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CASE REPORT

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Rosai Dorfman Disease —A rare case of cervical lymphadenopathy

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Abstract

Rosai Dorfman disease is a rare cause of sinus histiocytosis with massive lymphadenopathy. In developing countries, it often mimics some infectious diseases and malignancies and is often mismanaged. A high index of suspicion is necessary for its diagnosis. It is seldom life threatening therefore observation is currently the best advocated approach for its management.

KEYWORDS

cervical lymphadenopathy, Rosai Dorfman disease, sinus histiocytosis

1 | INTRODUCTION

Rosai-Dorfman disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy, It is a benign disease of histiocytic proliferation with unknown etiology. Some theories suggest it is thought to be due to immune dysregulation or infections like HHV-6, HHV-8, parvovirus B19, EBV, CMV, VZV, brucella, and klebsiella however, the evidence is inconclusive.[1,2]

Common clinical presentation is fevers with painless massive cervical lymphadenopathy or it may involve other sites like brain, eyes, upper respiratory tract and skin.[3] The peak incidence is in the second or third decade and predominantly occurs in males.

Common abnormalities in the laboratory investigations are an increased erythrocyte sedimentation rate, leukocytosis, neutrophilia, normocytic normochromic anemia, and hypergammaglobulinemia. Histopathological examination of the lymph node remains the mainstay of diagnosis which shows massive sinusoidal dilation containing histiocytes positive for S-100 and CD68, and negative for CD1a.

RDD is seldom life-threatening disease which commonly does not require therapy. There are no defined therapeutic algorithms for its treatment. In many cases spontaneous regression is observed therefore usually the "watch and wait" approach is advocated. Surgery and systemic treatment for instance use of steroids or chemotherapy is rarely required.[4]

2 | CASE PRESENTATION

We report a case of a 1 year and 10 months old girl, who is the 5th child born child to non- consanguineous parents. She presented with fever and anterior neck swelling for 3 months. Fevers were high grade in nature, non-specific periodicity and relieved by paracetamol. The neck swelling initially started on the right side which then gradually increased to involve the whole neck. This was associated with difficulty in swallowing solid food. There was no history of difficulty in breathing or chest pains, or drenching night sweats. There was no history of headaches or blurry vision or history of

open TB contact. She had lost 2 KG over the course of illness. Her developmental milestones were appropriate for her age and she had received all immunization according to our national schedule. She was treated with Anti-TB's for one month at the primary health care center and had no improvement in the symptoms which necessitated referral to a tertiary hospital for further management.

On admission she was febrile with temperature ranging from 38 to 39 degrees, she had some palmar pallor but was not jaundiced, she also had multiple smooth surfaced preauricular, submandibular, anterior and posterior cervical and supraclavicular lymphadenopathy, which was firm, fixed and matted (Figure 1).

Other systemic findings were normal. We provisionally diagnosed her for Hodgkin's lymphoma.

In the ward a thorough septic work and re- evaluation of the diagnosis was done. Full blood picture showed leukocytosis (34.8 x 10^9/L), neutrophilia (36.4 x 10^9/L), normal lymphocyte count (2.2 x 10^9/L), microcytic hypochromic anemia (Hb 8.65g/dl; MCV 73fL; MCH 22pg), thrombocytosis (654 x 10^9/L). Peripheral smear showed anis poikilocytosis and no blast cells were observed.

She had raised C- reactive protein (CRP) 296, Erythrocyte sedimentation rate (ESR) 245, Adenine deaminase (ADA) 218 and Lactate dehydrogenase (LDH) 295 levels. HIV test and gastric aspirate for gene expert were negative. Viral screening for EBV IgM and IgG, CMV IgM and IgG, Herpes simplex virus I and II IgM and IgG were also negative.

We performed 2 Blood cultures one week apart and urine culture and sensitivity which showed no growth after 5 days. Cerebrospinal fluid analysis was normal. CT scan of the head and neck revealed multiple matted supraclavicular, cervical, submandibular and sublingual lymph nodes. Abdominal Ultrasound revealed multiple para aortic lymph nodes. Fine needle aspiration (FNAC) was done from the left anterior cervical lymph node which was reviewed by a team of haemato-pathologist.

Histopathology results revealed partial effacement of lymph nodes architecture by marked expansion of Sinuses by Large Histiocytic cells. Reminiscent granulomatous process and no necrosis. Immunohistochemistry was strong for CD 68 AND S-100 positivity. CD 1 a and ZN stain were negative to rule out Langerhans histiocytosis and extrapulmonary tuberculosis respectively. A diagnosis of ROSAI DORFMAN disease was made.

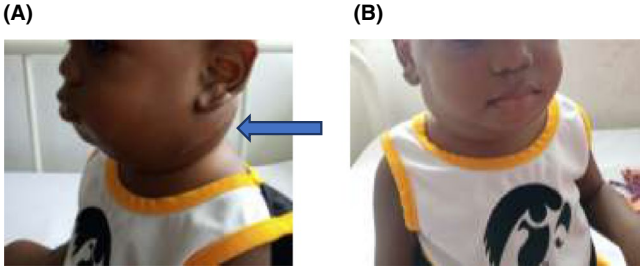

FIGURE 1 A and B, Bilateral neck swelling

We stopped Anti TB drugs and initiated oral prednisolone 10 mg twice daily for 4 weeks then to taper off slowly over another 4 weeks. Proton pump inhibitor like oral pantoprazole 20 mg once daily and calcium and vitamin D supplements once daily were prescribed to prevent gastritis and osteoporosis respectively which are side effects associated with prolonged steroid exposure. She was discharged and followed up monthly for the first 3 months to monitor response to treatment. Her mother was advised to check the baby's body weight every week and test for random blood glucose at least two times in a week at a nearby health center while she was on treatment. She showed improvement in her symptoms after one week of treatment as the fevers and the neck swelling started to subside and she gradually started taking solid foods. Currently, she is followed up every 3 monthly for the next 2 years in the outpatient clinic to assess for the possibility of relapse.

3 | DISCUSSION

Rosai-Dorfman disease (RDD) also known as sinus histiocytosis with massive lymphadenopathy, a rare disease with a variable presentation and course. Specific incidence and prevalence is not known for this disease with only about 1000 reported cases worldwide.[5] It is common in males than in females 4:1 and it affects all age groups but more frequently reported in young children and adolescents especially in the first two or three decades. Its pathogenesis remains unknown, though there is no clear causative agent in most cases a link between human herpes virus 6 (HHV-6), Epstein-Barr virus and parvovirus B19 has been suggested though not conclusive.[4]

Though the clinical presentation of RDD is variable however, the most common is site is nodal involvement that is painless bilateral cervical lymphadenopathy and it has been reported in nearly 90% of the cases.[1,4] This was consistent with our patient who presented fevers and multiple painless cervical, sublingual, submandibular and supra clavicular lymphadenopathy. Extra nodal involvement is also observed in approximately 40% of cases and can occur anywhere in the body with the most common sites including the skin, gastrointestinal tract, eyes, external and internal ear, skeletal system, upper and lower respiratory tracts, oral cavity, paranasal cavities, and the central nervous system.[1,3,6,7] However, this was not observed in our patient.

The histopathology of this disease is very characteristic. Lymph nodes shows massively distended sinuses, presence of numerous large histiocytes with vesicular nuclei, distinct nucleoli and abundant pale cytoplasm and emperipolesis. Emperipolesis, a biological phenomenon defined as the

active penetration of one cell by another which remains intact. The histiocytes will be positive for immunohistochemical stains CD68 and S100 and are typically negative for CD1a. Laboratory findings in RDD include leukocytosis, neutrophilia, normocytic anemia, thrombocytosis, an elevated C- RP, ESR, ferritin levels and hypergammaglobulinemia.[8] Similar histopathological and laboratory findings were observed in our patient.

In our setting this presentation can easily be misdiagnosed as it mimics infections like TB adenitis, reactive lymphadenopathies and sometimes malignancies like lymphoma and metastatic carcinoma which occur more frequently than RDD.

Fine needle aspiration cytology (FNAC) was used in our patient as compared to surgical core or excisional biopsy. FNAC can at times be misinterpreted due to limited or non-representative sampling and it does not permit examination of the tissue architecture, diagnosis can be further confounded. Despite these limitations, FNAC is still a very useful tool for the diagnosis of RDD.[9,10]

There is no unified therapeutic protocol for the treatment of this disease, spontaneous remission is observed and " wait and watch" approach is recommended.[2,4] For symptomatic patients requiring systemic therapy steroids are first-line therapeutic option that produces responses in both nodal and extra-nodal disease however, the reliability and durability of these responses is unpredictable. Furthermore, its duration of treatment is also not known.[3,4,10] Our patient was symptomatic and steroids were initiated using similar protocols that were used in some symptomatic patients with RDD.[3,8] Very limited clinical trials have been done using chemotherapy and radiotherapy therefore the effectiveness of these methods still remains to be uncertain. In cases of disseminated disease chemotherapy has been used with agents such as vinca-alkaloids, anthracyclines, and alkylating agents with varying response rates. Radiotherapy is considered a palliative method in patients with symptomatic disease.[2,4]

RDD has a remitting and relapsing pattern, however the recurrence rate is unknown. We aim to follow up our patient for at least 2 years to assess for the possibility of future relapse.

4 | CONCLUSION

RDD is a rare disease that has a relatively benign clinical course, it often mimics infectious diseases and other malignancies and it can easily be misdiagnosed. A high index of suspicion is necessary for its diagnosis. Definitive diagnosis is made by histology which show emperipolesis, sinus dilatation and histiocytic cells infiltration. Immunohistochemistry is positive for CD68 and S100 markers. Because the disease generally resolves spontaneously observation is currently the advocated approach however, for systemic symptoms steroids and chemotherapy have also been used for its treatment.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

AUTHOR CONTRIBUTIONS

IA, HS, EK, and LL: admitted the baby and were attending the baby daily in pediatric ward; U.M: was following up this baby in pediatric oncology; IA: prepared the manuscript; LM, AM, and HM: are specialists who provided their expert opinion in the management of this baby.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was not applicable. Consent for participation was given by the biological mother.

DATA AVAILABILITY STATEMENT

Data sharing not applicable.

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