CASE REPORT

ROSAI DORFMAN DISEASE WITH EXTENSIVE BONY INVOLVEMENT- A DIAGNOSTIC DILEMMA

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Previously classified as Non Langerhan cell histiocytosis by the Working Group of Histiocytic Society in 1987 Rosai Dorfman Destombes disease was first described by Destombes in 1965 and later in 1969 by Rosai and Dorfman as a rare histiocytic disorder with sinus histiocytosis and massive lymphadenopathy. They exist in both nodal and extranodal forms. Immunohistochemistry is an essential part of diagnosis to differentiate between Langerhans cell histiocytosis and another malignant histiocytosis. Some overlap has also been reported with IgG4-related diseases. We hereby reflect upon a patient who presented to our facility with pyrexia of unknown origin, the challenges faced to reach a diagnosis and the management offered.

Keywords: Pyrexia of unknown origin; Histiocytic disorder; Non-Langerhans cell histiocytosis; Immune-Mediated

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INTRODUCTION

Previously classified as non-Langerhans cell histiocytosis by the Working Group of Histiocytic Society in 1987 Rosai Dorfman Destombes disease was first described by Destombes in 1965 and later in 1969 by Rosai and Dorfman as a rare histiocytic disorder with sinus histiocytosis and massive lymphadenopathy. They exist in both nodal and extranodal forms. Immunohistochemistry is an essential part of diagnosis to differentiate between Langerhans cell histiocytosis and another malignant histiocytosis. Some overlap has also been reported with IgG4-related diseases.[1,2]

Rosai Dorfman Disease with Extensive Bony Involvement- A Diagnostic Dilemma

CASE REPORT

A 35years old male farmer by profession with no known comorbidities and no known drug allergies presented to us with a generalized feeling of unwell, a history of fever documented up to 102F, weight loss (unintentional >10% from baseline in <6 months), drenching night sweats, abdominal discomfort and back aches for 1.5years. He denied any addictions. His past medical history was significant for Focal segmental glomerulosclerosis (FSGS) which was treated 5 years ago with a 6-month course of prednisolone and was in complete remission. Clinical examination revealed anaemia with koilonychia and multiple palpable lymph nodes in the neck, axilla and inguinal region with a maximum size of 2×2 cm. Abdomen examination revealed a palpable liver 3 fingers below the costal margin with a smooth texture and borders and a span of 16 cm. Chest, neurological and cardiovascular examination was unremarkable.

Over the last 1.5 years, he had been in and out of multiple facilities and had extensive workup done but did not reach a conclusive diagnosis. His baseline labs (over the last 1.5 years) revealed anaemia with microcytic indices, normal white cell count and reactive thrombocytosis. Kidney functions and liver functions were normal. His total protein revealed low albumin of 1.8g/l with raised globulin of 7g/L. Numerous sets of blood cultures were done which did not reveal any bacterial growth. He also had CT Chest abdomen and pelvis with contrast from outside which revealed multiple enlarged lymph nodes in the left supraclavicular, bilateral axillary, mediastinal, para-aortic, aortocaval, iliac and inguinal nodes with the largest measuring about 2.3×1.4 cm. Soft tissue density nodule at the apical segment of the right upper lobe of the lung. The liver measures 19.4 cm with few small soft tissue density areas in segments II, V, VI and VIII one of these being 0.5×0.5cm which may represent a metastatic deposit. After this scan, he had excisional lymph node biopsies from the neck and axilla and both of them showed reactive changes, gene expert for tuberculosis was negative on the lymph node specimen.

He presented to our care as pyrexia of unknown origin. His labs at our facility revealed an Hb of 7g/dL with MCV 68, normal White blood cell (WBC) count and Platelet of 600. The peripheral film revealed hypochromic, microcytic red blood cells with thrombocytosis WBC appeared normal in

morphology. He had a corrected ESR of 140. Kidney, liver functions and coagulation profile were normal. Viral markers were non-reactive. Three sets of blood cultures were sent with fever spikes which did not reveal any growth. His workup of anaemia revealed Functional Iron deficiency with Transferrin saturation of 5% (Serum Iron 17 TIBC 350 with serum ferritin 119) normal B12 and folate levels. His total protein revealed low albumin of 1.8G/L and raised globulin 7g/L with reversal of Albumin/Globulin ratio. His urine DR showed trace protein with spot PCR of 0.1gm. His Stool DR was positive for occult blood. Serum protein electrophoresis revealed a polyclonal increase with no monoclonal band. Autoimmune workup was negative and IgG4 levels were in normal ranges. Upper GI Endoscopy was done keeping in view of anaemia and melena which revealed moderate pan gastritis and biopsy from that site showed features of H pylori associated chronic active gastritis. Baseline ECG, and ECHO were normal. A PET scan revealed FDG avid lymph nodes in the bilateral cervical region, axilla, anterior mediastinum lateral aortic region, and a bilateral para-aortic, iliac and inguinal region with maximum SUV uptake of 6.3. It also showed FDG uptake in the humerus, sternum, clavicle, C6, D1, D4, D5, D12 and L4, sternum, femur and bilateral iliac bones with SUV range 2.9–8.5 (Figure-1). An excisional lymph node biopsy from the inguinal region showed effacement of nodal architecture with the expansion of the sinus with numerous histiocytes. These histiocytes have abundant clear to eosinophilic cytoplasm and vesicular nuclei showing emperipolesis with engulfment of lymphocytes. In the background plasma cells were also noted, these histiocytes were positive for CD-68 and S-100 and negative for Cd1a and the biopsy was conclusive for Rosai Dorfman disease (Figure-2). A bone marrow biopsy was done which was unremarkable.

He was started on H pylori eradication therapy and was started on prednisolone 1 mg/kg, since his GI symptoms were expected to worsen and clinically did worsen and keeping in view of his prior prolonged course of steroids due to FSGS he was planned for a short course of steroids with rapid tapering of over 6 weeks (rather than conventional 12–16 weeks). A steroid sparing agent Methotrexate at 20 mg/m2 weekly was added upfront with folinic acid and iron supplementation. His feeling of generalized unwellness improved by 2 weeks and fever and night sweats settled by the end of 4 weeks. He was planned to continue methotrexate for 6 months with a repeat PET scan at the end of 6 months

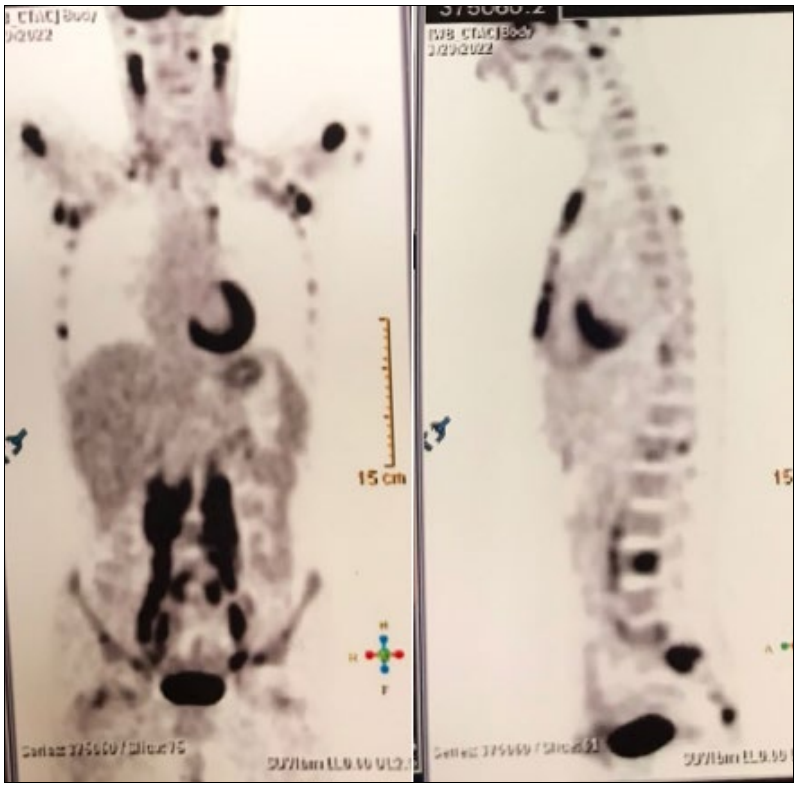

Figure-1: PET scan images showing FDG uptake in bilateral cervical region, axilla, anterior mediastinum, lateral aortic region, bilateral Para aortic, iliac, inguinal region, humerus, sternum, clavicle, C6, D1, D4, D5, D12 and L4, femur and bilateral iliac bones.

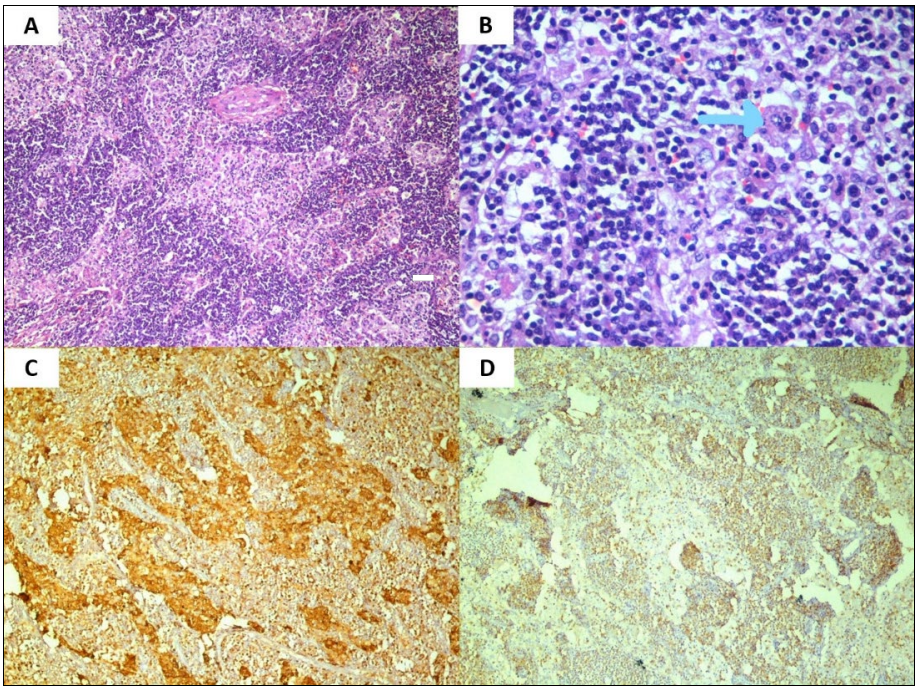

Figure-2: Histopathologic features of Rosai-Dorfman disease on lymph node biopsy. A. Low-power view showing the marked expansion of the sinuses by histiocytic infiltrate (H&E, ×100). B. High-power view showing many histiocytes, lymphocytes and plasma cells. One of the histiocytes is exhibiting emperipolesis (arrow). (H&E, ×400). C. Medium-power view of CD68 immunohistochemical staining showing positivity of histiocytes. S-100 showed similar positivity. (CD68, ×200). D. Low-power view of CD1a immunohistochemical staining showing negativity of histiocytes. (CD1a, ×100).

DISCUSSION

Rosai Dorfman disease is a rare non-Langerhans cell histiocytosis which is distinguished from another histiocytosis with the positivity of Cd68 and S-100 and negative for Cd1a. There are multiple case reports published until now mostly with lymph node involvement. Two case reports published from Pakistan showed cutaneous involvement and GI Tract involvement with intra-abdominal lymphadenopathy and ascites.[3,4]

The clinical course of Rosai Dorfman disease is usually benign however it can have a lethal outcome if any vital organ is involved. Extranodal involvement can occur in up to 40% of cases, and in less than 10% of cases, bone involvement has been reported. Primary RDD without lymphatic involvement has also been reported with the largest case series including 15 patients. [5]

Histology is the gold standard mode of diagnosis in these patients but the stage of disease at which the patient is biopsied may affect the diagnostic yield as the classical features are more easily picked during the stable phase of the disease. This histological variation throughout the disease process can be reflective of a diverse cytokine milieu. Sampling during the stable phase of the disease may yield diagnostically conclusive material whereas sampling during involution and exacerbation phases may lead to inconclusive diagnosis as in our patient leading to diagnostic delay.[6]

The most common clinical presentation in these patients included pain and swelling however it appeared as an incidental finding in a few patients. Lesions are mostly reported as intramedullary and lytic with some occasional sclerosis. Extensive bony involvement has been rarely reported in literature and data depicts that if the patient has an extensive disease with bony involvement, treatment options and outcomes were not affected. Surgical excision is the most commonly offered treatment modality if the disease is localised.[5,7]

We opted for systemic treatment for our patient, considering extensive disease and constitutional symptoms. After an MDT discussion and published literature review, we tailored the treatment in accordance with our patient's needs. A short course of steroids with the addition of steroid-sparing agents was offered upfront. Treatment led to clinical resolution of symptoms and the patient tolerated well without any documented side effects. We will repeat the PET Scan in 6 months to document the treatment response.[8,9]

CONCLUSION

Rosai Dorfman Destombes is a rare entity with very few cases with extensive disease reported. To our knowledge, this is the first case with such extensive disease and bony involvement reported. Due to the paucity of data from our region, this case report will help clinicians to offer treatment for the extensive disease in our population.

REFERENCES

1. Bruce-Brand C, Schneider JW, Schubert P. Rosai-Dorfman disease: an overview. J Clin Pathol 2020;73(11):697–705.
2. Foucar E, Rosai J, Dorfman R. Sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease): review of the entity. Semin Diagn Pathol 1990;7(1):19–73.
3. Parkash O, Yousaf MS, Fareed G. Rosai-Dorfman's disease, an uncommon cause of common clinical presentation. J Pak Med Assoc 2019;69(8):1213–5.
4. Soomro IN, Hameed K. Arthritis and rosai-dorfman disease of the skin: a diagnostic dilemma. J Pak Med Assoc 1999;49(11):280–2.
5. Mosheimer BA, Oppl B, Zandieh S, Fillitz M, Keil F, Klaushofer K, *et al*. Bone involvement in Rosai-Dorfman disease (RDD): a case report and systematic literature review. Curr Rheumatol Rep 2017;19(5):29.
6. Mallick S, Ghosh R, Iyer VK, Jain D, Mathur SR. Cytomorphological and morphometric analysis of 22 cases of Rosai-Dorfman disease: a large series from a tertiary care centre. Acta Cytol 2013;57(6):625–32.
7. Demicco EG, Rosenberg AE, Björnsson J, Rybak LD, Unni KK, Nielsen GP. Primary Rosai-Dorfman disease of bone: a clinicopathologic study of 15 cases. Am J Surg Pathol 2010;34(9):1324–33.
8. Abla O, Jacobsen E, Picarsic J, Krenova Z, Jaffe R, Emile JF, *et al*. Consensus recommendations for the diagnosis and clinical management of Rosai-Dorfman-Destombes disease. Blood 2018;131(26):2877–90.
9. Goyal G, Ravindran A, Young JR, Shah MV, Bennani NN, Patnaik MM, *et al*. Clinicopathological features, treatment approaches, and outcomes in Rosai-Dorfman disease. Haematologica 2020;105(2):348–57.

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