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Rosai-Dorfman Disease with Neck Swelling: Case Report of a Child

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Case Report

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Abstract

Rosai-Dorfman disease (RDD) is a rare disease, particularly in children characterized by histiocyte proliferation within the sinusoids of lymph nodes and in extranodal tissue that progresses with extensive lymphadenopathy. Massive cervical lymphadenopathy as the initial manifestation tends to raise the initial suspicion of lymphoma. We report a 12-year-old boy presented with right-sided extensive neck swelling, Initial lymph node biopsy, and S 100, CD68 positive in immunohistochemistry confirming the diagnosis of Rosai-Dorfman disease. Although spontaneous resolution occurs, in our case, even after chemotherapy the child presented with recurrent neck swelling, and needed neck dissection.

Keywords: Rosai-Dorfman Disease (RDD); Histiocytosis; Sinus; Histiocytosis; Non-Langerhans-Cell; Lymph Nodes; Child

Abbreviation

RDD: Rosai-Dorfman Disease

Introduction

Rosai-Dorfman disease (RDD) was described by Rosai and Dorfman in 1969, as a rare benign histiocytic disorder [1]. Classically, it presents as painless cervical lymphadenopathy but is increasingly showing extranodal involvement [1]. Recent studies have pointed out the diverse clinical presentations and their evolving understanding. It affects every age group, with mostly children and young adults being primarily affected, though the exact pathogenesis remains unknown, hence the various theories of infectious and genetic predisposition [2]. The most characteristic histological feature here is the presence of classical emperipolesis, wherein intact lymphocytes are phagocytosed by the histiocytes [3,4]. Recent genetic findings indicate that MAP2K1 pathway mutations may contribute to certain cases, enabling targeted therapies [2]. Histiocytosis, sinus, and non-Langerhans-cell histiocytosis are key features distinguishing this disease. This study reviews the clinical, histological, and radiological features of RDD while addressing differential diagnoses and therapeutic progress. It also presents the statistical analysis of prevalence and outcomes, hence offering insights into the prognostic trajectory of the disease. The involvement of lymph nodes is a critical hallmark, particularly in pediatric cases, which makes understanding RDD in children essential.

Case Report

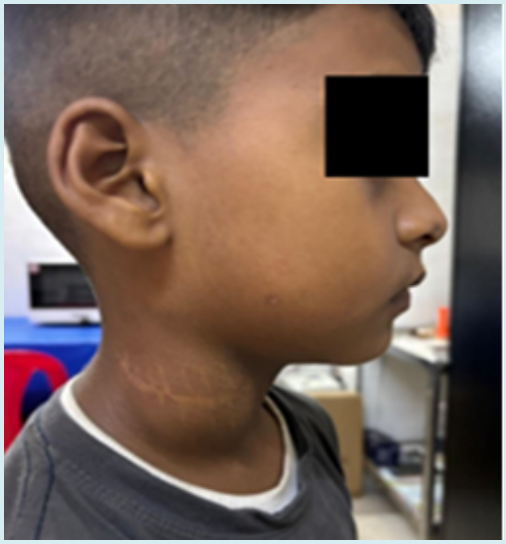

Figure 1: Clinical Picture.

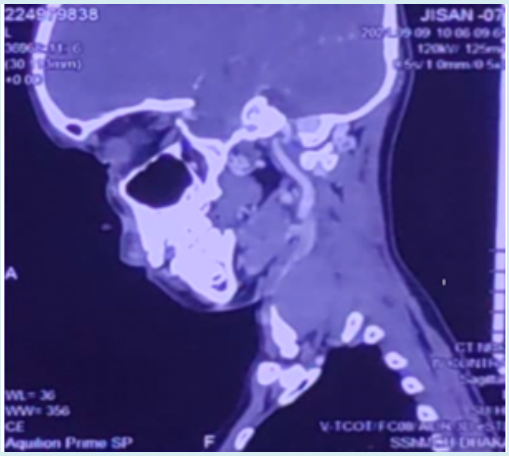

Figure 2: CT Scan Film.

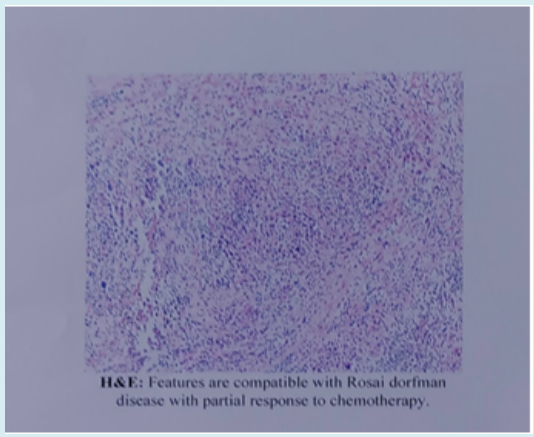

Figure 3: Histology Clinical Photograph.

A seven-year-old boy Figure 1 presented with a 4-month history of progressive right cervical lymphadenomegaly without signs of inflammation, fever, weight loss, or night sweats. The lab tests revealed Hb 11.7g/dl, WBC 3.83k/Ul, ESR 29 mm/h. a high blood sedimentation rate (BSR: 103 mm/h), An Ultrasound scan of the neck showed multiple right-sided cervical nodes at levels I II, III, and IV, the largest one measuring about 4.15X2.15 cm. The CT scan of the neck showed a similar picture (Figure 2). On physical examination, the child was found to be in good overall condition but presented with a cervical mass of elastic consistency, without signs of adherence or inflammation. No pathologies were observed in the lungs, heart, abdomen, or extremities. The child was submitted to cervical lymph node biopsy, the histopathological analysis of which revealed a lymph node measuring 4.5X3 cm. Embedded 4 blocks. Microscopic pictures showed multiple matted lymph nodes, these revealed diffuse proliferation of histocytes with enlarged round nucleoli and abundant eosinophilic cytoplasm (Figure 3). The immunohistochemical examination was positive for PS100, and CD68, and negative for CD1alfa, thus compatible with Rosai-Dorfman disease. The child was referred to oncology for medical treatment with chemotherapy, after having 27 cycles of vinblastine, the child presented to our hospital with recurrent right-sided cervical lymph nodes. He underwent selective neck dissection. At present, he has been sent for medical oncology support.

Discussion

RDD is a complex condition that necessitates comprehensive evaluation and treatment. Over 40% of patients appear as asymptomatic, bulky cervical lymphadenopathy [5,6]. Recent literature suggests a near 43% prevalence of extranodal involvement, complicating diagnosis and therapy [7,8]. Common extranodal sites include the skin, orbit, and central nervous system, though the involvement of the respiratory or gastrointestinal tracts is not unknown [9]. Indeed, some of these extranodal manifestations may be similar to other diseases, cancers, autoimmune diseases, and infective conditions that mostly present delayed diagnosis of the disease. The histiocytosis associated with RDD, especially non-Langerhans-cell histiocytosis, provides a key diagnostic marker.

Radiological findings in RDD are frequently nonspecific, posing challenges for definitive diagnosis. CT and MRI commonly show well-defined, non-enhancing soft tissue masses or lymphadenopathy, which may appear similar in neoplastic conditions or inflammatory disorders. Research shows that several cases revealed soft tissue mass with the need for histopathology confirmation [10,11]. Histologically, the disease features large histocytes with emperipolesis and immune-histochemical markers like S-100 positivity,

with negativity to CD1a [2,8]. These constitute important features in the differentiation of RDD from some disorders like Langerhans cell histiocytosis. The involvement of lymph nodes remains a prominent feature in the presentation of RDD, emphasizing the need for detailed histological evaluation.

The etiology of RDD remains speculative, with infectious agents like Epstein-Barr virus and Klebsiella pneumoniae implicated but not definitively proven [6,4]. Some MAPK/ERK pathway mutations in RDD patients show clonal histiocytic proliferation, relating it to neoplastic illnesses rather than reactive circumstances [12,13]. The concept of Rosai-Dorfman disease pathogenesis has increased, evolved, and reshaped the understanding of its underlying pathogenesis. This progress enables the possibility of targeted therapies, with MEK inhibitors among others indicated for refractory cases [14]. Such treatments make promising outcomes, given that they target the molecular pathology of the disease. Consequently, they represent an overwhelming shift in therapeutic approaches to RDD. Such developments usher in a new era in the effective management of this rare histiocytic disorder. The role of sinus histiocytosis is highlighted in recent studies as a critical aspect of RDD's pathology.

RDD could also be caused by immune dysregulation. Sickness progression in affected individuals might be attributed to cytokine increases, including IL-6 and TNF-α, in affected individuals. The association of RDD further with autoimmune diseases, notably systemic lupus erythematosus, points to the immunological origin of the disorder [15-17]. In light of these findings, immunomodulatory drugs targeting cytokine pathways that act in combination with current treatments are under investigation. Insight into the immunological system of RDD will provide new therapeutic modalities and better management. Understanding the prevalence of histiocytosis and its implications for lymph node pathology in children highlights the complexity of RDD.

Treatment strategies for RDD vary according to disease severity and site involvement. Many cases are asymptomatic and self-limiting; therefore, the illness can resolve itself [18]. Systemic or symptomatic illness requires corticosteroids, immunosuppressants, and chemotherapy [19,20]. New MEK inhibitor trials have shown potential, especially in refractory cases [21]. Surgical treatment is effective only in localized disease, and the inability to address systemic manifestations is a limitation [2]. Despite these advances, relapses occur in some cases, thus necessitating protracted follow-up. The impact of lymph nodes and their histiocytic involvement is a major focus in surgical and systemic treatment planning.

The prognosis of RDD is generally favorable, with survival rates exceeding 90% across most cohorts [15,22,23]. However, systemic involvement the more so in vital organs like the lungs far worsens the prognosis [11]. Ongoing development of imaging, histopathology, and molecular studies will improve diagnosis and treatment of this disease. The involvement of lymph nodes and extranodal manifestations underscores the need for continued exploration of sinus histiocytosis and non-Langerhans-cell histiocytosis in prognosis and treatment [24].

Analyzing Rosai-Dorfman's disease epidemiology and clinical features provides insights into its natural history and therapeutic outcomes [8,25]. In a retrospective review, 150 cases showed slight male predominance, as the male-to-female ratio was 1:5. This result is consistent with other studies also [2]. The median age at the onset was noted to be 50 years, though all age groups, from infancy to well-advanced adulthood, could be affected [2].

In other cases, cervical lymphadenopathy remains the most common symptom, occurring in 83% of cases, and thus presents as a hallmark feature. Of the 64 patients, 8% had classical (nodal only) and 92% had the extra-nodal disease (67% extra-nodal only). About 43% of the patients experience Extranodal involvement, mainly in the skin 52%, followed by lymph nodes (33%) [8,26]. Systemic symptoms include fever, night sweats, and weight loss identified in about 20% of the cases; most of them can present similarly to lymphoma or tuberculosis among other conditions.

Radiological findings further highlight the disease's complexity. Among the imaged patients, 68% had soft tissue masses, and 32% of the patients had isolated lymphadenopathy. These imaging findings, however, are nonspecific and have to be confirmed histologically to enable an appropriate diagnosis. All cases examined in histopathology showed the characteristic features of RDD, such as emperipolesis and S-100 positivity [8,27,28]. Immunohistochemistry was especially valuable for diagnosing RDD among other histiocytic disorders, thus signifying the importance of tissue biopsy for diagnosis [1]. The frequent involvement of lymph nodes and sinus histiocytosis is evident from the histological and immunohistochemical findings.

Treatment outcomes varied significantly depending on disease presentation and severity. About 32% were cases of spontaneous remission without intervention, while in a percentage of patients with RDD, the disease tends to be self-limiting [8,29,30]. Corticosteroid therapy was necessary in about 21%, primarily in patients with systemic or symptomatic disease, and surgical excision in 12%, mostly in those with localized extranodal disease causing functional impairment [2]. Targeted therapies include the use of MEK inhibitors in 5% of refractory cases, which induced partial or complete remission in these patients [30]. Despite such

therapeutic advances, 14% of cases relapsed, indicating that for a subset of patients, this is a chronic active disease with the tendency to relapse. Histiocytosis of the sinus and its role in prognosis, especially in pediatric cases, are areas of active investigation.

Survival analysis revealed a favorable five-year survival rate of 94%, consistent with the generally benign course of RDD [31,32]. However, this number considerably went down to an extremely low level in the cases of systemic organ involvement that implicate vital organs like the lungs or kidneys. The poor prognostic factors include advanced age, systemic symptoms, and more extensive organ involvement; early intervention and personalized treatment are justified [8,33,34]. These results again underline timely diagnosis and long-term management for better outcomes for the patients. The involvement of lymph nodes in children remains a consistent feature, guiding therapeutic decisions. Larger cohort studies with extended follow-up are essential to validate findings and improve prognostic models. Research should be directed toward the development of novel therapies for refractory or relapsing cases to optimize outcomes. Such efforts will also deepen the understanding of the natural history and progression of RDD.

Conclusion

Rosai-Dorfman disease, though rare, is a unique histiocytic disorder with diverse clinical and pathological manifestations. Advances in imaging studies, histopathology, and molecular genetics have enormously improved both diagnostic skills and treatment. Also, although self-limiting with systemic involvement, it can cause great morbidity requiring timely interventions pertinent to all patients for a universally optimal outcome. Statistical analyses reveal a slight male predominance, a broad age range of onset, and survival rates exceeding 90%. The systemic involvement of vital organs is a big challenge and carries a poor prognosis; it always requires continued follow-up and management. Newer therapies, especially MEK inhibitors, do hold promise in cases of refractory or relapse. This provides optimism for better outcomes and improved patient care. The variable clinical course of the disease necessitates a major multidisciplinary diagnosis and management. Further research is required since there is a need not only to understand its etiology properly but also to develop targeted treatment modalities. Patients in this difficult condition will receive state-of-the-art outcomes as model prognostics improve.

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