Rosai-Dorfman Disease

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Abstract

A young male presented with recurrent neck swellings with initial leucocyte count of 16800/mm³, with non-caseating glands on ultrasonography neck. FNAC showed mixed cellularity with histiocytic and marked lymphohagocytosis as seen in Rosai Dorfman Disease. Immunohistochemistry demonstrated CD 25, Ki 67 and CD 68 in histiocytes. Her responded to supportive treatment alone.

Introduction

Rosai-Dorfman disease was initially described as a separate entity in 1969 by Rosai and Dorfman under the term sinus histiocytosis with massive lymphadenopathy (SHML).¹ Although Rosai-Dorfman Disease can occur in any age group, but frequently seen in children and young adults. Patients presenting with isolated intracranial disease tend to be older. In fact, many viruses like Herpesvirus 6 (HHV-6) and Epstein-Barr virus (EBV)² have been implicated as potential causative agents, but strong evidence is lacking for this at the moment. The causes of RDD are not fully understood, and treatment strategies can be different according to severity or vital organ involvement.

Case Report

A 20 year old male, presented with history of intermittent fever without chill and rigor, associated with headache and weakness for 7 days duration. On examination he had mild rise of temperature, no pallor or icterus, multiple cervical lymph nodes were enlarged (Figure 1), tender and firm in consistency. He did not have any sign of respiratory difficulty or pressure effect to any structure in the neck. His other systems were normal and there was no other lymph node group enlargement. His fundus and cranial nerves were normal. His chest X-ray was normal, ultrasonography of whole abdomen was unremarkable. His white cell count was 16800/mm³ on admission and became normal after three days along with ESR of 30 mm. Ultrasound examination of neck demonstrated multiple enlarged lymph nodes without any caseation. FNAC from submandibular lymph node showed a mixed cellular infiltrate consisting mainly of lymphocytes, plasma cells and occasional eosinophils (Figure 2). Histiocytic proliferation with marked lymphohagocytosis is seen throughout the smears.

The histological impression was reactive features with prominent lymphohagocytosis suggesting Rosai-Dorfman’s disease. Results of Immunohistochemistry from excised submandibular gland showed absence of CD 30, random staining with CD 25, Ki 67 was positive in histiocytes and CD 68 was positive in histiocytes.

Results of immunohistochemistry from excised submandibular gland showed random staining for CD 25, positive Ki 67 and CD 68 in histiocytes.

Discussion

Rosai-Dorfman Disease (RDD) is a well described entity, the etiology of which is still unknown. It often occurs in the setting of nonspecific immune dysfunction with many cases occurring after a viral illness. Human herpes virus 6 and to a lesser extent Epstein Barr virus may be involved in the aetiology as proposed by Levine et al.

The mean age of onset with nodal disease is 20.6 years with a male to female ratio of 1.4:1³. Patients who develop intracranial involvement, however, become symptomatic at a mean age of 34.9 years, with a strong male preponderance. Ninety percent of the patients present with massive painless bilateral cervical lymphadenopathy. Fever, anaemia, leukocytosis, elevated erythrocyte sedimentation rate, and polyclonal hypergammaglobulinemia may also be found. Extranodal involvement, such as in the eyes, skin, upper respiratory tract, bone, salivary gland, testis and in extremely rare circumstances, the central nervous system can be affected in about a third of the patients.⁴ Massive cervical lymphadenopathy is not always seen with intracranial RDD.

Cheng et al have reported two cases of RDD with locally aggressive features and dural sinus invasion. RDD can also present as pachymeningitis. Suprasellar involvement in CNS has been reported about five cases and hypothalamic-pituitary axis dysfunction has been described in only one case, in which diabetes insipidus was present.⁴ The differential diagnosis for Intracranial RDD includes meningoia, histiocyte X, Wegener’s granulomatosis, sarcoidosis, tuberculosis, gliosarcomas, Hodgkin’s disease, plasma cell granulomas, and in suprasellar lesions also includes germinoma, hemophagocytic lymphohistiocytosis, and metastasis. Radiological and at histological level they can mimic granulomatous

Fig. 1: Multiple enlarged cervical lymph nodes

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lesions. Thus histological and immunohistochemical confirmation is essential for a definitive diagnosis of RDD. On microscopic examination a polymorphous infiltrate of histiocytes, lymphocytes and plasma cells in a fibrous stroma can be seen. In RDD two subsets of histiocytes, differentiated by size, are present. The large histiocytes typically exhibit emperipolesis, which is an active penetration of one cell by another. In RDD, the large histiocytes contain well preserved lymphocytes and are usually S-100 positive. The medium-sized histiocytes may not exhibit emperipolesis, are representative of a histiocyte at an earlier stage, and are typically S-100 negative. In RDD with intracranial involvement, the treatment of choice is surgery. Leaving residual tumour has lead to recurrence of the disease.

Treatment modalities: Patients with RDD without vital organ involvement should be followed closely without any active treatment. Associated systemic symptoms or those with sudden enlargement of nodes may be treated with prolonged course of low-dose prednisone; the optimal duration of low dose steroid is yet to be defined. For patients with vital organ compression, surgery and high-dose corticosteroids is to be tried first, but radiotherapy may be needed in resistant cases or whenever surgery is not feasible.

Since RDD is self-limited in most patients, the use of chemotherapy should be restricted to patients with life-threatening disease or for those non-responsive cases and or cases with multiple relapses. Combination therapy with low-dose Methotrexate and 6 Mercaptopurine seems justifiable in patients with multiple reactivations. Till more novel and more effective treatment strategies are available reassurance with wait and watch policy remains applicable for most of these cases.

**Conclusion**

RDD as differential diagnosis is to be considered in cases of recurrent lymphadenopathy mostly in the cervical region. A high degree of clinical suspicion is needed to make the diagnosis because the differential diagnosis includes both malignancy and other histiocytic disorders.

**Abbreviations**

RDD Rosai-Dorfman Disease; SHML Sinus histiocytosis with massive lymphadenopathy; ESR Erythrocyte sedimentation rate; AEFH At the end of first hour; CT Computerised tomography; CNS Central Nervous system

**References**