eg, central nervous system, renal).[12] Current consensus guidelines advocate for close monitoring and surveillance, with intervention (corticosteroids, chemotherapy, or surgery) reserved for cases involving vital organ compression or progressive extranodal disease.[2] In this case, a confirmatory excisional biopsy was appropriately recommended to fully characterize the disease extent and exclude rare concurrent malignancies. The unfortunate loss to follow-up poses a critical public health and clinical management challenge. While RDD is often self-regressing, the patient remains at risk for potential disease progression, especially if extranodal sites were subclinically involved, or if the initial cytological diagnosis was incomplete. This outcome underscores the necessity for robust patient tracking systems and emphasizes the global imperative for maintaining surveillance in the management of rare chronic diseases, ensuring that even presumptively benign conditions receive complete diagnostic workup and appropriate long-term surveillance.[12,15]

Limitation

Lack of confirmatory biopsy and molecular data.

Conclusion

This case report documents the diagnosis of RDD, a rare non-Langerhans cell histiocytosis, in a 12-year-old male presenting with classic massive, bilateral cervical lymphadenopathy. The diagnosis was made by FNAC, which demonstrated the pathognomonic finding of emperipolesis, highlighting the utility of FNAC as a high-yield, cost-effective diagnostic tool in resource-limited settings. While nodal RDD typically follows a benign, self-limiting course, the potential for recurrence or aggressive behavior necessitates complete pathological characterization and long-term surveillance. Finally, the patient's subsequent loss to follow-up underscores a persistent challenge in global health systems regarding continuity of care for rare, chronic disorders.

Ethics Approval

Institutional ethical approval was not required to publish the case details.

Consent for Publication

Written informed consent was obtained from the patient's legal guardian for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Author Contributions

All authors made a significant contribution to the work reported, took part in drafting and reviewing the article, gave final approval of the version to be published, have agreed on the journal to which the article has been submitted, and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no conflicts of interest in this work.

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