CASE REPORT

Rosai-Dorfman Syndrome: Report of Two Cases

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ABSTRACT

Aim: To report and discuss two cases of Rosai-Dorfman Syndrome.

Summary: Cervical lymphadenopathy is a common clinical condition in paediatric age group ranging from benign reactive lymphadenopathy to malignant lymphoma. Rosai-Dorfman disease is an extremely rare self limiting disorder presenting as bilateral cervical lymphadenopathy. Rosai-Dorfman disease is a rare disease characterized by sinus histiocytosis with massive lymphadenopathy. Occasionally non lymphnodal sites such as central nervous system, eyes, upper respiratory tract and skin may be involved. The commonest presentation is bilateral massive painless cervical lymphadenopathy. Spleen and bone marrow is not usually involved. The disease has a self limiting course and spontaneous resolution without therapy occurs over a period of months to years.

Keywords: Rosai-Dorfman disease, RDD, Cervical lymphadenopathy, Lymphoma.

INTRODUCTION

Rosai-Dorfman disease (RDD) or sinus histiocytosis with massive lymphadenopathy (SHML) was first reported by Rosai and Dorfman in 1969.[1] It is a rare, benign proliferative disorder of histiocytes, sometimes showing familial incidence. SHML is a self-limiting disorder of unknown etiology usually presenting with cervical lymphadenopathy, fever, elevated ESR and hematological abnormalities.[2] It presents mainly in the first or second decades of life, but any age group can be affected. Without suspicion, the diagnosis of RDD is an unexpected and surprising finding. Especially in South East Asian countries where certain lymphadenopathies such as tuberculosis, metastatic nasopharyngeal carcinoma and lymphomas are common, RDD is unnoticeably missed, and its revision would seem worthwhile with this case illustrating the disappearance of the lymphadenopathy without treatment.

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CASE REPORTS

Case 1

A 16 year old boy presented with multiple bilateral painless swellings in neck which had gradually progressed over one and half years [Fig. 1a]. There was an initial history of fever for one month with no history of pain, respiratory tract infection or similar swellings elsewhere in the body. He had no loss of appetite or weight. There was no past history of tuberculosis or contact. General examination showed bilateral symmetrical cervical lymph node enlargement (2-5 cm in size), rubbery in consistency, non tender and matted which were clustered mainly in the upper posterior triangles. No abnormal findings were noted in examination of chest, abdomen and limbs. Fine needle aspiration cytology (FNAC) was done on the right upper cervical lymph nodes mass which showed emperipolesis (lymphocytophagocytosis) in the background of a mixed inflammatory infiltrate, consisting of moderately abundant plasma cells and lymphocytes, which are the classical histopathological features of Rosai-Dorfman's disease [Fig. 2]. The diagnosis of RDD was reconfirmed on excision biopsy of an isolated enlarged lymph node in the posterior triangle. No lymphomatous change was noted. Patient received no specific treatment and kept under observation. His neck nodes gradually decreased in size and were clinically non palpable over the follow-up period of 14 months after the initial presentation [Fig. 1b].

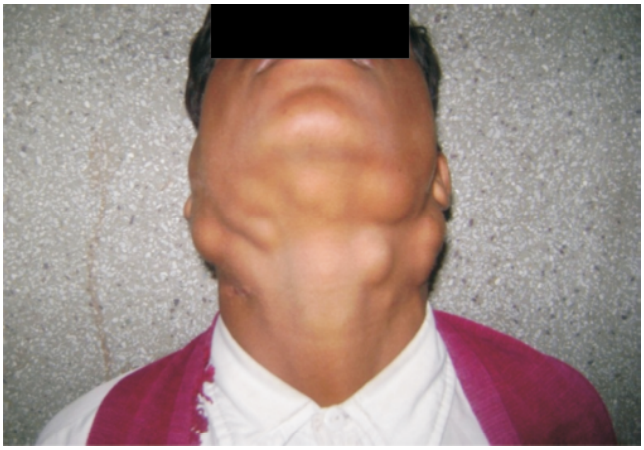

Figure 1a: Case 1 showing bilateral cervical lymphadenopathy

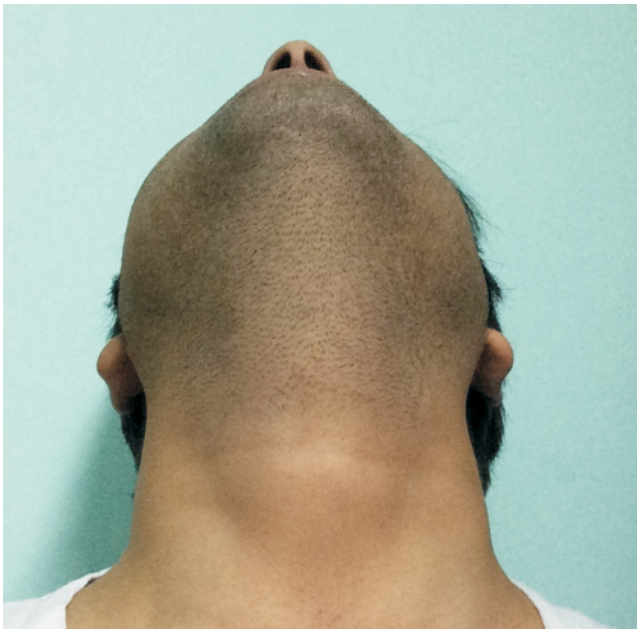

Figure 1b: Patient with completely resolved Lymph nodes at 5 year follow up.

Case 2

A 7 year old boy presented with multiple bilateral painless swellings in submandibular region which was slowly progressive in nature [Fig. 3]. There was no past history of pain, tuberculosis, respiratory tract infection, anorexia & significant weight loss. On examination there was bilateral symmetrical cervical lymph node enlargement about 3-5 cm in size and which was matted and rubbery in consistency. Examinations of chest, abdomen and limbs showed normal findings. Fine needle aspiration cytology (FNAC) from the lymph node showed features of Rosai-Dorfman's disease. Routine investigation of blood and biochemical examination showed values within normal range. Confirmatory diagnosis of Rosai-Dorfman's disease was made by excisional biopsy. Patient was under follow up at a regular interval of 3 months, the size of lymph nodes regressed gradually over a period of 18 months.

DISCUSSION

Rosai-Dorfman disease (RDD) was first described as giant cell sinus reticulosis by Robb-Smith in 1947, though this name was given by Rosai and Dorfman in 1969.[1] Literature search has shown about 600 cases reported till 2004. RDD is commonly seen in white males in first and second decades of life.[3] Chief complaints are massive, painless, bilateral cervical lymph node enlargement with fever in up to 90% of patients although multiple extranodal sites including the central nervous system, eyes, upper respiratory tract, skin, and head and neck region can be simultaneously involved in up to 43% of cases.[3] But most cases present with painless progressive, often symmetrical lymph nodal enlargement. Interestingly, hepatosplenomegaly and bone marrow involvement unlike in other histiocytic disorders , is uncommon.[4] The exact etiology of this disease is unknown though suggestions has been made that it may be an

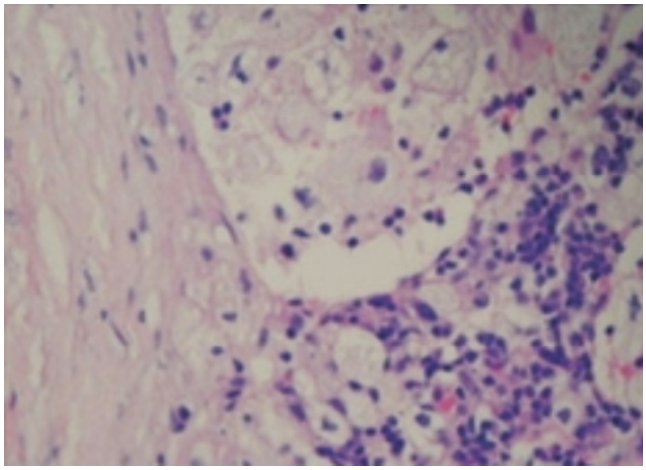

Figure 2: Magnification at 200x showing emperipolesis (lymphocyto-phagocytosis) in the background of a mixed inflammatory infiltrate.

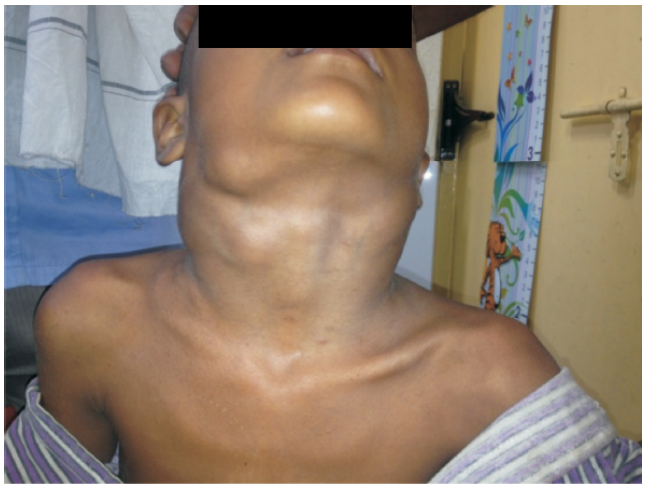

Figure 3: Case 2 showing bilateral cervical lymphadenopathy

unusual reaction to a Klebsiella infection.[3] Hematological abnormalities such as normocytic or microcytic anemia, polyclonal hypergammaglobulinemia, elevated ESR and reversal of A:G ratio.[4,5] Pathological differential diagnoses of RDD include reactive sinus hyperplasia, langerhans cell histiocytosis, Hodgkin's disease, metastatic carcinoma, malignant melanoma, and lymphoma.[5] Rosai-Dorfman disease is a non-Langerhans cell histiocytosis where sinuses of the lymph nodes are infiltrated with distinctive histiocytes with round or oval vesicular nuclei with well-defined, delicate nuclear membranes and a single prominent nucleolus and interfollicular area of the lymph nodes is less commonly involved.[1,2,5] The characteristic pathologic feature is emperipolesis (lymphocytophagocytosis) in the background of a mixed inflammatory infiltrate, consisting of moderately abundant plasma cells and lymphocytes.[8-10] Diagnosis can be readily established on fine needle aspiration cytology. Emperipolesis is mediated by Fc-receptor bearing lymphocytes[11] and can be demonstrated by a strong positive reactivity for S-100 protein in the histiocytes, a unique feature.[6] RDD cells are also positive for CD68, CD163, α-1antichymotrypsin, α1-antitrypsin, fascin and HAM-56 while CD1a is typically negative Fu on immunohistochemical staining. In situ hybridization has shown Human herpes virus 6 (HHV- 6) genomes or Epstein -Barr virus (EBV) within the histiocytes.[4] Rosai-Dorfman disease may show a remitting and relapsing course, where the timing and duration of each phase is entirely unpredictable. Stable course is seen in 54% of cases, spontaneous regression in 21%, and progressive disease in only 1%.[4] In light of the uncertain aetiological origin of the disease and of its frequent spontaneous remissions, treatment still does not have any set guidelines. Only about 50% of patients with Rosai-Dorfman disease need some form of treatment.[12] Most aymptomatic cases progress to resolution with time of several months and no therapy is needed. Surgical debulking may be required in patients with vital organ compromise, but in most cases it is limited to biopsy. Systemic corticosteroids in form of prolonged course of low dose prednisone, chemotherapeutic agents like low dose methotrexate (MTX) and 6 mercaptopurine (6MP) or prolonged therapy with Interferon-α have been used in refractory cases.[13] There is no conclusive role for Radiotherapy or antimetabolite therapy.[14]

CONCLUSION

The diagnosis of Rosai Dorfman disease (RDD) is of exclusion. The diagnostic and therapeutic implications of this disorder should be in the armamentarium of the treating surgeon, as it will reduce pitfalls in the management of this condition owing to its rarity, benign nature and excellent prognosis.

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