Rosai-Dorfman Disease in African children

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Citation

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Abstract

We present a report of Rosai-Dorfman disease in African children, as well as highlight its familial tendency and draw attention to the different orbito/ocular presentations of this disease. An observational case review was performed. Two siblings, one with multiple subcutaneous eye lid nodules in a 12 year old female, and the younger brother who demonstrated a right fungating proptosis, participated in the review. Clinical diagnosis of Endemic Kaposi's Sarcoma and Rhabdomyosarcoma respectively were made. However, immunohistochemical examination confirmed Rosai-Dorfman disease. Patients were referred to the pediatric oncologist for systemic review and treatment. In the African setting, blindness may become a consequence of Rosai-Dorfman disease. The disease may simulate other known causes of proptosis and should be considered in differential diagnosis of orbito/ocular conditions in African children.

INTRODUCTION

Rosai-Dorfman in 1969 first described a clinicopathological entity, of Idiopathic histiocytic proliferation which was characterized by sinus histiocytosis with massive painless lymphadenopathy (SHML) or Rosai-Dorfman disease (RDD) [1,2]. It is considered to be a non hereditary and rare disorder in children and young adults of African ancestry. A male preponderance has been described in literature with the male to female ration of 2: 1 [3]. Histiocytic disorders are accurately diagnosed based on Histochemical l and immunohistochemical studies in combination with clinical evaluation. Rosai-Dorfman disease is currently classified as a member of the non Juvenile Xanthogranuloma (non-JXG) family under the sub group of the non Langerhans Cell Histiocytosis (non-LCH) [4]. The underlying cause of RDD is vague, Epstein-Barr virus[2] and human herpes virus 6 [5] have been implicated, but no clear association has been identified. Autoimmune disease, immunocompromise, and neoplastic cell disease may be a cause, but remains uncertain. There are rare associations with polycythemia vera, joint disease, glomerulonephritis, haematological antibodies, and Wiskott-Aldrich syndrome[2].

Extra nodal involvement represents 30% of cases and has been reported in diverse anatomic sites, including the skin, orbit, and upper respiratory tract [2,3,6]. Absence of nodal presentation has been reported [7]. Although involvement of the orbit and lids has been reported in 12% of cases, intraocular involvement is rare [1]. We present two cases of Rosai-Dorfam disease from Sub-Saharan Africa and in siblings. To the best knowledge of the authors, no documentation of the disease and its familial tendency has been reported in literature from Sub-Saharan Africa.

CASE REPORT 1

A 12 year –old female African, living in South region of Nigeria presented with a 1 year history of a bilateral progressive ptosis and slowly enlarging painless periocular masses of two months duration. There was no associated systemic illness. Examination of the eye showed normal visual acuities and a normal globe bilaterally. Further examination revealed, a non tender, firm, multinodular freely mobile, well defined subcutaneous mass in both upper lids. There were no associated preauricular or submandibular lymphadenopathies. Dental anarchy was present. Further systemic examinations were within normal limits and retroviral study was negative. A clinical diagnosis of endemic karposis sarcoma to rule out multiple Chalazia was entertained. An incisional biopsy was taken under general anaesthesia and the specimen sent for Histopathology diagnosis.

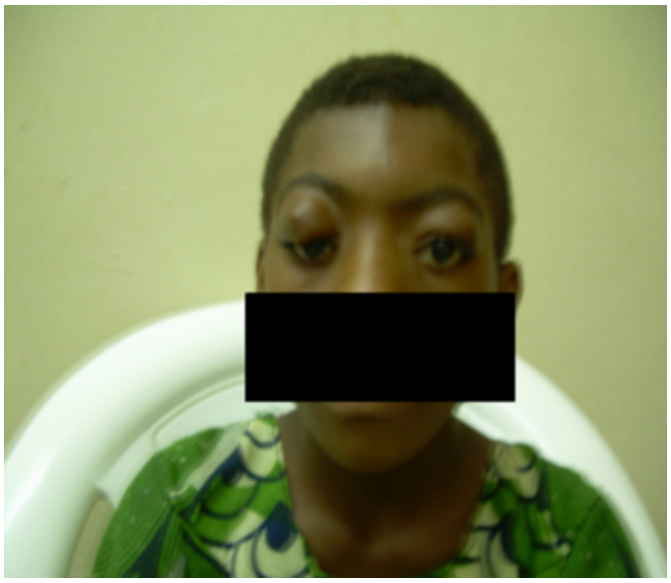
The tissue report was as follows: Macroscopy: Part of a firm cream white rubbery nodule 25x22x10mm. The cut surface shows solid white and yellow nodular areas. Microscopy: Histology shows features of extra-nodal Rosai-Dorfman disease. This is characterised by the presence of CD68 and

S100 positive histiocyte type cells showing emperipolesis. No infective agent or vasculitis is identified.

Unfortunately, the patient was lost to follow up.

Figure 1

Figure 1: Child in case 1



CASE REPORT 2

The 9 year-old , younger brother of the above girl, presented with a 7 weeks history of painful rapidly progressive protrusion and loss of vision in his right eye. There was no antecedent trauma or febrile illness. However, this was a preceded by a three months history of catarrh. He denied application of traditional eye medications. On examination, the right visual acuity was no perception of light. There was a right gross periorbital swelling more prominent inferiorly associated with lower lid ecchymosis. In addition to a non tender, gross orbital protrusion and a fungating globe, in a frozen orbit. A congested right turbinate was noted. There were associated multiple, discrete, non tender preauricular, and cervical lymphadenopathy. Vision was normal in the left eye. As in the older sibling, other systemic evaluation including the lung fields were normal. A diagnosis of advanced Rhabdomyosarcoma was considered. A modified exenteration was performed and tissue sent for histology:

The tissue report was as follows: Macroscopy; Multiple fragments of nodular cream white tissue; the largest 18mm. Cut surface is solid white. Microscopy; The histology shows the features of extra nodal Rosai-Dorfman. This is characterised by the presence of CD68 and S100 positive histiocyte type cells showing emperipolesis. No infective agent or vasculitis is identified.

The patient was referred to the ear, nose and throat surgeons and pediatric oncologist for further management. Similar to the first case, he too was lost to follow up.

Figure 2

Figure 2: Child in case 2

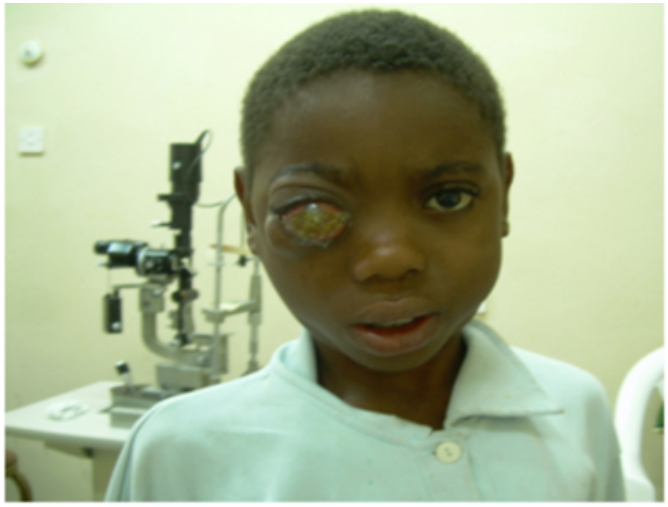


Figure 3: histochemical slide picture of Rosai-Dorfman. This is called emperipolesis and is well recognised in Rosai-Dorfman.

Figure 3

3 (a) Images show the larger histiocyte type cells and the background shows lymphocytes and plasma cells.

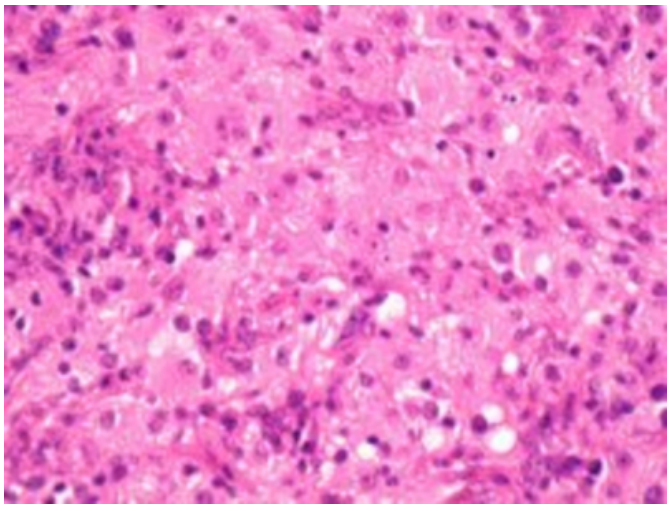


Figure 4

3 (b) The picture below with the single brown cell in the centre-note how the histiocyte type cell has engulfed lymphocytes into its cytoplasm.

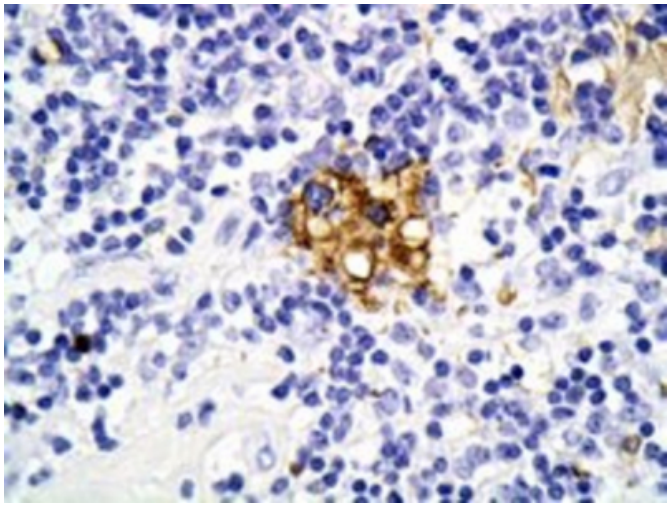
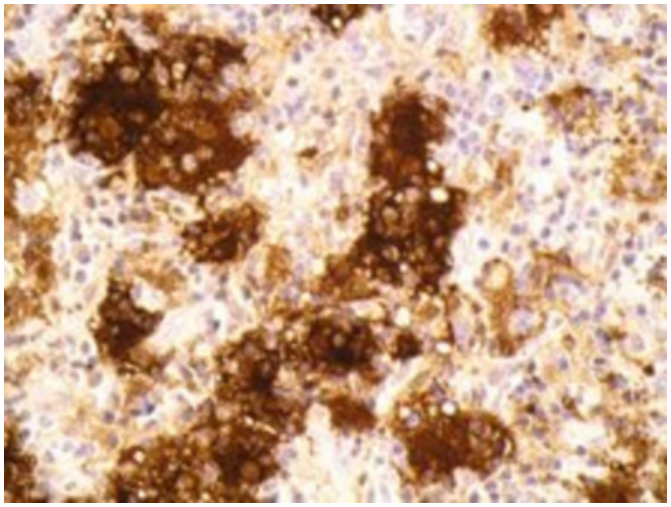


Figure 5

3 (c) The immunohistochemistry images demonstrate that these larger histiocyte type cells are positive for S100 (brown is positive).



DISCUSSION

Rosai-Dorfman Disease has not been documented in literature as occurring in or reported from sub-Sahara Africa. This may probably be due to missed diagnosis and a deficiency in diagnostic support in sub-Saharan Africa, and therefore may not be as rare as has previously been documented. To the best of the authors' knowledge this are the first cases to be documented in an African family, from Sub-Saharan Africa. Familial cases though rare have been seen. Observation of congenital disease and reports of familial cases with seven pairs of siblings including three sets of identical twins suggests a genetic predisposition in some patients with this condition [8].

In a review of extra nodal Rosai-Dorfman disease seen in 11 cases, the disease was isolated to the central nervous system. This suggested the ability of this entity to mimic meningiomas, lymphomas and chronic inflammation [9]. In another report, RDD mimicked a testicular malignancy [10]. Moreover, molecular studies have found no evidence of clonal rearrangement implying that this disease is a reactive rather than a neoplastic condition.

Most cases have spontaneous remission after several years, usually without treatment. However, treatment modalities for RDD include: surgery, radiotherapy or medications such as corticosteroids, cyclophosphomide and more recently interferon [11, 12]. However, the results of chemotherapy or radiation treatments have generally been disappointing. Surgical debulking has been effective. This is now recommended as the first line of interventional therapy to be considered along with adjuvant steroids or more aggressive chemotherapy or radiotherapy when necessary [12].

The orbit and eye lids are common extranodal sites and were the presentation in this review which was confirmed by immunohistochemistry. The first case was purely extra nodal while the second case had a nodal component. It may appear that the first case is an early presentation of the disease compared to the second case. Nodal involvement maybe a hallmark of disease severity. This may explain the loss of vision in the second case. On the other hand, it may be possible that there is an acute and chronic form of the disease hence the difference in the duration of presenting symptoms and signs. Lower eye lid involvement in RDD has been reported [2]. This is the fourth common site of extra nodal disease. However, our first case presented with upper eyelid masses.

Prognosis is good, but severe cases can often lead to morbidity and mortality especially if multiple organs are involved or there is an underlying auto immune dysfunction. The rate of recurrence is often high even in cases of successful treatment [1]. In our environment, patients patronize alternative medicine practitioners and use traditional eye medications before they eventually present at the terminal stage of disease to eye health facilities. This situation is suspected to have been the case in case 2, in which there was visual loss before presentation. Visual loss in orbital disease has been documented to be a result of compressive optic neuropathy which responded to chemotherapy [13]. In our case, there was in addition, an irreversible corneal cause of loss of

vision. Rosai-Dorfman disease in the African setting would pose a challenge in both its diagnosis and treatment. Although believed to be rare, Rosai-Dorfman disease from this report can in children clinically mimic other pathologies such as Rhabdomyosarcoma, advanced Retinoblastoma, Burkkits lymphoma, and Panophthalmitis. Some of these differentials have been documented as such in a previous report [7],[14,15]. While the differential diagnosis of eye lid involvement could include: multiple eye lid Chalazion and Endemic Kaposi's sarcoma as was initially assumed.

Early recognition of this benign entity as a masquerade for neoplasm in African children will prevent misdiagnosis, allow for appropriate treatment and prevent loss of vision.

Moreover, it should be noted that an accurate diagnosis can only be made with the aid of at least histochemical examination; therefore emphasising the importance and need for adequate, suitable and superior ocular histopathogy services. This would compliment ophthalmic clinical services, ensure early and appropriate diagnosis of this disease.

In conclusion, a high index of suspicion of RDD with adjunct facility for confirmation is necessary. We suggest that for Africa, eye health promotion and education which should presumably encourage early uptake of eye care services and discourage the use of alternative and harmful traditional eye medications needs to be advocated. These should result in early diagnosis, appropriate care, including prevention of permanent visual loss in African children with Rosai-Dorfman disease.

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