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Rosai dorfman disease-A rare disease in India

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Abstract
A 27 year old male presented with complaint of painless cervical lymphadenopathy which was progressively increasing in size and low grade fever on and off since one and a half year. Bilateral Cervical and axillary lymphnodes were palpable. The lymphnodes were firm, mobile and painless. Liver was palpable, non-tender and smooth in consistency. Hematological parameters and ESR in this case were in normal range. FNAC was suggestive of Hodgkin's lymphoma but immunohistochemistry showed S-100 protein expression and lesion demonstrated emperipolesis. Hence the diagnosis of RDD was made. Patient was initially non-compliant to medical advise and presented after 5 years with similar complaints. He was managed using Rituximab and Chemotherapy with cyclophosphamide and Adriamycin. Also, oral prednisolone 100 mg was started. The patient responded very well to treatment over a period of two weeks and showed no signs of recurrence after 12 months follow up.

Keywords: rosai dorfman disease, disease

Introduction

Rosai Dorfman disease (RDD) is a rare form of non-Langerhans cell histiocytosis which is a histopathological diagnosis. It is characterized by accumulation of CD68 & S100 positive histiocytes and CD1a-negative histiocytes with frequent emperipolesis [1]. The disease was first described by a French pathologist, Destombes in the year 1965 in a four African young children and adults. Initially, RDD was termed "adenitis with lipid excess" as the condition is associated with lipid laden histiocytes in the tissue specimen [2]. Later, in 1969, Rosai and Dorfman reported massive cervical lymphadenopathy with specific histiopathological features in a series of patients. The disease was termed "sinus histiocytosis with massive lymphadenopathy" or Rosai Dorfman disease [3].

The disease has been reported in all races but it is relatively common in Caucasians (43%). RDD can be observed in any age group, but is common in first and second decade. Males are commonly affected as compared to females and male: female ratio have been reported as 2:1.[4] Typically, the patients presents with fever, leukocytosis and painless cervical lymphadenopathy. Though the disease has higher predilection for the lymph nodes in the head and neck, it may also involve extranodal sites such as skin and soft tissue, CNS. RDD is a non-malignant disease and histology & immunohistochemistry are helpful in establishing its definitive diagnosis. The disease is considered as self-limiting which rarely require systemic therapy but few patients may have adverse outcomes [5].

Case Details

A 27 year old male presented with complaint of painless cervical lymphadenopathy which was progressively increasing in size and low grade fever on and off since one and a half year. He was not addicted to tobacco smoking/chewing or alcohol. Also, no history of comorbidities could be observed. His weight was 62.6 kg and height was 153 cm. His body surface area was 1.56m^2. On general examination, he was afebrile, pallor was present. On local examination, bilateral Cervical and axillary lymphnodes were palpable, maximum size being 8x10 cm. The lymphnodes were firm, mobile and painless. Liver was palpable, non-tender and smooth in consistency. He was advised investigations such as USG abdomen, HIV, LDH and ESR. Hematological parameters and ESR in this case were in normal range.

Biopsy of lymphnode was taken and subjected to immuno Histopathological examination. FNAC was suggestive of Hodgkin's lymphoma but immunohistochemistry showed S-100 protein expression and lesion demonstrated emperipolesis. Hence the diagnosis of RDD was made.

He was given Inj solumedrol 125 mg stat, Injection Endoxane 1gm IV stat, Inj VCR 2 mg stat and Inj Epirubicin 50 mg IV stat. He was advised Tab Endoxane 50 mg 1 OD for 1 month and Tab Omnacortil 40 mg OD for 15 days. The patient was non-compliant to medical advice and returned for visit after one month. His symptoms persisted and he was given Inj Endoxane 1 gm, Inj cytocristin 2mg, Inj Solumedrol 1 gram IV and Inj Doxorubicin 50 mg IV stat. Following this, patient did not report for follow up.

He again presented after 5 year with bilateral neck swelling and difficulty in swallowing. On local examination, bilateral cervical level I to VI, axillary, supraclavicular and inguinal lymphnodes were palpable which were tender, non-matted and mobile. He gave no history of fever at this time.

Complete hemogram was done which was normal. Oesophago-gastro-duodenoscopy was done which revealed normal findings.

FNAC of Lymph node was performed from various sites. Smears were stained with MGG, PAP, and H&E stains. On microscopic examination, cytological smears revealed the presence of diffusely distributed uninucleated, binucleated as well as multinucleated histiocytes throughout the FNAC smears, but no nuclear atypia. The cytoplasm of these histiocytes exhibited numerous intact lymphocytes (emperipolesis) as well as neutrophils. Again immunohistochemistry was also done which was reactive to S100 histiocytes. Based on these features, diagnosis of Rosai- Dorfman disease was made.

He was subjected to CECT neck which revealed bilateral enlarged cervical lymphadenopathy at level I to VI, largest measuring 2.5 cm, along with few enlarged mediastinal lymphnodes. Mucosa of paranasal sinus showed signs of inflammation.

He was managed using Rituximab 500 mg in 1 unit NS over the period of 3 hours under strict observation. Also, Tab prednisolone 100 mg OD for 5 days was given. After checking for RFT, Chemotherapy with cyclophosphamide and Adriamycin was started using standard protocol. The patient responded very well to treatment over a period of two weeks. Symptomatically he improved. Subsequently, the patient was given tapered doses of oral prednisolone over the next two weeks and asked to report monthly for follow up. There was no evidence of recurrence on follow-up over a period of 12 months.

Discussion

Rosai Dorfman disease (RDD) is a rare disease in India. Only 2 cases have been reported in Indian adults.[4,6] Though, the patient presented with low grade fever which was occasionally present, his hematological parameters as well as ESR was in normal range. These findings were contrasting with the previous two reports in which ESR was raised.[4,6]

Rosai and Dorfman in their serioes of patients described the disease which is characterized by well-defined, histiocytic proliferation and spontaneous remission. The patient usually present with typical massive bilateral cervical lymphadenopathy which is classically mobile and non-tender. Though the nodes are non-matted, but may become matted due to pericapsular fibrosis. The patients may also present with lowgrade fever with, normocytic normochromic anaemia, elevated ESR, leucocytosis, and hyperglobulinaemia [3]. Our case had persistent lymphadenopathy which was progressive in nature. In present scenario, patient presented with multiple lymph node enlargement. Initially, bilateral cervical and axillary lymph nodes were palpable but after five years even supraclavicular and inguinal lymphnodes were palpable. The lymphnodes initially were non tender but later they were tender. Similarly, Mehrotra *et al.* [7] in his case demonstrated a patient with multiple lymph node swellings at various sites involved. However, Warpe BM *et al.* reported the disease in 12 year old child with only cervical lymph nodes along with extranodal, nasal mass [8].

The exact aetiology of Rosai Dorfman disease remains unclear. However, familial or infection have been proposed as possible etiological factors. As the disease is associated with a similar immune response which is observed in response to an infectious agent. Epstein Barr Virus (EBV), and Human Herpes Virus 6 (HHV-6) have been associated with RDD but exact relationship is still lacking [9]. Also, the role of familial factors have been postulated. Stimulation of monocytes/macrophages via macrophage colony stimulating factor (M-CSF) has been observed in RDD. Such stimulation is associated with formation of numerous large histiocytes. Some macrophages demonstrate phagocytosis of lymphocytes or neutrophils, which is called "emperipolesis" [9, 10]. The disease is characterized by accumulation of CD68 & S100 positive histiocytes and CD1a-negative histiocytes [1]. In this case diffusely distributed uninucleated, binucleated as well as multinucleated histiocytes throughout the FNAC smears were observed with emperipolesis. Immunohistochemistry was reactive to S100 histiocytes.

RDD is usually a self-limiting disease and rarely require chemotherapy. The disease may be managed using corticosteroids, chemotherapy, antibiotic therapy, radiation therapy, and surgical treatment [11]. In present scenario, the patient was initially managed using conservative therapy. Though, he responded well to the treatment, the disease could not be cured as he was non-compliant. Later he presented after five years and managed using chemotherapy. He was more vigilant towards medical advice and followed all the instructions this time. He responded well to the treatment and disease did not recur even after 12 month of follow up.

Since the disease is rare, but present with typical clinical presentation, careful interpretation FNAC is required for presence of histiocytes especially in presence of bilateral massive cervical lymphadenopathy. FNAC must be supplemented with immunohistochemistry for definitive diagnosis as the disease typically has accumulation of CD68 & S100 positive histiocytes and CD1a-negative histiocytes [1].

Thus if an adult patient comes with history of cervical lymphadenopathy with or without fever, after ruling out common diseases, possibility of RDD has to be kept in mind for prompt management.

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