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Rosai Dorfman disease- A rare entity: Case report in North Indian male

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ABSTRACT

Rosai Dorfman disease is a rare disease characterized by histiocytic proliferation of lymph node in young adults. We present here the case of a 67 years old Indian male presenting with lymphadenopathy and pyrexia of unknown origin for 16 months duration. Histopathological examination of lymph nodes revealed emperipolesis consistent with the diagnosis of Rosai Dorfman disease. The patient recovered with steroid treatment.Our case is one of the few cases of adult onset Rosai Dorfman Disease reported from India.

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Key words: Rosai Dorfman disease, Lymphadenopathy, Histiocytosis, Emperipolesis

INTRODUCTION

Rosai Dorfman Disease or sinus histiocytosis with massive lymphadenopathy was first described by Juan Rosai and Ronald F Dorfman in 1969 as a separate clinic-pathological entity.[1] Patients with this disease presents with massive lymphadenopathy with systemic symptoms like fever, neutrophilia, leucocytosis, raised ESR and polyclonal gammopathy.[2,3] The Etiology of this disease entity is still unclear. Less than 1000 cases have been reported in literature worldwide with young adult males being most affected. Cervical, axillary, para-aortic and inguinal nodes are most frequently affected with extranodal manifestations reported in 43% of the cases.[4] We present here a case of Rosai Dorfman disease in a 67 years old Indian male with massive enlargement lymph nodes who presented to our hospital with intermittent fever of 16 months duration.

CASE REPORT

A 67-years-old Indian male reported to the internal medicine outpatient department of Dr. Ram Manohar Lohia hospital, a tertiary care hospital located in New Delhi. The patient presented with intermittent low grade fever not accompanied with chill and rigor of 16 months duration. He complained of weakness and fatigability since last 12 months and reported frequent nausea along with loss of appetite during the last 6 months. He had also lost around 6 kg of weight during this period. For these symptoms he had consulted private doctors twice earlier when he was prescribed antipyretics along with broad spectrum antibiotics for 5-7 days period.

The patient has been taking amlodipine 5 mg OD irregularly for the last 15 years. The patient was also operated in this hospital 2 years back for hydrocele. The family history was non contributory. There was no history of any drug allergy. There was no history of tobacco or alcohol abuse.

The clinical examination done at RML hospital revealed that the patient had tachycardia (pulse rate 110/min) along with pallor and his mouth temperature was 99.2 degree Fahrenheit. Detailed physical examination also revealed multiple, bilateral cervical and bilateral inguinal lymphadenopathy. The lymph nodes were discrete 3 × 3 cm in size, 3-4 in each group, firm, non tender, mobile and free from skin. There was no overlying sinus or discharge. Pathological investigations revealed ESR-39 mm 1st hour, hemoglobin -10 g/dl, TLC-22,200/mm^3, platelet count-6.5 lakh/mm^3 and peripheral blood smear-microcytic hypochromic Red Blood Cells with abundant

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platelets (Table 1). Biochemical investigation revealed total protein-10.1 g/dl, albumin-2.5 g/dl and globulin-7.6 g/dl, montoux was 6 x 8 mm. Other investigations like VDRL, sputum for AFB, HIV, Serological investigations for CMV and EBV were also negative along with negative ds DNA and anti nuclear antibodies. On radiological investigation it was found that chest X ray show bilateral hilar prominence. USG abdomen revealed multiple enlarged retroperitoneal lymph nodes. This was confirmed by CECT abdomen which revealed para aortic and bilateral inguinal lymph nodes.

Fine needle aspiration from the left inguinal swelling showed cellular smear composed of large number of histiocytes engulfing intact small and viable lymphocytes and plasma cells with a background of mature small lymphocytes and plasma cells. Histopathological examinations of lymph node revealed effacement of the architecture with pronounced dilatation of the sinuses (Figure 1). Sinuses were occupied predominantly by histiocytes along with lymphocytes and plasma cells. Many histiocytes also showed emperipolesis in the form of engulfment of lymphocytes within the cytoplasm of histiocytes (Figure 2). Immunohistochemical staining of the histiocytes was positive for S-100.

Based on blood picture, CT findings and histopathological examination a diagnosis of Rosai Dorfman disease with extensive lymph node involvement was established. Patient was put on prednisolone 40mg OD during the first month follow up. The patient has reported relieve from constitutional symptoms along with improvement in appetite and weight. The cervical and inguinal lymph node sizes have also slightly regressed.

Tabel 1: Principal Laboratory findings

	Laboratory findings	Normal range
Hemoglobin	10 g/dl	13.3-16.2 g/dl
Total leucocyte count	22.2×10^3/mm^3	$3.54\text{-}9.06\times10^3$/mm^3
MCV	75.3 µm^3	79-93.3 µm^3
MCHC	33.7 g/dl	32.3-35.9 g/dl
RBC	4.35×10^6/L	$4.30\text{-}5.60\times10^6$/L
Platelets	650×10^3/mm^3	$165\text{-}415\times10^3$/mm^3
ESR	65 mm/h	0-15 mm/h
Sodium	136 mmol/l	136-146 mmol/l
Potassium	4.4 mmol/l	3.5-5 mmol/l
Calcium	9.6 mg/dl	8.7-10.2 mg/dl
Urea	23 mg/dl	15-40 mg/dl
Creatinine	1.1 mg/dl	0.6-1.2 mg/dl
Uric acid	5.4 mg/dl	3.1-7 mg/dl
Total Bilirubin	0.6 mg/dl	0.3-1.3 mg/dl
SGPT	127 U/L	7-41 U/L
SGOT	27 U/L	12-38 U/L
Total Protein	10.1 g/dl	6.7-8.6 g/dl
Albumin	2.5 g/dl	4-5 g/dl
Cholesterol	108 mg/dl	<200 mg/dl
Triglyceride	107 mg/dl	30-200mg/dl
Amylase	30 U/L	20-96 U/L
Lipase	95 U/L	3-43 U/L

DISCUSSION

Rosai Dorfman Disease (RDD), an uncommon idiopathic disease of the young, is a rare entity in the Indian population. Very few cases have been reported in adult population in Indian context.[5] The histopathological features of RDD was first described by Destombes in 1965 and later by Juan Rosai and Ronald F Dorfman in 1969 as non langerhans cell histiocytosis.

Etiology of RDD is unknown but many viruses like herpes virus 6, Epstein barr virus, parvo virus, brucella and klebsiella have been implicated although their role is not confirmed.[6] This disease is also seen post bone marrow transplantation and also after Hodgkin and non Hodgkin lymphoma. Some authors have also proposed disturbance in

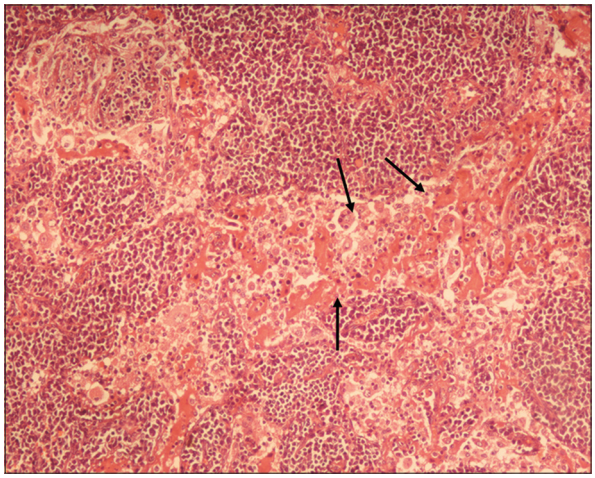

Figure 1: Distortion and dilatation of the sinuses due to infiltration of the histiocytes (100x, H&E staining)

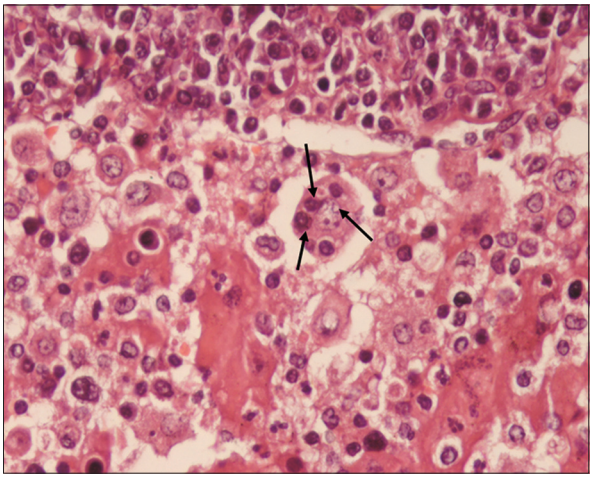

Figure 2: Slide showing emperipolesis of the histiocytes with a background of plasma cells and lymphocytes (400X, H&E staining)

immunological process, specifically cell mediated immunity as a cause of RDD. Middel et al have proposed that it is due to activation of monocyte/macrophage by M-CSF2.[7]

This disease is characterized by extensive lymphadenopathy, fever, weight loss, night sweats polyclonal gammopathy, auto immune hemolytic anaemia and raised erythrocyte sedimentation rate.[2] Forty-three percent of cases also shows extranodal manifestations with skin being the most common site.[8] Other sites are soft tissue, nasal cavity, eye, retro orbital tissue, GI tract, liver, pancreas, breast, urogenital tract, parotid gland and CNS.

Our patient was unique because he was a 67 yrs old male. As already discussed the usual age of presentation is childhood and adulthood although old age may not be an exception. In India most common cause of generalized lymphadenopathy at this age would be an infective etiology like tuberculosis of malignancies- particularly that of lympho reticular and hematological system. In our case the patient had presented with chronic constitutional symptoms along with Monteux 6 × 8 cm and generalized lymphadenopathy so it was very important to rule out these causes. Demonstration of AFB in cytological and histopathological sample or culture positivity is a gold standard in diagnosing tuberculosis. PCR for MTB from biopsy specimen was negative. FNAC followed by excision biopsy was hence done to achieve a confirmatory diagnosis. The HPE picture was consistent with RDD

Histopathology of RDD is characteristic-lymph nodes shows massively distended sinuses presence of numerous large histiocytes, vasicular nuclei, distinct nucleoli and abundant pale cytoplasm. Emperipolesis (engulfment of lymphocytes and erythrocytes by histiocytes) and S100 positivity is characteristically found in RDD. Immunohistochemical staining of RDD also shows CD163, α antitrypsin, lysozyme, fascin, HAM56, LEU M3, MAC 387, OKM5, KI-1 positivity along with increased IL-6, IL-1β and TNFα expression.[4,6,9,10]

Other Differential diagnosis includes reactive lymph nodes, lymphomas, langerhans cell histiocytois, malignant histiocytosis and melanomas.[11] Lymphomas are differentiated by immunohistochemistry (S100 negative and CD68 positive). Langerhans cell histiocytosis is characterized by birbecks granule and absence of emperipolesis. In the presence of extranodal manifestations the differential diagnosis also includes sarcoidosis, wegeners granulomatosis and syphilis. Biopsy is the modality used to differentiate these from RDD.

Treatment is usually not required as RDD follows an indolent course. In 50% of the patients disease resolves spontaneously, 33% have residual symptomatic lymphadenopathy and 17% have lymphadenopathy with clinical symptoms even after many years. Medical management includes use of corticosteroids to reduce symptoms and size of the lymph nodes. Use of acyclovir, antimetabolites, imitanib and interferon α have been postulated but could not be generalized.[12-15] Surgical treatment is usually restricted to debulking when vital organ involvement is associated.

Our case showed a good response to steroids with disappearance of constitutional symptoms over 1 month follow up period with regression of lymph node size. Since the patient is still under follow up, he is being observed for resolution of lymph nodes with plan to titrate steroid as per the response. No surgical option was considered.

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Authors Contribution:
AB - Designed, analyzed data, wrote the manuscript and revised the manuscript; **PG** - Wrote the manuscript and revised the manuscript; **KLR** - revised the manuscript.

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