ROSAI-DORFMAN DISEASE: A DIAGNOSTIC ALBATROSS IN A FEMALE PATIENT WITH BILATERAL PERSISTENT NECK MASSES. A CASE REPORT.

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Abstract
RosaiDorfman disease (sinus histiocytosis with massive lymphadenopathy) is an uncommon benign and often self limiting lymphoproliferative disease of unknown aetiology which was first described by Rosai and Dorfman in 1969. It usually presents with a multiple progressive painless bilateral cervical lymphadenopathy, low grade fever, polyclonal hypergammaglobulinemia and raised erythrocyte sedimentation rate. Extranodal diseases are uncommon but have been documented. Due to the rarity of this condition, the diagnosis may not be suspected clinically and fine needle aspiration cytology of neck nodes may miss the diagnosis. In this study, we present a 24 year old female who presented with bilateral cervical lymphadenopathy and right breast lump since childhood.

Key words: *Histiocytes, Rosai-Dorfman disease, massive lymphadenopathy*

Introduction
Sinus histiocytosis with massive lymphadenopathy as initially described by Rosai and Dorfman in 1969 is a distinct pathologic entity from Langerhans' cell histiocytosis (Histiocytosis X) whose histopathologic hallmark is the presence of emperipolesis and expression of S-100 protein by the histiocytes with feathery borders.[1,2]

Extranodal sites may be involved in 10% of cases with the skin and subcutaneous tissue being most common followed by upper respiratory tract, salivary gland oral cavity and genitourinary system.[13]

However, another study reported 30%% extranodal involvement with various sites in the head and neck region showing particular predilection.[4]

This disease runs a benign course and may be confused with disease entities like Langerhans' cell histiocytosis, reticulohistiocytoma, malignant histiocytosis, Hodgkin's lymphoma, eruptive xanthoma, and juvenile xanthogranuloma.[2]

Case presentation
A 24 year old Nigerian female who developed an illness which was gradual in onset and was characterized by slowly progressive bilateral painless right cervical swellings of 16 years duration, 12-year history of a painless left cervical swellings and one-year history of right breast lump (Fig 1 &2). There was no obstructive or pressure symptoms and no nasal, otological or ocular symptoms. She had no constitutional symptoms. She had full immunization in her childhood according to the National Programme on Immunization (NPI) schedule. Prior to presentation to the Ear Nose and Throat Department of the University College Hospital Ibadan, she had had one Fine Needle Aspiration Cytology (FNAC) of the neck masses and a cervical lymph node biopsy both of which were reported as chronic inflammation. Neck examination revealed right-sided upper lateral masses which measured about 9cm x 6cm with a healed surgical scar. The mass was mobile with mixed consistency. She also had a left supraclavicular mass which measured about 6cm x 4cm with similar physical characteristics to the contralateral neck masses. Breast examination revealed a freely mobile mass in the right outer upper quadrant which measured about 3cm x 2cm. Computerized tomography scan of the neck and upper chest showed multiple oval shaped soft tissue dense masses of varying sizes in the subcutaneous layer of the neck bilaterally. The right mass measured 8.1x5.0 in its longitudinal and transverse dimensions while the largest on the left measured approximately 5.3cm x 3.1cm. A similar attenuating

mass was seen in the upper outer quadrant of the right breast. It was lobulated and measured approximately 3.1cm x 2.0cm. No mediastinal or hilar mass was seen. The lung fields, heart and ribcage were within normal limits (Fig 4). Mantoux test was not significant and retroviral screening was negative. A repeat FNAC of the neck masses at the University college Hospital Ibadan was reported as reactive while FNAC of breast lump showed cohesive clusters of benign ductal epithelial cell disposed in stag-horn patterns and partly rimmed by bipolar cells. The overall features were suggestive of a fibroadenoma. Her erythrocyte sedimentation rate (ESR) was 48mm/hour by Westergreen Method. She had raised polyclonal gammaglobulin of 19.6g/dl (8-13.5g/dl). Due to inconclusive diagnosis, patient's anxiety and cosmetic considerations, she had a neck dissection and breast lump excision. The histological features of the cervical nodes (fig 5) and right breast lump were in keeping Rosai-Dorfman disease and fibroadenoma respectively.

She was discharged on Prednisolone tablets 5mg daily to be tailed off after two months and is being followed up at the clinic.

Literature review.

Rosai was reputed to have maintained a registry of cases of SHML since the description of this disease in 1969 and had accumulated 365 cases as at 1988.[5]

Majority of patients with Sinus histiocytosis with massive lymphadenopathy (SHML) are usually within the first 2 decades of life at the onset of the disease.

According to the analysis of the registry of Rosai and Dorfman of 1988, there is a slight predilection for blacks. About 49% of the cases were blacks whereas 46% and 5% of the cases were Caucasians and Oriental respectively. Many of the blacks were of African and Carribean origin.[5]

Ademiluyi et al[6] in a series of 105 Nigerian children with persistent cervical lymphadenopathy, put the incidence of SHML at 7.6%.

It is slightly commoner in males. The male to female ratio is approximately 1:4 to 1.[1]

The aetiology of this disease is unknown but occult chronic infection or an aberrant exaggerated immune response to an infectious agent or an antigen may be the cause of initial histiocytic infiltration.[7]

Human Herpes Virus 6, Epstein-Barr virus, Cytomegalovirus and bacteria like Klebsiella and Brucella have been suggested as possible causative agents.[8,9]

There may also be a genetic predisposition as the disease has been described in 2 pairs of siblings and a pair of identical twins.[10]

The commonest presenting symptom is painless progressive bilateral cervical lymphadenopathy.[11] Axillary, inguinal, hilar & mediastinal nodes may be affected in 80% of cases. However, not all affected lymph nodes become enlarged although all will show emperipolesis and other microscopic features of sinus histiocytosis with massive lymphadenopathy.[11]

The percentage of extranodal disease involvement varies in various reports & range from 10-40%.[11,12]

Documented sites of extranodal involvement include skin, respiratory tract, bone genitourinary system, oral cavity nasopharynx, nose, central nervous system, eye, salivary gland, tonsil breast and bone marrow, heart.[4,13-15.]

Extranodal disease may be the initial and sole manifestation of the disorder[16] although both extranodal and nodal disease may occur synchronously.[17]

Nasal obstruction, rhinorrhoea, epistaxis due to mucosal infiltration by mixture of histiocytes and chronic inflammatory cells are the typical clinical presentation of nasal and nasopharyngeal sinus histiocytosis with massive lymphadenopathy and thus may simulate a sinonasal or nasopharyngeal cancer.[5,18]

Involvement of the trachea or bronchus may present with stridor or dyspnoea which may be life threatening whereas orbital disease characteristically manifests with progressive proptosis[5]

In the analysis of the cases in his registry, Rosai found that when massive lymphadenopathy is present, fever (up to 102^0F), leucocytosis (up to 32,000/mm^3), neutrophilia and raised erythrocyte sedimentation rate are usually present and that about 80% of the patients had polyclonal hypergammaglobulinemia while 65% had hypochromic or normochromic normocytic anemia.[5]

Sinus histiocytosis with massive lymphadenopathy runs a benign course and spontaneous resolution occur in 50% of cases.[5] The longest reported clinical course before spontaneous resolution as at 1990 was for 30 years. [19]

One of the histopathologic hallmarks of sinus histiocytosis with massive lymphadenopathy is effacement of nodal architecture and dilatation of lymph node sinuses by lymphocytes, plasma cells and numerous characteristic histiocytes and sometimes red blood cells within their cytoplasms. This process whereby cells enter and transit through another cell without degradation is known as emperipolesis and was first described by Humble et al. [20]

Diagnosis of Sinus histiocytosis with massive lymphadenopathy may be missed in both FNA and surgical biopsy specimen. FNA can at times be misinterpreted due to limited or non-representative sampling and as FNA does not permit examination of tissue architecture, diagnosis is further made difficult. But despite these limitations, FNA is considered to be superior to surgical core or excision biopsy as emperipolesis tends to be more prominent in FNA materials than on tissue sections. [12]

Both Langerhans' cells and Histiocytes of Rosai-Dorfman's disease demonstrate S-100 protein on immunohistochemical staining but the reaction of Langerhans' cells is stronger. [17,21,22]
The presence of emperipolesis and positive s-100 protein is regarded as diagnostic of sinus histiocytosis with massive lymphadenopathy. [21]
There is no treatment protocol for Rosai-Dorfman's disease. Modalities of treatment seen in literature include excisional biopsy followed by observation.[18]

Oral corticosteroid (Prednisolone) has been tried with varying responses. In one report, approximately one third of patients achieved a complete or partial response to treatment. [23]

In another report, a 4 month course of Prednisolone was prescribed for a patient with laryngeal Rosai-Dorfman's disease but she had recurrences after discontinuation of treatment.[18]

Chemotherapy has been used with some success. Documented agents that have been used include Vincristine, Chlorambucil and Methotrexate.[11]

Although the disease is benign, radiotherapy has been used as a treatment modality. In a review of 418 cases of Rosai-Dorfman's Disease, Kompo [24] found 34 patients that were treated with radiotherapy with varying responses to radiation dose ranging from 30-40Gy

Conclusion

Rosai-Dorfman's Disease is a disease that is not commonly suspected as a cause of persistent palpable swellings in both nodal and extranodal sites, thus posing a diagnostic dilemma. However, we recommend that clinicians should be weary of a possibility of Rosai-Dorfman's Disease in a patient with long standing painless slowly progressive nodal or extranodal swelling especially if the patient is within the second decade of life.

Suspicion should be heightened if there are bilateral cervical lymphadenopathy and no weight loss. Clinical suspicion of the disease will assist the histopathologist in looking out for the diagnostic features of this disease.

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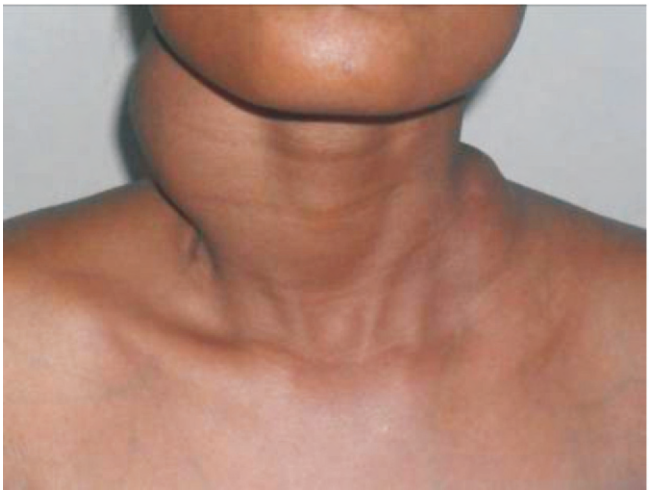

Fig 1

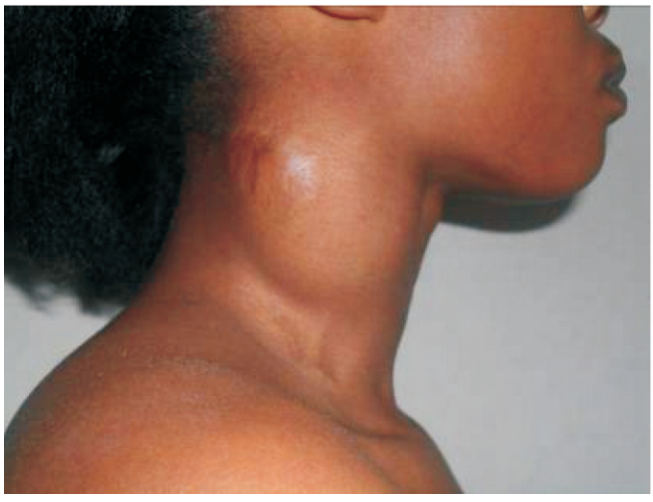

Fig 2

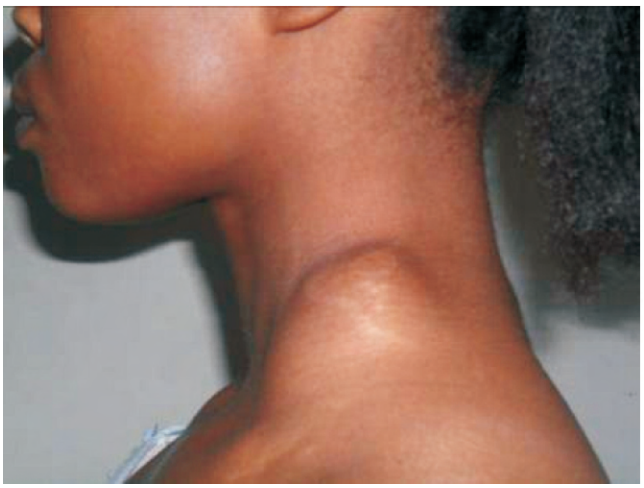

Fig 3

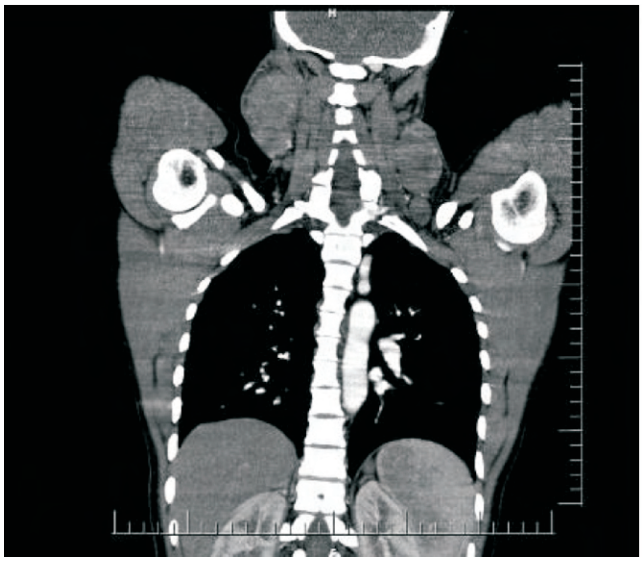

Fig 4

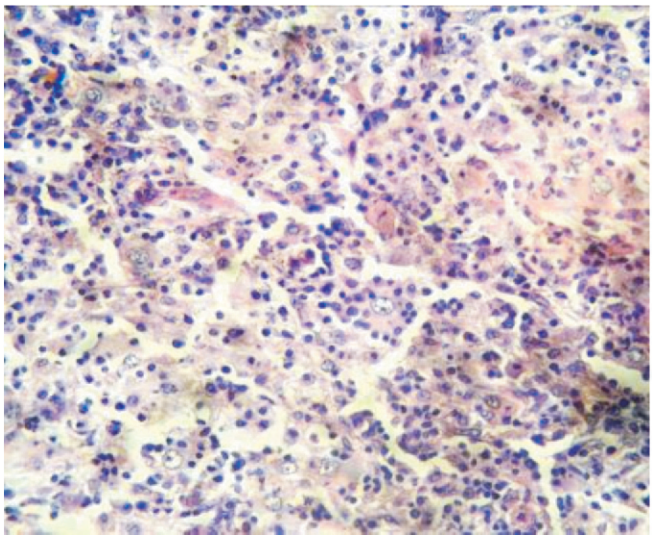

Fig 5