

CASE REPORT

Multifocal nodal and extranodal Rosai-Dorfman disease initially diagnosed as histiocytic lymphoma

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Abstract

Rosai-Dorfman disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy (SHML), is a systemic disease involving nodal and extranodal tissues. We report a 48-year-old female with recurrent nasal obstruction due to polypoidal masses involving the nasal sinuses, turbinates and septum bilaterally, and lumps in the right infra-orbital region and region of the right lacrimal sac. A 4 cm right upper neck mass was also noted, which was initially diagnosed as histiocytic lymphoma. Histopathology of the nasal and infraorbital lesions revealed fibro-inflammatory masses containing histiocytic cells with large vesicular nuclei and abundant foamy cytoplasm exhibiting emperipolesis and lymphophagocytosis, admixed with scattered plasma cells and lymphocytes. These histiocytes revealed immunohistochemical positivity for S-100 protein and CD68, but were negative for CD1a. The findings supported a diagnosis of RDD. This report serves to remind pathologists and clinicians of the extranodal manifestations of RDD and its potential confusion with lymphomas.

Keywords: Rosai-Dorfman disease, sinus histiocytosis with massive lymphadenopathy, multifocal, nodal, extranodal

INTRODUCTION

Rosai-Dorfman disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy (SHML), is a systemic disease involving nodal and extranodal tissues. Though rare, it is a well-established disease with distinct clinicopathological features. Typical histological findings include characteristic large, pale histiocytic cells exhibiting emperipolesis and lymphophagocytosis. RDD usually runs a benign course and extensive treatment is not required. However, some patients undergo transformation into conditions similar to those of lymphoma and immune deficiency status, or have extranodal involvement that compress respiratory organs, which can be life-threatening. We report a case of RDD which occurred in the nasal cavities, then recurred a year later with multifocal nodal and extranodal manifestations.

CASE REPORT

A 48-year-old lady presented in April 2005 with recurrent nasal obstruction. She had had a polypectomy done for similar problems the previous year. Clinical examination revealed polypoidal masses involving the nasal sinuses, turbinates and septum bilaterally, associated with small lumps at the right infra-orbital region and in the region of the right lacrimal sac. A 4cm mass was also noted at the right upper neck region. An initial histopathological diagnosis of histiocytic lymphoma was made.

A second review of the slides from the nasal and infra-orbital lesions revealed fibro-inflammatory masses containing histiocytic cells with large vesicular nuclei and abundant foamy cytoplasm exhibiting emperipolesis and lymphophagocytosis, admixed with scattered plasma cells and lymphocytes (Figure 1).

Immunohistochemically, these histiocytes revealed positive staining for S-100 protein and CD68, but were negative for CD1a. Slides from the neck mass revealed only remnants of nodal tissue with necrosis and fibrosis.

The above histopathological and immunohistochemical features confirmed the diagnosis of Rosai-Dorfman disease (RDD).

These masses recurred 6 months post-surgery, and the patient was then referred to an oncologist. However, she has subsequently defaulted follow-up.

DISCUSSION

Rosai and Dorfman described a distinctive clinicopathological entity characterized by sinus histiocytosis with massive lymphadenopathy (SHML) in 1969.¹ SHML may affect all ages, but the majority of patients present within their first 2 decades of life.² SHML was originally described as a nodal-based disease presenting as painless enlarged lymph nodes of the neck, axillae, inguinal region, hilum and mediastinum. However by 1988, it was apparent that lymph nodes were not always affected and that any organ of the body may be involved, and a designation of Rosai-Dorfman disease (RDD) was preferred.

Extranodal involvement occurs in 43% of cases,² and out of these, 75% occur within the head and neck region, mostly affecting the nasal cavity and paranasal sinuses, followed by the salivary glands, oral cavity, pharynx, tonsils, trachea, orbit, and eyelid.² The common head and neck manifestations include fever, weight loss, rhinorrhea, nasal obstruction, epistaxis, and tonsillitis.² Extranodal involvement is more frequently found among elder individuals and those with an underlying immune deficiency status, which may contribute to a poorer prognosis.³

Histopathologically, involved lymph nodes show peri-capsular fibrosis with sinuses expanded by numerous distinctive proliferative histiocytes with round vesicular nuclei, distinct nucleoli and abundant pale to clear cytoplasm, intermixed with variable numbers of mature plasma cells. A characteristic, but not pathognomonic, finding is the presence of lymphophagocytosis or emperipolesis.^{1,2} The phagocytized cells are usually lymphocytes, but also occasionally plasma cells, erythrocytes, and polymorphonuclear leukocytes.^{2,3} Immunohistochemically, the histiocytes are positive for S-100 protein, CD68 and alpha-antichemotrypsin, but are negative for CD1a.²

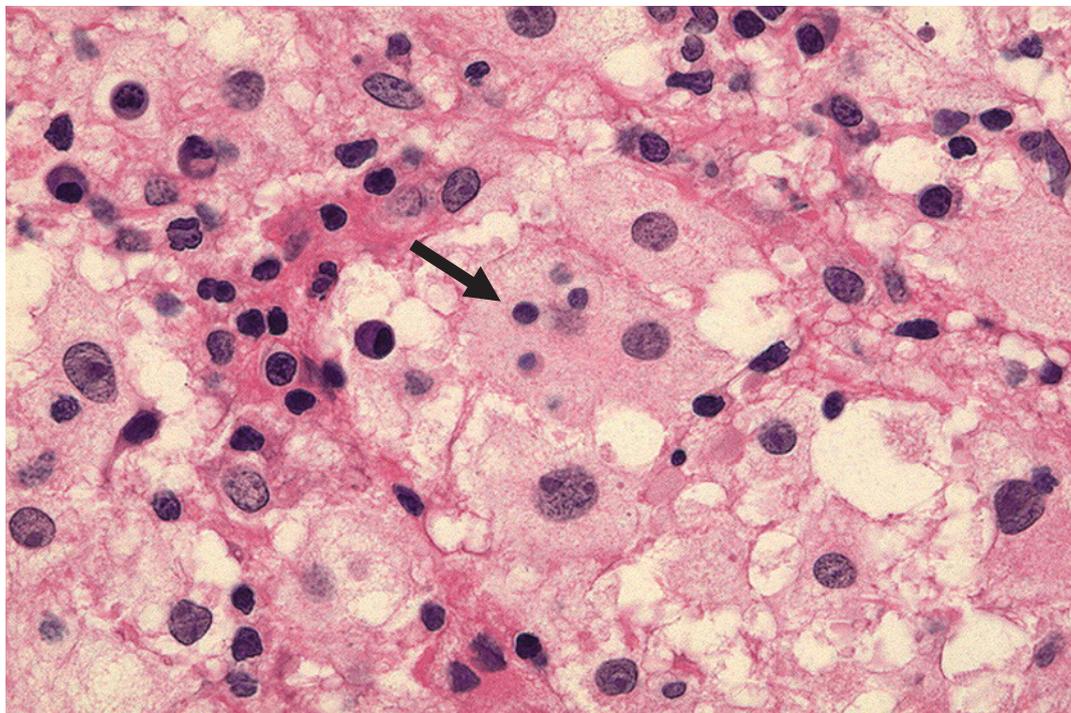


FIG. 1: Characteristic pale histiocytes in Rosai-Dorfman disease, exhibiting emperipolesis and lymphophagocytosis (arrow) (H&E x 400)

The negativity for CD1a excludes a diagnosis of Langerhans cell histiocytosis, which is an important differential diagnosis. Histiocytic lymphoma (histiocytic sarcoma) shows similar immunohistochemical staining as RDD, but was excluded on routine stains by presence of the typical RDD features seen above, and absence of defining histopathological characteristics of histiocytic lymphoma such as invasive margins, abundant eosinophilic cytoplasm, binucleated and multinucleated giant cells, nuclear atypia, mitotic activity and spindle cell sarcomatoid areas. Furthermore, the clinical presentation of extranodal RDD shows a predisposition for the nasal cavity and paranasal sinuses, while extranodal manifestations of histiocytic lymphoma are usually found in the skin, soft tissue and gastrointestinal tract. Also, histiocytic lymphoma is a very rare neoplasm in which many previously published cases were likely misdiagnosed examples of non-Hodgkin lymphoma.⁴

To date, the aetiology of RDD remains uncertain. Two hypotheses have been proposed; a disturbance of cell-mediated immunity, and a primary viral infection.⁵ The immunohistochemical findings in RDD confirm the presence of functionally activated macrophages; the activation possibly following an immune or infectious challenge, and EBV and HHV-6 have both been implicated.⁵

RDD is usually considered an indolent and self-limited disease,² although clinical courses have been noted to vary.⁶ McAlister *et al* reported that approximately 50% of patients with this disease resolved spontaneously, 33% had residual asymptomatic lymphadenopathy, and 17% had persistent symptoms.³ Recurrences and progression of disease may also occur.² Unfavourable prognostic factors include disseminated nodal disease and involvement of multiple extranodal organ systems.^{2,3}

Extensive treatment is not necessary in most patients with RDD because it usually does not aggravate and is sometimes self-limiting.⁶ However, some patients undergo transformation into conditions similar to those of lymphoma and immune deficiency status, or have extranodal involvements compressing respiratory organs, which can be life-threatening. In these cases, surgical resection is necessary, but the use of steroids, radiation, thalidomide and chemotherapy has been unsatisfactory.

In conclusion, RDD is a distinct clinical and pathological entity, which is often overlooked

initially in extranodal sites and may be confused with other neoplastic disorders, namely lymphomas. There are varying clinical courses of RDD and a confirmed diagnosis is important to inform patients regarding therapy and prognosis. Long-term follow-up is usually necessary, due to the nature of the disease. It is thus important for otorhinolaryngologists, pathologists, and other clinicians to be familiar with the head and neck manifestations of this disease in order to facilitate a correct diagnosis of RDD, particularly those in extranodal sites.

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