



Case Report

Extra nodal Rosai Dorfman disease of nasal septal mucosa without lymphadenopathy

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ABSTRACT

Rosai–Dorman disease, also known as sinus histiocytosis with massive lymphadenopathy, typically presents as massive enlargement of lymph nodes accompanied by systemic symptoms. Extranodal involvement is also known usually in head and neck regions. Rarely the disease presents at extranodal sites only without involvement of lymph nodes.

We present a case of 58 years-old female who presented with mass in nasal septum without involvement of lymph nodes. The mass was removed surgically and diagnosis was made on histological grounds with classical findings of histiocytic proliferation and emperipolesis.

INTRODUCTION

Rosai–Dorman disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy (SHML), a rare and usually self limiting disease, was originally described by Destombes in 1965.¹ Subsequently; in 1969, it was characterized as a distinct clinicopathological disorder by Rosai and Dorfman.² It is a pseudolymphomatous nonneoplastic lymphoproliferative disease of unknown etiology that presents with systemic symptoms.³ The presentation is bilateral cervical, axillary or inguinal lymphadenopathy that is painless, accompanied with pyrexia, leukocytosis and hypergammaglobulinemia.³

In 43% cases disease may have extra nodal involvement⁴, most common sites being nasal cavities, skin, eyes, orbit, eyelids, bones, soft tissue, the central nervous system, upper respiratory tract and less commonly, the gastrointestinal tract, But it may present itself at extra nodal sites only in absence of obvious lymphadenopathy.⁵⁻¹¹

Rosai–Dorman disease typically manifests in childhood or in early adulthood, mostly in the second and third decades of life.¹² Caucasians have a higher prevalence than African Americans. A male predominance is observed.¹² Rosai–Dorman disease is rare in India, till 2007 only about a dozen cases have been reported, all in children and none in adults. No case of extra nodal involvement has been reported. The disease usually follows an insidious course but could be fatal due to involvement of vital organs.

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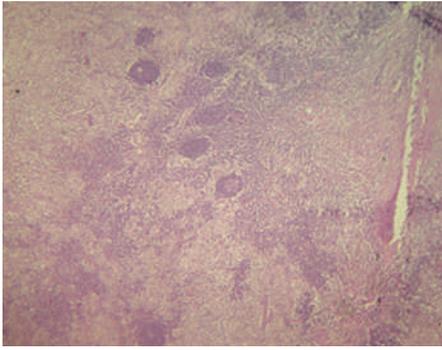


Figure 1: Low power view of the lesion, nasal mucosa with histiocytic proliferation underneath; Extensive histiocytic proliferation. And few lymphoid follicles [HE stain, X100]

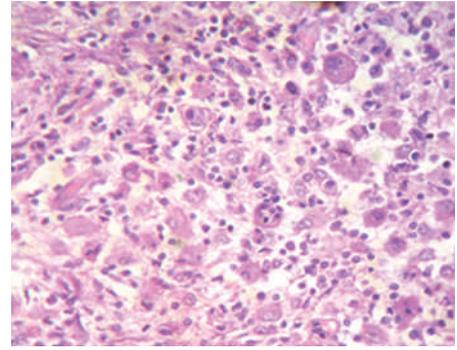


Figure 2: High power view of the lesion, extensive emperipolesis. [HE stain, X400]

Histopathologically, it is characterized by flooding of lymphatic sinuses by histiocytes and plasma cells. The most important diagnostic finding is emperipolesis which is active penetration of a smaller cell into or through a larger cell more commonly phagocytosis of intact lymphocytes, plasma cells or red blood cells by histiocytes.¹³ In extranodal diseases emperipolesis is seen less frequently but in our case it was quite frequent. Immunohistochemistry like positivity for S100 and CD68(+) and negativity with CD1a protein help differentiate RDD from malignant disorders such as lymphoma.

CASE REPORT

A 58-year-old female patient presented to the outpatient department with complaints of difficulty in breathing and frequent episodes of epistaxis since three months. Endoscopic nasal examination revealed a mass originating from the nasal septal mucosa.

Computed tomography images of right paranasal sinus showed a large well defined homogeneously enhancing soft tissue density mass lesion in the right half of nasal cavity measuring 5x3.7x2.5 cm polyp arising from right nasal septum. The lesion was causing expansions of the nasal cavity with smooth scalloping and remodeling of adjacent bones. It was obliterating all drainage pathways. Left nasal cavity and paranasal sinus were unremarkable.

The mass was endoscopically excised which was soft in consistency, largest 3.5x3x1 centimeters. The histopathological examination revealed a polypoid lesion lined by pseudostratified columnar epithelium. Stroma showed sheets of histiocytes along with a large number of mature plasma cells, lymphocytes and few lymphoid follicles with prominent germinal centre.(fig.1) Most of the histiocytes did not show any foamy cytoplasm. Bi and multinucleation was also seen, however popcorn cells were absent. There was no fibrocollagenous proliferation. Many

histiocytes had large and vesicular nuclei and showed lymphocytic emperipolesis. (fig.2). The histiocytes were S100(+), CD68(+) and negatively stained with CD1a. Histopathological and immunohistochemical findings were consistent with the diagnosis of RDD– extranodal involvement.

DISCUSSION

Rosai–Dorman disease is a disease of unknown etiology. Histiocytic proliferation could be due to a long standing occult infection or an altered immune response against an antigen. Epstein Barr Virus and Human Herpes Virus-6¹¹ have also been implicated in the pathogenesis of SHML. It could be a disorder of the mononuclear and immunoregulatory effect system with a speculated association with EBV and HHV-6.^{11,12-14} Expression of HHV-6 antigen has been identified in the histiocytes present in RDD, while lymphocytes express EBV and parvovirus. Eventually the infected lymphocytes are phagocytosed by histiocytes.¹⁴⁻¹⁵

Differential diagnosis of RDD involves other causes of lymphadenopathy especially nonmalignant conditions like tuberculosis, reactive sinus hyperplasia. Wegener's granulomatosis, sarcoidosis, IgG4-related disease, juvenile xanthogranuloma, Gaucher's disease and other disorders of histiocytic proliferation such as Langerhans cell histiocytosis.

Malignant conditions causing lymphadenopathy include Hodgkin's lymphoma, non-Hodgkin lymphoma, melanoma, leukemia, and Langerhans cell sarcoma. In addition, due to the localization and the development of a nasal mass, primary nasopharyngeal carcinoma and olfactory neuroblastoma should also be considered in the differential diagnosis.

Clinical, laboratory and histopathological findings

considered together help differentiate chronic inflammatory diseases such as tuberculosis, sarcoidosis and reactive sinus histiocytosis. A marked difference in the histopathology and simultaneous CD4 and CD8 positivity exclude Hodgkin's and non Hodgkin's lymphoma. Langerhans cell histiocytosis is differentiated from RDD by the absence of emperipolesis and CD1a positivity. Nasopharyngeal carcinoma is differentiated by means of cell type and its aggressive behavior.

RDD is usually a self limiting benign disease. Most of the cases do not require any treatment¹⁶ In few cases it follows a more aggressive course due to widespread involvement of vital organs. In occasional cases a fatal outcome is also reported. Treatment options in non self limiting cases or those with massive enlargements of lymph nodes or extranodal sites are steroids, chemotherapy, radiation, monoclonal antibody treatment, acyclovir, interferon and thalidomide.

Surgery is usually undertaken when the mass causes a functional impairment in an organ or is life threatening. This case presented with nasal obstruction and difficulty in breathing and was subjected to endoscopic removal of the mass. No other treatment was given.

CONCLUSION

Since most of the times RDD is a benign self limiting disease that does not require any aggressive treatment it is imperative to differentiate it from other causes of lymphadenopathy. For the same reason both clinicians and pathologists should have a high degree of suspicion for patients presenting with generalized lymphadenopathy with/without extra nodal involvement or masses with histiocytic proliferation in extranodal sites. Presence of emperipolesis is an important diagnostic finding.

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