ROSAI-DORFMAN DISEASE: REPORT OF A RARE CASE OF PERIPHERAL LYMPHADENOPATHY.

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ABSTRACT

Introduction: Rosai-Dorfman disease (RDD), also called Sinus histiocytosis is an uncommon proliferative disorder of unknown aetiology. Though, the lymph node is the revelation mode of several diseases particularly in the tropics, RDD typically presents with painless bilateral lymphadenopathy in the neck associated with fever and leukocytosis, sometimesmimics lympho-proliferative disorders. Recently research has unveiled gene mutation in the tumour with potential of malignant transformation. Case report:We report case of 4 year old boy who had massive cervical lymphadenopathy with extranodal manifestation of fever. Sepsis screening was negative, while imagingshowed hilar,mediastenal andmesenteric lymph nodes enlargement in addition to massive hepatomegaly. The histology is suggestive of the diagnosis of RDD. The patient was treated with corticosteroids, with remarkable remission. Conclusion: We report the clinicopathological characteristics of RDD in order to increase our awareness of its diagnosis and treatment and to re-emphasize that the disease is rare in our environment.

Keywords: Rosai-Dorfman disease, lymphadenopathy, sinus histiocytosis.

INTRODUCTION

Rosai-Dorfman disease (RDD) also known as sinus histiocytosis with massive lymphadenopathy is a rare disease of unknown aetiology. It is a non-neoplastic disorder of which the evolution is often self-limiting over a period of few months.[1]It usually presents with painless cervical lymphadenopathy with or without extranodal manifestation. The prognosis of the disease is dependent on the extranodal involvement.[1]The disease was first described by Juan Rosai and Ronald F Dorfman in 1969.[2]Clinically it manifests as massive lymphadenopathy mainly of the cervical region. Other lymph nodes involvement is however, not exceptional.[3] Diagnosis of the disease is often delayed partly due to higher prevalence of cervical lymphadenopathy caused by infectious diseases. To Our knowledge this is the first Paediatric case reported in North-Eastern Nigeria, therefore, the rarity of the disease in our setting prompted the need for this case report.

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CASE REPORT

The patient is a 4-year old boy who was referred to the Paediatric Haemato-oncology unit of our hospital from State Specialist Hospital, Maiduguri with one year history of cough, fever, progressive neck swelling and seven months history of progressive weight loss, cough was not paroxysmal, not barking and no associated difficulty in breathing.There was no history of

contact with adult having chronic cough. At thesame time thechild developed low grade intermittent fever with drenching night sweats but no chills or rigors. Few days later,the mother noticed bilateral neck swelling of peanut size which progressively increases to the size at presentation. Neck swelling was painless and there was no associated difficulty in swallowing or noisy breathing. There was significant weight loss, but no history of bleeding diathesis, bone or joint pains. He had immunization in accordance with National Program on Immunization (NPI). Clinical examinationof thepatient revealed anafebrile child with axillary temperature of 37.2^{0}C, no conjunctival pallor, not jaundiced, acyanosed, not dehydrated, no dysmorphic facie, but with significant and generalized peripheral lymphadenopathy, with the largest measuring 6x4 cm at the right anterior triangle of the neck. The lymph nodes were firm, discrete and mobile, not tender, no differential warmth, no change in colour of overlying skin, no pedal oedema. He weighed 12.5kg (78% of the expected for age). Examination of the respiratory system revealed respiratory distress, tachypnoeicwith a respiratory rate of 42 breath/min. Abdomen was full, moves with respiration, hernia orifices were intact. There was hepatomegaly 8cm below the right sub-costal margin that is firm in consistency, smooth and not tender. There was no splenomegaly and no demonstrable ascites. The other physical examination findings including ear, nose and throat were essentially normal.

Haematologic examination revealed microcytic hypochromic anaemia with a haemoglobin concentration of 8.3 g/dl, total leukocyte count of 6,600/mm^3 with neutrophil constituting 67%, lymphocyte 30%, and monocyte 3%, thrombocytosis with a platelet count of 650,000/mm^3, red cell morphology showed anisocytosis and spherocytosis, along with few target cells. Blood chemistry, liver and renal function tests were within normal limits, Mantoux test and HIV serology were negative. The Chest X-ray showed multiple lobulated masses of soft tissue density in the mediastinum and both hilar regions compressing both main bronchi. Abdominal ultrasound showed para aortic lymphadenopathy (Figure 1). The excisional biopsyof cervical lymph node suggested RDD(Figure2). The patient was treated with corticosteroid for 6 weeks with a favourable response of weight gain and regression of lymphadenopathy with no evidenceof steroid impregnation. The haemoglobin concentration increased from 8.3 to 9.7 g/dl without transfusion or haematenics supplementation. Following clinical and laboratory evidence of improvement, a maintenance dose was continued with gradual dose reduction over six weeks. The patient was eventually lost to follow-up and no phone number was documented in the case file for possible contact, attempt to trace location from the documented address was not successful.

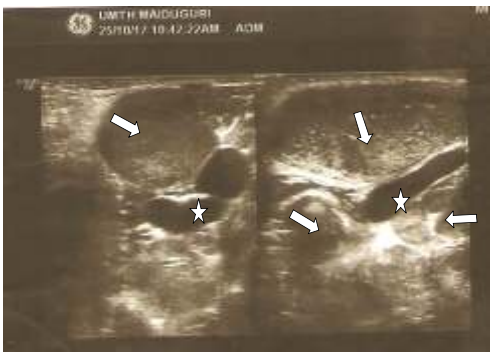

FIGURE 1: Abdominal ultrasonography (transverse and longitudinal views) showing multiple para-aortic lymph nodes (white arrows). Aorta was depicted by the white star.

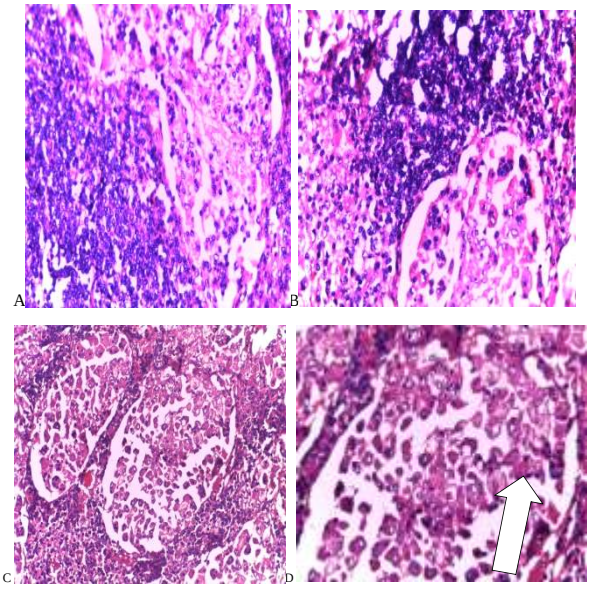

FIGURE2: Photomicrograph of lymph node tissue (A and B) showing partial architectural effacement and marked expansion of the sinuses by histiocytes and plasma cells. Photomicrograph (C and D) show numerous histiocytes having large vesicular nuclei with abundant eosinophilic cytoplasm some of the cells exhibits lymphocytophagocytosis (emperipolesis) indicated by an arrow on D. (H and E; B & C X 200 and X 400).

DISCUSSION

Rosai-Dorfman Disease is a rare chronic disease characterized by benign self-limiting histiocytic proliferation of non-Langerhans histiocytosis cells.[3] Its aetiology remains obscure, even though its association with infectious nature is often reported, including infections with EBV, CMV, measles, rubella and toxoplasmosis which are still common in our setting, but at the same time disorders of the immune system with abnormal histiocytes reaction have also being reported.[4]

This rare disorder was first reported by Juan Rosai and Ronald F Dorfman in 1969,[2] in 1990, Rosai reported 423 documented cases.[1] Since then several hundreds of isolated cases of RDD have been reported worldwide, only a few cases were reported from Africa.[1,5-8] There was only a case reported from Nigeria.[9] Extranodal involvement is found commonly in the head and neck regions.[10,11] Our patient had hepatomegaly which may suggest hepatic involvement, which is even more rare and in consistent with the case reported by Maheshwari *et al*.[12] Fever and weight loss may also be presenting symptoms of this disease as was the case for our patient which are in consistent with the two case reported by Atoumane Faye *et al.*[1] Other rare presenting features include tonsillitis, nasal obstruction which were not seen in our patient. The disease may occur at any age,in our case, the patient is aged 4 years. Lymphadenopathy constitute a classical mode of presentation of the disease, and are chronic, non-inflammatory often localized to the cervical region but may rarely involve other nodal regions as was the case with our patient where there were axillary, inguinal and deep mediastenal and hilarlymphadenopathy clinically consistent with reported cases in the literature.[1]The masses are typically voluminous cervical lymphadenopathy that can measure up to 7cm in their long axis.[13,14] More often bilateral, asymmetric, firm in consistency, painless without necrosis or tendency to suppuration or fistula formation as the case with our patient. In our observation, the most voluminous lymphadenopathy was 5cm of long axis with the same characteristics described as in the index case. The lymphadenopathy can last for several months or years. Our case had hepatomegaly at variant with many reported cases having both liver and spleen been consistently normal.[2,5,8,9] This long standing hepatomegaly may be from various aetiologies commonly implicated particularly in tropics including hepatic schistosomiasis and visceral leishmaniasis.[15,16]

Histology was suggestive of RDD using Haematoxylene and Eosin in our case, although other mimics such as tuberculosis was rule out by Mantoux negative test and genexpert. Unfortunately for our patient, immunohistochemistry was not done because of its unavailability in our centre, however, if done it can assist in ruling out Langerhans histiocytosis and lymphoproliferative disorders especially in atypical RDD.

To date, there is no consensus on the initiation of systemic treatment of the disease,[2,5] except in rarecases where the life is threatened such as airway compression. Our patient presented with life threatening respiratory distress, low grade intermittent fever, along with painless non-tender bilateral cervical, mediastenal and hila lymphadenopathy, and hepatomegaly was observed. However, corticosteroids remain important in the management of RDD, this is confirmed with the work of Lampert.[18] Promising results were obtained with prednisone or a combination with vinblastine or chlorambucil. We used prednisolone at a dose of 1mg/kg/day for 8 weeks with remarkable clinical and laboratory improvement without steroid impregnation in this index case. It was difficult to assess the long-term effect of the corticosteroid treatment, keeping in mind the self-limiting possibility of RDD, and therefore, assessment of corticosteroid therapeutic effect remains difficult.

Rosai-Dorfman disease has shown somatic *KRAS* and *MAP2K1* mutation in 33% of cases,[19] and molecular evidence has also revealed the benefit of targeted therapy particularly for refractory and aggressive disease.[19] Similarly, *RAF* inhibitor, venurafenib has revolusionalized treatment of patient with *BRAF*-mutated histiocytes.[20] Few reported cases indicating transformation of RDD to diffuse large cell lymphoma, has been observed.[20] Therefore, it is always necessary to rule out

malignant transformation in especially refractory and aggressive RDD.

CONCLUSION

Rosai Dorfman Disease is an uncommon histiocytic disorder presenting with diverse clinical manifestations. The main presenting feature is massive cervical lymphadenopathy. Approximately one-third of RDD patients may require systemic corticosteroids therapy that gives remarkable remission as in this index case. As the molecular events of the disease are unveiling many gene mutations have been discovered, so molecular targeted therapy will be the feature treatment.

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