case report

Rosai-Dorfman disease of the paranasal sinuses and orbit

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Hematol Oncol Stem Cell Ther 2011; 4(2): 94-96

DOI: 10.5144/1658-3876.2011.94

Rosai-Dorfman disease, also known as sinus histiocytosis with massive lymphadenopathy, is a benign indolent disorder, characterized by enlarged lymph nodes filled with histiocytes. Extranodal involvement is uncommon. The disease rarely affects the nose and paranasal sinuses. We report a case that presented with a right nasal mass, extending into all the paranasal sinuses and right orbit without any accompanying lymphadenopathy. Because of the absence of lymphadenopathy it posed a diagnostic challenge until the pathology was confirmed on histopathological examination.

Rosai-Dorfman disease is an uncommon disorder featured by histiocytic proliferation in the lymph nodes, clinically presenting as lymphadenopathy and/or extranodal involvement in one-fourth to one-third of cases. Being a benign disorder, it needs to be differentiated from malignant causes especially lymphomas. The diagnosis comes from histopathology and the majority require no treatment.

CASE

A 30-year-old woman presented with progressive right-sided nasal blockade and protrusion of the right eye of 2 years duration. The disease was accompanied by progressive diminution of vision on the right side for the previous 6 months. Prior to this, the patient had been complaining of bilateral nasal discharge for ten years, for which she had undergone nasal surgery twice, once in 2002 and again in 2006, the records of which she had lost. She denied any history of local pain, fever, weight loss or night sweats. There was no history of diabetes mellitus, tuberculosis or hypertension.

Examination revealed pallor, right eye proptosis with slight restriction of ocular movements medially and a visual acuity of 6/12 with normal pupillary reflexes and a fleshy nasal mass filling the right cavity, completely pushing the nasal septum to left side. The pharynx was clear. There was no fever, lymphadenopathy or organomegaly. Investigations revealed a hemoglobin of 5.9 g/dL, with a normal total leukocyte count, different leukocyte count, and platelets. A peripheral smear showed microcytic, hypochromic anemia, possibly iron deficiency anemia. The erythrocyte sedimentation rate was 32 mm the first hour. Blood glucose, renal function tests, liver function tests, and uric acid were normal. Chest x-ray, echocardiography, and CT abdomen were also normal. Non-contrast CT of the paranasal sinuses revealed a heterogeneous mass arising in the right nasal cavity, extending into all the sinuses and also eroding the medial walls of both the orbits. The lobulated lesion in the right orbit was abutting the optic nerve, the right medial and inferior recti muscles and causing lateral displacement of the globe. The lesion also extended into the right buccal space, the infratemporal fossa and soft tissue of the cheek on the right side (**Figure 1**).

For the mass lesion, the patient underwent endoscopic nasal mass excision under general anesthesia. A right-sided nasal mass that filled the entire nasal cavity was debulked. The mass engulfed the nasal septum and all the sinuses bilaterally. Disease was cleared from the sinuses and part of the nasal septum was removed. The post-operative period was uneventful. Orbital mass clearance was not attempted, but planned for a later date.

The histopathological examination revealed a dense mixed inflammatory cell infiltrate, rich in plasma cells and histiocytes, which showed emperipolesis. No granuloma or necrosis was seen. Stain for fungus was negative and on immunohistochemistry, the histiocytic cells were positive for S-100. Overall features were consis-

tent with Rosai-Dorfman disease (**Figure 2a, 2b**). The patient was given CVP (cyclophosphamide, vincristine, prednisolone) therapy, concurrent with iron.

DISCUSSION

In 1969 two pathologists, Juan Rosai and Ronald Dorfman, reported a distinct histiocytic disorder in young black males who presented with bilateral, painless, massive cervical lymphadenopathy that in most instances was associated with fever, anemia, neutrophilia, an elevated erythrocyte sedimentation rate, and polyclonal gammopathy.[1] They named it sinus histiocytosis with massive lymphadenopathy and it was later renamed Rosai-Dorfman disease.[1]

The disease has a worldwide distribution and can occur at any age, although it is common in adults. The male-female ratio is 2:1. Painless lymphadenopathy is the most common presentation and involves the cervical region in up to 90% of patients.[2] Other locations such as inguinal (26%), axillary (24%) and mediastinal lymph nodes (15%) are also reported to be involved.[2] Extranodal disease is seen in 25% to 43% of patients, with or without associated lymphadenopathy.[2] The most common extranodal sites, in decreasing order of frequency, are the skin, nasal cavity and paranasal sinuses, eyelid, orbit, bone, salivary gland and the central nervous system. Hepatosplenomegaly, unlike in other histiocytic disorders, is uncommon.[2] Laboratory findings include hematological abnormalities such as normocytic or microcytic anemia, hemolytic anemia, an elevated erthrocyte sedimentation rate and polyclonal hypergammaglobulinemia.[2]

The etiology of the disease remains obscure, but two hypotheses have been proposed: a disturbance in cell mediated immunity, and a focus of infection due to Epstein-Barr virus, *Klebsiella*, *Brucella* or human herpesvirus-6. According to Foucar et al[3] the most frequent otorhinolaryngologic manifestations are found in the nasal cavity (50%), followed by the pharynx (25%), the paranasal sinuses (18.7%) and the trachea (6.3%). In the orbit, the most commonly affected sites are the soft tissue (84.6%) and eyelids (45.5 %), which manifest as exophthalmus (53.8%), clouding of vision, conjunctival infiltration, diplopia, increased or reduced lacrimation, and slight ocular irritation.[4] The diagnosis of Rosai-Dorfman disease is made on the basis of clinical suspicion and confirmed by histopathologic examination. Histopathologic findings include lymphoid aggregates intercalated with areas consisting of histiocytes, lymphocytes, and plasma cells. The hallmark of Rosai-Dorman disease is lymphophagocytosis or emperipolesis, wherein the viable lymphocytes are located in well-

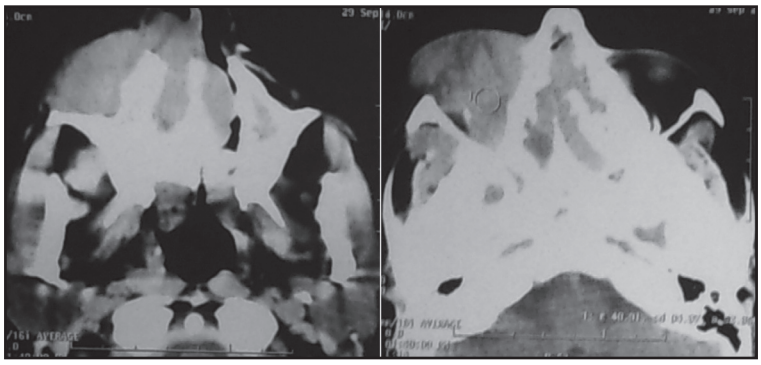

Figure 1. Heterogenous mass in both nasal cavities, maxillary sinuses and the right orbit causing proptosis (non-contrast CT scan).

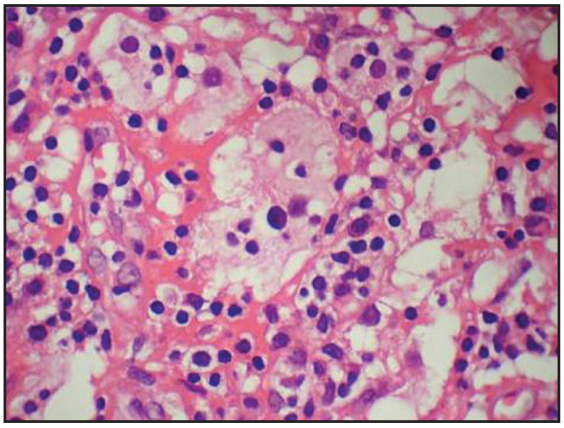

Figure 2a. Inflammatory infiltrate, rich in histiocytes showing emperipolesis (hematoxylin and eosin, 40×).

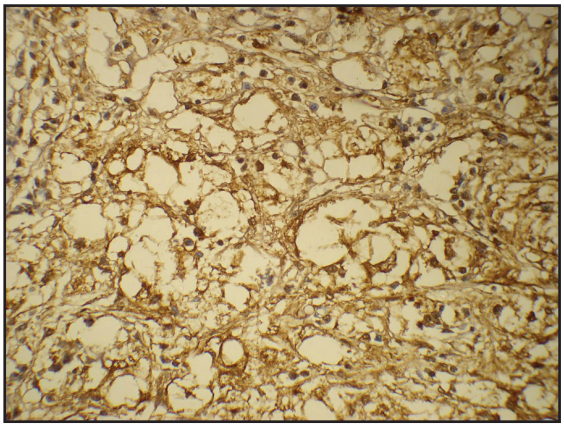

Figure 2b. S-100 positive histiocytes (±immunohistochemistry with S-100, 20×).

defined cytoplasmic vacuoles of intact histiocytes. The involved histiocytes are activated macrophages with features of phagocytic cells as well as immune accessory cells and thus express S-100 protein, HAM 56, α1 antitrypisn, α1 chymotrypsin, lysozyme, Mac 387, Ki-1 (CD 30, Ber-H2), but are negative for CD1a.[5] The histological differential diagnosis includes hemophagocytic syndromes, storage disorder, inflammatory lesions, necrobiotic xanthogranuloma and lymphoreticular malignancies.[6] The presence of benign histiocytes with emperipolesis, an absence of cellular atypia, the immunohistochemical profile, and associated clinical features distinguish Rosai-Dorfman disease from other similar disorders.

The clinical course of Rosai-Dorfman disease is chronic and variable with the majority achieving remission in the long run. The ideal treatment for Rosai-Dorfman disease is as yet unestablished. Only about 50% of patients with Rosai-Dorfman disease need some form of treatment.[7] Management options include observation for mild manifestations with no cosmetic or functional abnormality, surgical excision or debulking for lesions in surgically accessible locations, systemic corticosteroids, chemotherapy (which may include vincristine, 6MP, methotrexate, alkylating agents) or radiotherapy in patients with severe symptoms or where vital organ function is compromised.[8] The treatment of orbital manifestations of Rosai-Dorfman disease aims to control the functional and cosmetic abnormalities. The treatment may include surgery, systemic corticosteroids, chemotherapy or radiotherapy for massive or recurrent orbital disease or significant residual lesion following surgical debulking. Chemotherapy has also been used to relieve sight-threatening optic nerve compression.[3] Goldberg et al[9] treated a patient with Rosai-Dorfman disease with compressive optic neuropathy with a combination of cyclophosphamide, vincristine and prednisolone and found excellent results with 6 months therapy. Komp[7] also showed the superiority of CVP over other chemotherapeutic regimens. Horneff et al[10] demonstrated the efficacy of methotrexate and 6-mercaptopurine (6-MP) in a 3-year-old girl with cervical lymphadenopathy. However, Pulsoni et al[11] disfavored chemotherapy. Jubran et al[12] treated one child with rituximab after a suboptimal response with steroids, methotrexate and 6-MP and showed complete resolution of lymphadenopathy. Jabali[13] cured a patient with chemotherapy with no reccurrence of the disease after 5.5 years.

Author contributions

Dr Afaq made contributions to conception and design, acquisition of data, drafting the article or revising it critically for important intellectual content; and final approval of the version to be published. Dr Shyam Aggarwal had first contact with the patient and later on treated her. Dr Fouzia did the histopathological examination.

No conflict of interest declared

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