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CASE REPORT

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Histiocytosis in Nigerian children: A report of two variants

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Abstract: Histiocytoses are a rare group of proliferative disorders with very similar clinical and histological pictures.
We present a case report of two variants seen in an eight-month-old female and five-month-old male in a tertiary hospital in southern Nigeria. They both presented with painless neck swellings and fever, leucocytosis, neutrophilia and lymphopenia. Initial histologic examinations of the cervical lymph nodes biopsy posed a diagnostic conundrum. However, Immuno-histochemical analysis done on both sample showed CD1a, positive S100 in keeping with Langerhans cell histiocytosis in the former. While, that of the latter showed strongly positive CD68, positive S-100 in 30% cells in keeping with Sinus histiocytosis with massive lymphadenopathy (SLMH) in the latter.
Clinicians should have a high index of suspicion for histiocytosis in children presenting with generalised lymphadenopathy. Also, apart from the routine histology, immunohistochemistry analysis is recommended for all cases

Keywords: Histiocytosis, Children, Nigeria, Immunohistochemistry

Introduction and Background

The histiocytoses are a group of rare diverse proliferative disorders characterized by the accumulation and infiltration of variable numbers of macrophages, dendritic cells, or monocyte-derived cells in tissues and organs of the body.[1]

Although, many subtypes of histiocytic disorder exist with variable clinic pathological features,[1] we are only reporting the two variants seen in our facility to highlight the similarities in clinical presentation and the diagnostic challenges.

Langerhans cell histiocytosis (LCH)

Langerhans cell histiocytosis is a heterogeneous disease of the myeloid cells characterised by the accumulation of clonal dendritic cells in various organs.[2]
LCH can affect patients of all ages, although it appears to be more common between the ages of one and three. There is a male preponderance, with a male-to-female ratio of 1.5:1.[3]
Clinically, the spectrum is broad, ranging from an asymptomatic bone lesion to a life threatening condition. Children with isolated bone lesion typically present between five and fifteen years of age. While those with multisystem LCH tend to present before age five.[3]
The diagnosis is based on immune-histochemical examination staining of a biopsy of lesion tissues and positivity for CD1a, S100 and or CD207 is required for definitive diagnosis of LCH.[1,3]

Rosai-Dorfman Destombes disease (RDD) described as Sinus histiocytosis with massive lymphadenopathy (SLMH) is a form of class 2 histiocytosis syndrome.
There is a predilection of the disease for the black race, a slight male preponderance with early manifestation of the disease in the first decade of life. In the classical form, the patient presents with bilateral multiple painless cervical lymphadenopathy associated with systemic symptoms such as fever, weight loss, anaemia and immunologic abnormalities.[2] Histologically the lesions are characterised by a proliferation of polyclonal S-100 positive histiocytes, often multinucleated with obvious emperipolesis and negativity for CD1a.[1,2]

The prevalence of this group of the rare disorderis uncertain. Among histiocytic disorders, LCH is the most common one, affecting an estimated four to five per million children under fifteen years of age each year.[1, 2]
Rosai-Dorfman disease has a low incidence, with less than 100 cases diagnosed per year in the USA.[4] Though, there have been previous case reports of histiocytoses in Africa and Nigeria in particular, No national prevalence has been reported. In Eastern Nigeria, RDD accounted for 0.7% of all cases of histologically diagnosed lymph node biopsies in a tertiary hospital.[5] While sinus histiocytosis constituted 7.6% of cervical lymph nodes enlargement in Nigerian Children in Lagos.[6] This is the first reported variants of histiocytic disorders in Uyo which was based on immunohistochemistry analysis,

and the overall challenge with making this diagnosis in a resource-poor setting like ours, hence, our decision to publish this rare clinical entity.

Case report 1

An 8-month-old female was brought to our hospital with a three month history of painless neck swelling sand fever with progressive weight loss of two weeks duration. She was the second child of her parents in a monogamous setting of social class 4 according to Oyedeji classification.[7]
Physical examination revealed a febrile child with a temperature of 38.8^0C. She was severely pale, in respiratory distress, with depigmented hair and hypopigmented lesions in the trunk. She had bilateral, non-tender, matted cervical lymph node swellings, measuring 3-cm-to-6-cm in diameter. She also had occipital, pre-auricular and bilateral axillary lymph nodes enlargement measuring 2cm to 4cm in the largest diameter.
She was malnourished with a weight of 5.6kg (65.8% of expected weight for age), length of 65cm, WHZ z-score <-3. Her full blood count findings showed a packed cell volume of 13%, total white blood cell count (WBC) of 20.1x 10^9/l with neutrophils and lymphocytes making up 83% and 15% respectively, platelet count was 277x 10^9/l, She had negative Mantoux, Gene-Xpert and HIV antibody tests.

Her chest radiograph revealed, mediastinal widening with a predominantly right sided lobulated soft tissue mass in the anterosuperior mediastinum, extending down towards the right cardio-phrenic angle.
Histologic examination of the cervical lymph node biopsy, showed distortion of the nodal architecture by benign proliferation of haematopoietic and fibrous tissues, composed of circumscribed sheets of polygonal and spindle histiocytes. Also, seen were pale eosinophilic histiocytic cells that engulf lymphocytes (emperipolesis) as well as multinucleated cells. These were in keeping with a sinus histiocytosis with massive lymphadenopathy (Rosai Dorfman Destombes Disease).
However, report of samples sent to India for IHC was CD1a positive, S100-Strongly and diffusely positive, positive CD68 and a low Ki67 index. These findings were in keeping with Langerhans cell histiocytosis.
She was commenced on oral prednisolone at 1.5mg/kg once daily prior to the result of immuno-histochemistry staining. Also, she was transfused with fresh whole blood which raised her packed cell volume to 24%. There was a gradual reduction in the size of the lymph nodes within a week of treatment. She was discharged home with an improved weight of 6.2kg after two weeks of oral prednisolone for a follow-up visit in the out-patient clinic. Unfortunately, the child was lost to follow up and was later reported to have died from an unknown complication.

Case report 2

A five month old male was brought to our children out-patient clinic on account of neck swelling of one month duration and fever of two weeks duration. Painless swellings involving the anterior neck were initially the size of a peanut but increased in size extending to the supraclavicular regions.
He was treated at a private facility with oral antibiotics and rifampicin for two weeks before referral to our hospital. Examination findings revealed a right neck mass extending from the angle of the jaw into the neck anteriorly and posteriorly, measuring 9cm by 8cm in the longest diameters. They were firm, non-tender and not attached to the overlying skin. There was also supraclavicular lymph node enlargement.
Investigations showed a TWBC of 32.4x 10^9/l, platelet count of 382 x 10^9/l red blood cell count was 23.0 x10^9. Differential WBC showed 81% Neutrophils, 9% lymphocytes. Histologic section of supraclavicular lymph node biopsy was in keeping with RDD. The IHC report showed strongly positive CD68 +++; positive S-100 in 30% cells; low proliferative Ki-67 index and negativeCD19. A diagnosis of Rosai-Dorfman disease was made.
Oral prednisolone 1mg/kg was commenced with no significant reduction in the size of the neck mass six weeks later. He was thereafter commenced on a combination therapy of prednisolone, methotrexate and mercaptopurine. The mass significantly regressed within two months of treatment with the regime and he is on a regular follow-up in the out-patient clinic.

Discussion

Our patients with histiocytoses fitted into the one to three age group which has been reported to be the age with a higher prevalence. Two Nigerian studies have reported 0.7%-7.6% rate of RDD cases among lymph node biopsies carried out.[5-6] This low incidence might be due to the infrequent and poor habit of reporting cases in the developing world and the challenges of making a diagnosis in resource-constrained environments. We noted that histiocytosis was not primarily a disease of poverty as one each of the children was from a high and low socioeconomic class. This is unlike other endemic tropical disease- causing lymphadenopathies such as Tuberculosis and Lymphomas which are primarily diseases of poverty.[8]

Our patient with RDD presented, with multiple painless cervical lymphadenopathy of a bull neck appearance and systemic symptoms of fever. These findings are in keeping with previous reports where cervical lymphadenopathy has been recognised as the commonest lymph node group in addition to other nodal sites like the axillary and mediastinal lymph nodes in 80% of cases.[1]
Besides, our patients presented with other constitutional symptoms like weight loss, recurrent fever and anaemia. Previous reports have observed these symptoms.[1,2] These constitutional symptoms can pose a diagnostic challenge especially in areas endemic for tuberculosis

and HIV like our setting. Both cases had a similar histologic picture which was in keeping with Rosai-Dorfman diseases. However, IHC of the lymph node biopsy sent to India was able to differentiate the two variants of histocytoses.

Challenges encountered were the high cost and lack of diagnostic facilities for IHC.

Conclusion

We have presented two cases of histiocytic disorders with very similar clinical and histologic features. The diagnosis was differentiated using IHC. We therefore recommend that facilities for immuno-histochemistry be set up by our policymakers and hospital administrators to aid in the early diagnosis and treatment of such challenging cases.

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