Extranodal Rosai Dorfman Disease: Report of Two Cases and Review of Literature

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Introduction:
Rosai Dorfman Disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy is an uncommon disorder characterized by non malignant proliferation of distinctive histiocytes within lymph node sinuses and/or extranodal sites. The disease was initially described in 1969 by Juan Rosai and Ronald Dorfman. The causes of RDD are not fully understood, and treatment strategies differ according to severity or vital organ involvement. It is most frequently seen in children and young adults, although it may occur in any age group. Painless lymphadenopathy is the most frequent systemic presenting symptom and involves the cervical region in up to 90% of patients. Extranodal involvement of at least one site is documented in 43% of patients, and only 23% exclusively have extranodal disease in which lymphadenopathy may or may not develop later in the disease course. The most common extranodal sites in decreasing order of frequency, are skin, nasal cavity and paranasal sinuses, eyelid, orbit, bone, salivary gland and central nervous system (2). Head and neck involvement has been reported in 22% of cases, most commonly the nasal cavity followed by the parotid gland (5). The simultaneous involvement of multiple extranodal sites is not unusual. Hepatomegaly is not a feature, unlike other histiocytic disorders (2). Here we present two cases of extranodal disease; a patient with RDD of the orbit and a second patient with Cutaneous RDD.

Case one:
The first patient is a 14 year old male with history of cerebral palsy, mental retardation, and bilateral chronic uveitis. The patient developed enlargement of the right lacrimal gland as described by magnetic resonance imaging. An anterior orbitotomy was performed and a mass tightly adhered to the medial portion of the lacrimal gland was identified. The intraoperative consultation reported the presence of fatty tissue and the patient with Cutaneous RDD.

Discussion:
Rosai-Dorfman disease is a non-Langerhans cell benign histiocytosis where predominantly the sinuses of the lymph nodes, and less commonly the interfollicular areas, are distended by pale staining histiocytes with round or oval vesicular nuclei with well-defined nuclear membranes and a single prominent nucleolus, intermixed with a variable number of plasma cells. Nuclear atypia and mitoses are infrequent. The phenomenon of emperipolesis is considered diagnostic, although not unique of RDD (2). In emperipolesis the lymphocytes are not attacked by enzymes and appear intact within the histiocytes. Because lymphocyte emperipolesis is thought to relate to antigen presentation, RDD may represent a derangement of the method by which histiocytes contact lymphocytes for antigen delivery (3).

The involved histiocytes are activated macrophages with features of phagocytic cells as well as immune accessory cells, and thus phagocytosis related antigens (CD64, Fc receptor for immunoglobulin G), lysosomal activity (lysosome α1-antichymotrypsin) and immune activation and adhesion molecules (transferrin receptor, interleukin 2 receptor). The most consistent reliable phenotype for RDD is strongly positive S100, variably positive CD68 and negative CD1a (1, 2, 5). RDD lesions have a moderate expression of IL-6, which could be related to the associated polyclonal plasmacytosis and hypergammaglobulinemia. Furthermore, the lesions tend to express strongly IL-1β and TNF-α. This cytokine production may be related to the systemic symptoms associated with RDD (5). Rosai-Dorfman disease involving extranodal sites shows similar morphologic features to its nodal counterpart with more fibrosis and fewer histiocytes with emperipolesis (2). As pathologists we need to be aware of the microscopic features of this condition to be able to diagnose it accurately, specially when it has an extranodal presentation. Although benign and usually self-limited, in some cases it can have a relapsing remitting course and present significant morbidity to the patient. Timely diagnosis spares unnecessary interventions to the patient.

Case two:
The second patient is a 27 year old male with a biopsy diagnosis of nasal and skin xanthogranulomas. He visited the dermatology clinic for evaluation of his condition. He presented multiple violaceous indurated plaques and nodules with central yellow hue on the back and face, along with subcutaneous indurated nodules on both arms. A skin biopsy of one eyelid, orbit, bone, salivary gland and central nervous system (2). Head and neck involvement has been reported in 22% of cases, most commonly the nasal cavity followed by the parotid gland (5). The simultaneous involvement of multiple extranodal sites is not unusual. Hepatomegaly is not a feature, unlike other histiocytic disorders (2). Here we present two cases of extranodal disease; a patient with RDD of the orbit and a second patient with Cutaneous RDD.

References: