

Rosai-Dorfman Disease with Intracranial Involvement in a Young Female

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Abstract: Sinus histiocytosis with massive lymphadenopathy (SHML) or Rosai Dorfman Disease (RDD) is an uncommon benign, idiopathic disease that mimics lymphoma clinically. Strong clinical suspicion is required to diagnose this disease. Laboratory investigations may be non-specific. RDD most commonly affects lymph nodes, but extranodal involvement of multiple organs has been reported in literature. CNS involvement by RDD is an uncommon finding and may mimic meningioma radiologically. Histopathology is the gold standard for the confirmation of diagnosis. Histological diagnosis is obtained after incisional biopsy or excision of the lesion. We report a case of a young girl who presented with massive bilateral cervical lymphadenopathy and headache. MRI brain showed extra-axial, lobulated right CP angle mass. Her CSF examination, Fine needle aspiration cytology of cervical lymph nodes and excision biopsy of one lymph node showed histological hallmark of RDD, which is lymphophagocytosis or emperipolesis displayed by the histiocytes. Controversy exists about the etiology and pathogenesis of RDD. It has a relapsing and remitting clinical course and therefore therapeutic management varies with the clinical presentation of the patient.

Key Words: Sinus histiocytosis, Emperipolesis, Lymphadenopathy.

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Introduction

Castleman's disease, dermatopathic lymphadenitis, mucocutaneous lymph node syndrome (Kawasaki's disease), histiocytic necrotizing lymphadenopathy (kikuchi's disease), vascular transformation of lymph nodes¹ and Langerhans cell histiocytosis are among the rare causes of lymph node enlargement. Sinus histiocytosis with massive lymphadenopathy (SHML) is an important addition to this list of rare diseases. A physician comes across cases of massive lymphadenopathy almost every other day with a clinical picture difficult to differentiate from malignant lymphomas. Histopathology is the gold standard for the diagnosis in such cases.

Since it is a rare disease, a high degree of clinical suspicion is required to diagnose this disease.

Histopathology report usually surprises the physician if he was not suspecting it and at the same time provides relief to the physician and the patient, as this is essentially a benign and self-limiting disease. RDD predominantly affects the children and young adults with a slight male to female predominance (male: female = 1.4:1)². Concurrent involvement of nodal and extranodal areas by RDD is seen in 28% of the cases³. The central nervous system can be involved in less than 5% of cases².

Case Report

A 12 years old girl resident of Rawalpindi was in her usual state of health six years back when she noticed multiple small swellings in the cervical region, bilaterally. Swellings were insidious in onset, gradually increased in size and painless. There was

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accompanying history of headache without seizures and intermittent low grade fever, lasting for a couple of days unaccompanied by chills, weight loss, night sweats or pruritis. Her past, personal, and family history has been normal. Clinical examination showed multiple, non-tender, firm, and matted lymph nodes in cervical region. Chest, cardiovascular and central nervous system examination was unremarkable.

Her investigations showed a hemoglobin of 10g/dl, WBC10,000/cmm, differential- N 63, E7, L30, platelets 190000/cmm. Peripheral blood film showed microcytic, hypochromic red blood cells. ESR 40 mm/hr. Biochemical profile revealed normal renal and liver function tests.

Her fine needle aspiration cytology (FNAC) was performed from the bilateral cervical lymph nodes which showed many large histiocytes with abundant cytoplasm containing intact lymphocytes occasional neutrophils and plasma cells (emperipolesis) against numerous small lymphocytes, plasma cells and immunoblasts in background. Diagnosis of Rosai Dorfman disease was made.

Her cervical lymph node excision biopsy was done. Specimen was received in formalin. It consisted of a tan coloured lymph node measuring 3.6 x 3.5 x 1.3cm. Cut surface was homogenous, tan yellow and firm in consistency (Figure 1).



Figure 1: Gross image of excised cervical lymph node. The cut surface is homogenous and tan yellow in color.

Microscopic examination showed a lymph node with markedly dilated sinuses containing sheets of histiocytes having eosinophilic cytoplasm and small nuclei; some of the histiocytes show emperipolesis characterized by small lymphocytes in the cytoplasm. There was no evidence of malignancy or granulomas

seen in sections examined. These features were consistent with a diagnosis of sinus histiocytosis with massive lymphadenopathy. (Rosai-Dorfman Disease). (Figures 2a & b).

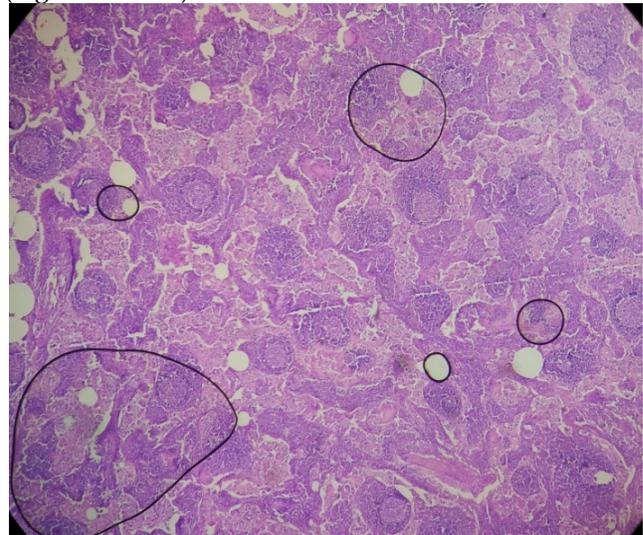


Figure 2a: Low power view of lymph node showing markedly dilated lymphoid sinuses with infiltration by the histiocytes. (H&E X 100)

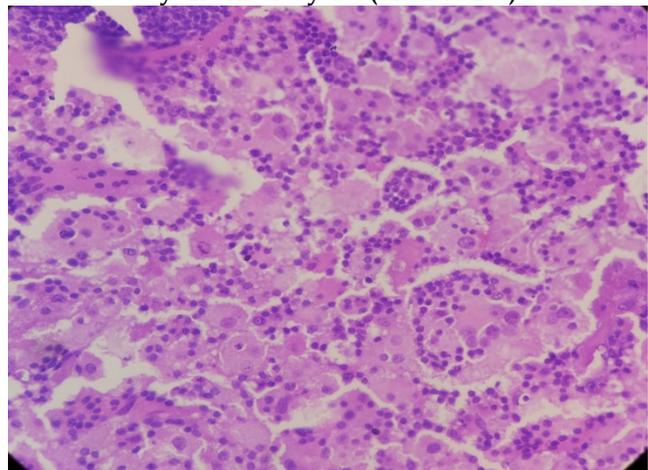


Figure 2b: High power view of the dilated sinus showing numerous histiocytes exhibiting emperipolesis (H&E X400)

Since she complained of headache her MRI brain with and without contrast was also done. It showed extra axial lobulated enhancing right CP angle mass with superior and inferior extensions into the right parasellar region and along the right lateral wall of medulla oblongata respectively, with enhancing dural deposits, suggestive of Rosai Dorman disease. Confirmation of diagnosis was done by cytologic analysis of the cerebrospinal fluid (CSF) which showed a mixed population of lymphoid cells and numerous histiocytes demonstrating emperipolesis,

characterized by engulfed lymphocytes with a surrounding prominent halo.

Discussion

Rosai Dorfman disease was first described by Robb-Smith in 1947 in children and was termed as giant cell sinus reticulosis¹. Sinus histiocytosis with massive lymphadenopathy was described by Destombes in 1965⁴. Subsequently, it was characterized as a distinct clinicopathological disorder in 1969 by Rosai and Dorfman⁵. By 1988, as it became evident that other nodal and extranodal sites could also be affected and the term Rosai-Dorfman disease (RDD) was preferred³. RDD predominantly affects the children and young adults with mean age of 20.6 years but can be seen in patients from 1 to 74 years old². Male population is affected more than the female population².

This disease is benign, characterized by lymphadenopathy, accompanied by fever, polyclonal gammopathy and leukocytosis with neutrophilia⁶. Lymphadenopathy appears in 87% of the patients and is often cervical, bilateral, massive and painless. Inguinal (25.6%), axillary (23.7%) and mediastinal lymph nodes (14.5%) may also be involved⁶. RDD only involves both nodal and extranodal sites in 28% of patients³. Our patient presented with both nodal and central nervous system (CNS) involvement.

CNS involvement in the setting of RDD is uncommon and has been reported in 210 cases in the English literature from 1970 to July 2013⁷. The mean age of patients is 39 years and a male prevalence has been reported⁷. As compared to the cases reported in literature, our case is interesting because CNS involvement is present in a 12 years old female. Neurological symptoms depend on the location of the lesion. Our patient presented with headache. CSF examination in cases of CNS involvement by RDD shows histiocytes with emperipolesis on cytological examination.

The etiological agent in Rosai Dorfman disease is still undetermined. The search for infectious agent has led to conflicting results, rendering RDD an idiopathic histiocytosis. Germline mutations in SLC29A3, have been reported in familial cases of RDD, suggesting that RDD may belong to a spectrum of disorders with SLC29A3 mutations, including Faisalabad histiocytosis, H syndrome, and pigmented hypertrichosis in the setting of insulin-dependent diabetes⁸. Our patient had no family history of RDD.

A high degree of clinical suspicion is needed to diagnose RDD, therefore detailed history and physical examination are required to rule out other causes of the lymphadenopathy. Important clue to diagnosis is absence of hepatosplenomegaly in RDD⁸, while it is commonly seen in other histiocytic disorders.

Laboratory investigations are often non-specific. Blood complete picture and peripheral blood film show normocytic or microcytic anemia, neutrophilic leukocytosis. 90% of the patients show elevated erythrocyte sedimentation rate. Polyclonal hypergammaglobulinemia is seen in 90% of the patients⁸. Histopathology is the gold standard for confirmation of diagnosis. Biopsy is done to confirm the diagnosis. Lymphophagocytosis or emperipolesis seen on microscopic examination is the hallmark of this disease.

There is a long list of non-neoplastic and neoplastic conditions that resemble the RDD histologically, but most important mimicker is langerhans cell histiocytosis. Immunohistochemically, RDD is positive for S100, CD68 and CD163. CD1a is an important distinguishing marker. It is negative in RDD but positive in langerhans cell histiocytosis⁸.

Multiple strategies of therapy have been used for intracranial RDD, including radiation therapy, chemotherapy, steroids, and surgery. Surgical resection is the most effective treatment. Recurrence after surgical therapy is rare and limited to incomplete debulking and multiorgan involvement⁹.

Prognosis of Rosai-Dorfman disease with involvement of the CNS is not poor. In a review of follow-up data of 43 patients, most patients (58%) were alive with disease. Only two patients (4.7%) had died. No death was reported as a result of isolated intracranial Rosai-Dorfman disease⁹.

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