Rosai-Dorfman Disease: A Case Report

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Abstract

Rosai-Dorfman disease (RDD) is a type of sinus histiocytosis. It is a rare disease (1:200000), particularly in children and commonly presents with massive, painless and usually bilateral cervical lymphadenopathy along with fever and weight loss. Leukocytosis, elevated erythrocyte sedimentation rate and hypergammaglobulinemia are common. A definitive diagnosis can only be made by histological analysis of affected lymph nodes. Emperipolesis and a typical immunohistochemical pattern characterized by positivity for S-100 protein and CD68 antigen and negativity for CD1a antigen are diagnostic for RDD. Here we report a case of RDD occurring in a 10-month-old child with progressive cervical lymphadenopathy and persistent fever. Histopathological and immunohistochemistry studies of a lymph node biopsy established the diagnosis. A watchful follow-up resulted in the resolution of fever and lymphadenopathy.

Keywords: Rosai-Dorfman disease, Infant, Sinus Histiocytosis, Emperipolesis.

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Introduction

Rosai-Dorfman disease (RDD) is a type of class II histiocytosis.[1] Histiocytosis is a group of disorders or syndromes resulting in an abnormal increase in the number of specialized white blood cells. RDD is also known as sinus histiocytosis with massive lymphadenopathy. It is a rare disease with a prevalence of 1:200000.[2] It often presents with massive, painless, bilateral cervical lymphadenopathy associated with fever and weight loss. The disease was first described by Destombes in 1965 and was recognized as a specific pathological entity in 1969 by Juan Rosai and Ronald Dorfman.[1] Although rare in children, RDD can mimic infectious disease and malignant lymphoproliferative disorders. The objective of this paper is to report a case of RDD occurring in a child.

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Case Report

A 9-month and 12-day-old child presented with a 2-month history of progressive swelling over the left cervical region. The mother gave a history of an evening rise of temperature for the same duration. Clinical examination of the playful child revealed the presence of pallor and a large painless swelling involving the angle of the mandible on the left side of the neck. Multiple, discrete, mobile, lymph nodes comprised the mass. The consistency of the mass was variable having solid and cystic components, not fixed with underlying structure or overlying skin and having no discharging sinus. There was no sign of bleeding or gum hypertrophy or bone pain. He did not have any hepato-splenomegaly or ascites. Other examination findings revealed normal findings.

Investigations revealed a high erythrocyte sedimentation rate (ESR, 103 mm in 1sthour), leukocytosis (15 x10^9/L) with normal distribution (45% neutrophil, 52% lymphocytes) and anemia (Hb 7.7 g/dL). Moderate microcytic hypochromic anemia with anisochromia and anisopoikilocytosis was found on the blood film. Left cervical lymphadenopathy was confirmed by ultrasonography, with the largest lymph node diameter of 25 mm. A negative mononuclear spot test excluded Epstein–Barr virus (EBV) infection. The chest radiograph showed normal findings with no mediastinal enlargement (Figure 1).

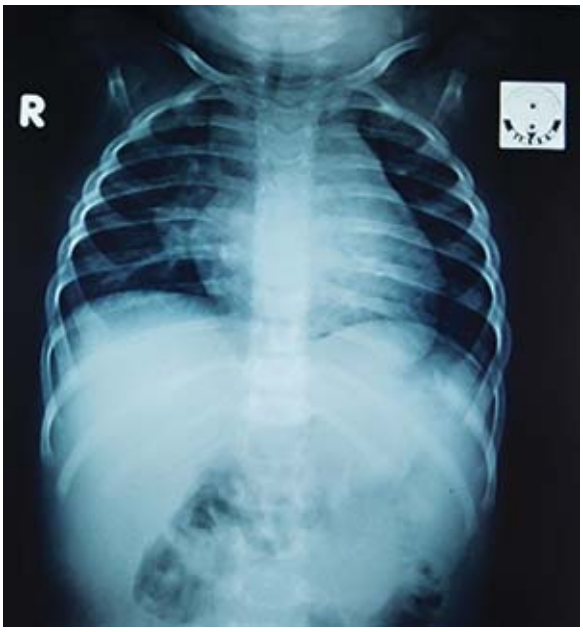

Fig.-1:*Chest x-ray showing normal findings.*

Assay of immunoglobulin levels revealed normal IgA, IgM, and IgE levels with slightly raised IgG levels. The quantitative rheumatoid factor (RA) test was normal but the indirect immunofluorescence assay of the antinuclear antibody (ANA) was positive. Histopathologic examination of biopsied cervical lymph node showed partial effacement of nodal architecture by marked dilatation of lymph sinuses. These sinuses contained histiocytes, lymphocytes, plasma cells, polymorphs and some eosinophils. Many histiocytes had intact lymphocytes and polymorphs in their cytoplasm exhibiting evidence of emperipolesis compatible with RDD (Figure 2). On immunohistochemistry, these cells displayed a positive reaction to CD68 and S-100 protein, whereas the reaction to CD1a was negative, which guided the diagnosis of RDD.

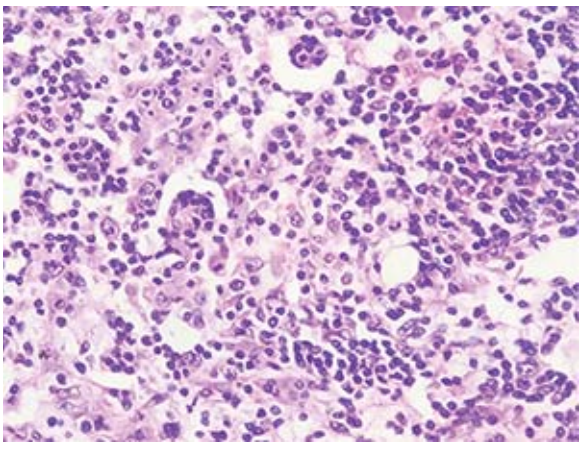

Fig.-2: *Histological sections of excised lymph node showing increased volume. A. Histiocyte containing numerous lymphocytes (emperipolesis) (hematoxylin and eosin at 400x magnification)*

A conservative approach was adopted. Regular follow was done in the outpatient department and eight months after diagnosis, the patient is clinically well and lymphadenopathy was resolved. No specific treatment was required.

Discussion

RDD is a bit more common among men (1.4:1) but significantly more common among Caucasians and Blacks than Asians.[3] Cervical lymphadenopathies are present in over 90% of patients. Typically, it is painless, bilateral and frequently massive. However, practically any group of lymph nodes can be involved; axillary (38%) and inguinal (44%), mediastinal (30%) and a hilar group of lymph nodes are involved.[4] Except for cervical nodes, the dimension of adenopathy in the other sites is usually smaller. Our case had painless unilateral cervical adenopathy.

Extranodal tissue involvement is documented in 43% of RDD patients and includes skin, soft tissues, upper airway, bones, urogenital system, lower airway and oral cavity.[5] No such involvement was found in our patient. Up to 30% of RDD patients report fever, frequently associated with a high ESR and polyclonal hypergammaglobulinemia (up to 90% of cases), anemia and neutrophilic leukocytosis.[6] Our patient presented with fever, had a high ESR, neutrophilic leukocytosis, anemia and raised immunoglobulin.

The etiopathogenesis and natural history of RDD are still not well known. The role of human herpes virus six (HHV-6) supported by reports of peculiar patterns of expression of HHV-6 antigens in abnormal histiocytes from RDD patients is described by some authors.[7] Some other authors believe the disease is the consequence of an exacerbated response of the immune system to infection by the EBV, cytomegalovirus, Brucella or Klebsiella.[8] It has been suggested that stimulation of monocytes-macrophage via M-CSF leading to immune suppressive macrophages may be the main pathogenic mechanism of RDD.[9] Recent molecular studies have revealed recurrent mutations involving genes in

the MAPK/ERK pathway in Langerhans cell histiocytosis.

A definitive diagnosis can only be made by histological analysis of affected lymph nodes or tissues. The association between emperipolesis, defined as the presence of phagocytized cells (mainly lymphocytes but also plasma cells, neutrophils or erythrocytes) in a histiocyte and atypical immunohistochemical pattern characterized by positivity for S-100 protein and CD68 antigen and negativity for CD1a antigen, is diagnostic for RDD. All of these parameters were present in our case. Emperipolesis alone is highly suggestive of the disease and in our case, it was present in histopathological examination of biopsied lymph nodes. But it can also be found in Langerhans cell histiocytosis (LCH), autoimmune hepatitis, lymphoma and rhinoscleroma.[10] Another characteristic is the absence of Birbeck granules, which are instead typical of LCH. LCH and RDD can be also distinguished by the CD1a pattern, being nearly always expressed in LCH.[11]

The differential diagnosis of RDD includes histiocytosis of Langerhans cells, histiocytic sarcoma, lysosomal storage diseases (such as Gaucher's disease), classic Hodgkin's lymphoma, melanoma and metastatic carcinomas and infections caused by Histoplasma and Mycobacteria involving the lymph node.[6]

Since the condition is most of the time self-limiting, it is often unnecessary to intervene, except when the airways are obstructed or vital organs are compressed. Several forms of therapy have been described involving corticosteroids, chemotherapy combined with alkaloids, anthracyclines, antimetabolics and alkylating agents, interferon, antibiotics, radiotherapy and partial or total surgical resection. A review of the literature revealed that 50% of patients with RDD require no treatment and that 82% of untreated patients experience spontaneous and complete disease regression.[8] In this case, after careful analysis of the biopsied specimen, a conservative approach was adopted.

The course of RDD is unpredictable. Episodes of remission and exacerbation may occur for several years. In approximately 70% of cases, the disease is permanent but stable, 20% experience spontaneous and permanent remission and 10% suffer from progressive and generalized disease.[12]

Conclusion

RDD has a relatively benign clinical course and generally resolves spontaneously. It often mimics infectious diseases and other malignancies and it can easily be misdiagnosed. A high index of suspicion is necessary for its diagnosis.

Consent:

We are grateful to the parents of this child who have been very understanding, supportive and co-operative with us throughout. They also give consent to publish it.

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