Rosai Dorfman Syndrome with Sinonasal Mucosa and Intraocular Involvement

M Kare*, S Dang **, A Dang***

Abstract
A 15 year-old-male presented with concurrent sinonasal polyposis and anterior uveitis with cervical lymph node enlargement. Cervical lymph node biopsy confirmed Rosai-Dorfman disease. Though patient’s eye symptoms did not respond well to topical corticosteroid treatment but he showed a remarkable regression in the size of nasal polyps and cervical lymph nodes after systemic corticosteroids. Intraocular involvement in such a case is rare. ©

INTRODUCTION
Sinus histiocytosis with massive lymphadenopathy (SHML) is a unique disease of unknown etiology which was initially described by Azoury and Reed and later it was described to have a benign course by Rosai and Dorfman in 1969 and is now widely known as Rosai-Dorfman disease or syndrome (RDD), a benign histiocytic proliferative disorder. Although it was initially considered to be a lymph node limited disease that involved the cervical stations in particular with a biphasic course (slowly progressive adenopathy followed some months later by gradual recovery), now is recognized as a distinct clinicopathological entity.

CASE REPORT
Fifteen years school boy from Bihar presented to ENT department with history of recurrent nasal polyposis. He complained of nasal blockade, running nose and difficulty in breathing for 1 year. Anterior rhinoscopy done six months back showed multiple anterior nasal polyps. He subsequently underwent nasal polypectomy. This only gave him relief for a short time and he had recurrence of similar symptoms. Biopsy of the tissue showed inflammatory reaction with no evidence of malignancy. There was no history of epistaxis. Three months prior he complained of difficulty in vision, redness and photophobia in the right eye. He also noticed swelling in the neck, bilateral which had progressively increased in size. General examination showed pallor, enlarged bilateral cervical lymph nodes, firm and non tender, measuring about 2-3 cm without any matting. Systemic examination was normal. On examining vision for right eye, perception of light was present with hand movement appreciation. On slit lamp examination, cornea showed mutton fat keratic precipitates, anterior chamber revealed aqueous flare, iris was muddy with the presence of posterior synechiae and exudative membrane in pupillary area. On USG B scan and ophthalmoscopy examination, posterior segment including retina was found to be normal. Anterior and posterior rhinoscopy showed multiple sinonasal polyps. The blood test revealed hypochromic microcytic anemia with high ESR (61 mm/hr) and total count of 10,000 cells/cmm. The RFTs, LFTs, serum albumin and serum globulin were within normal limits. HIV and tuberculin test was negative. FNAC of the lymph node showed chronic inflammatory non-specific reaction. A phenomenon known as emperipolesis or lymphophagocytosis was seen on taking biopsy of the lymph node which confirmed the diagnosis. He was started on ofloxacin (3 mg/ml) and prednisolone acetate (10 mg/ml) eye drops combination with QID dosage schedule along with flurbiprofen eye drops (0.5%) to be put 3 times a day. He was also given atropine sulphate (1%) TDS eye drops along with 1mg/kg body weight prednisolone as systemic therapy. Though patient’s eye symptoms did not respond well to topical corticosteroid treatment but he showed a remarkable regression in the size of nasal polyps and cervical lymph nodes within 6 weeks of starting the treatment, thereafter lost to follow up with us. This was one of the drawback with respect to our case report along with the fact that we could not confirm the diagnosis with immunochemistry i.e. histiocytic positivity for S-100 protein CD-68 protein, which is considered as gold standard, due to lack of laboratory set up in our hospital but a recent report do state that fine-needle aspiration cytology plays an important diagnostic role in SHML and may be...
conclusive in a typical clinical setting.² Hence with the classical features of massive bilateral cervical lymphadenopathy and evidence of sinus histiocytosis on histopathological examination of cervical lymph node, diagnosis of SHML or Rosai-Dorfman syndrome was made.

**DISCUSSION**

Rosai-Dorfman disease is a rare histiocytic proliferative
disorder. The etiology of the disease still remains obscure as precise origin of pathologic cells is still controversial and it is unclear if it is immune-mediated, of infectious origin, or related to some other pathological mechanism which is yet to be clarified, though sporadic cases have been associated with Klebsiella, Brucella, Epstein-Barr virus or herpes virus infections and few cases with malignant lymphoma. Using a broad panel of monoclonal and polyclonal antibodies the immunophenotype of the cell infiltrate of the lymph nodes of cases of RDD showed a heterogeneity of cell markers. Immunoreactivity of the histiocytes for S-100 protein and CD-68 positive large histiocytes displaying lymphocyte phagocytosis are characteristically seen.

Typical clinical features of the disease include massive painless cervical lymphadenopathy (the axillary, inguinal and mediastinal nodes may be affected), fever and weight loss, neutrophilia, elevated erythrocyte sedimentation rate, anaemia and hypergammaglobulinemia. Autoimmune hemolysis can also occur. Involvement of an extranodal site is present in approximately 43% of cases, either alone or in association with lymphadenopathy. Every organ system can be affected by RDD, the most common being head and neck, others include skin, lungs, bone, mucosa, orbits etc. The most common site of the ear, nose, and throat involvement was the nasal cavity, with the major salivary gland being the second most common site. Involvement of the extranodal head and neck sites appear to be more common in patients with immunologic abnormalities. Generally, patients present in their mid-20s but no age is exempted.

We report this case to draw attention to this unusual presentation of SHML confined to the sinonasal mucosa with intraocular involvement which to our knowledge is the first case of this kind being reported. In one report of SHML, uveitis with papilloedema was the only presentation and in another report the only site of the lesion was lacrimal sac with the duct but these patients later developed cervical lymphadenopathy. Another case with ocular involvement was reported with uveitis and marginal corneal infiltrates in association with cervical lymphadenopathy.

Fine-needle aspiration biopsy can be helpful in establishing the correct diagnosis. The characteristic pathologic feature of this disease is proliferation of distinctive histiocytic cells (with round or oval vesicular nuclei, delicate nuclear membranes, voluminous pale or eosinophilic cytoplasm and a halo around), in the background of a mixed inflammatory infiltrate, consisting of moderately abundant plasma cells and lymphocytes, a phenomenon known as emperipolesis or lymphophagocytosis that confirms the diagnosis.

Practically, the most common problem in differential diagnosis in cases of lymph node involvement is to distinguish the disease pathologically because many diseases can resemble Rosai-Dorfman disease morphologically.

1. Sinus hyperplasia (sinus histiocytosis): S100 protein is strongly expressed by RDD and negative in normal sinus histiocytes.
2. Langerhans cell histiocytosis: Nuclei of Langerhans cells are smaller and often irregular, with folding, grooves and fine chromatin without prominent nucleoli. Emperipolesis is not a feature of Langerhans cells and there is prominent eosinophilic component, including formation of eosinophilic abscesses.

There is no specific treatment for the Rosai-Dorfman syndrome. Treatment is required when the condition is organ threatening or life threatening. The treatment modes include corticosteroids, chemotherapy with a combination of vinca alkaloids and alkylating agents, low dose interferon, radiation therapy and surgery.

The condition is benign and has a long-term clinical course characterized by exacerbations and remissions and appears to undergo complete remission in most patients but some patients may have a fatal outcome. Mortality has been reported to be approximately 7%, possibly due to immune system dysfunction particularly at the level of the T-cell network and effacement of the node in a later phase. In others, an insidious course develops for years or decades, more common in the extranodal cases.

Acknowledgements
Dr. Wiseman Pinto, Head of Department, Pathology, Goa Medical College. Dr. Anita Spadigam, Head of Department, Oral and maxillofacial Pathology, Goa Dental College.

REFERENCES