

Rosai-Dorfman Disease in a Patient with Systemic Lupus Erythematosus

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ABSTRACT. Rosai-Dorfman disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy, is a clinically benign, frequently chronic, painless lymphadenopathy. It can also involve extranodal sites. We describe a 37-year-old man with a recent diagnosis of systemic lupus erythematosus and antiphospholipid antibody syndrome who had lacrimal gland and orbital involvement and nodal and extranodal sites with RDD. (J Rheumatol 2005;32:951–3)

Key Indexing Terms:

ROSAI-DORFMAN DISEASE
SINUS HISTIOCYTOSIS

SYSTEMIC LUPUS ERYTHEMATOSUS
MASSIVE LYMPHADENOPATHY

Rosai-Dorfman disease (RDD) or sinus histiocytosis with massive lymphadenopathy (SHML) is a rare, idiopathic histiocytic proliferation affecting the lymph nodes. It is characterized by painless lymphadenopathy with fever, leukocytosis with neutrophilia, high erythrocyte sedimentation rate (ESR), and polyclonal hypergammaglobulinemia^{1,2}.

The etiology of this disorder is unknown. A relationship with underlying immunodeficiency³, disordered immune mechanism⁴, or infectious agents like herpes virus, varicella zoster virus, Epstein-Barr virus, cytomegalovirus, brucella or klebsiella has been postulated.

Lymphadenopathy is a common clinical manifestation in patients with systemic lupus erythematosus (SLE), and histologically it is mostly reactive hyperplasia. However, other serious diseases have been associated with lymphadenopathy in SLE.

There are 2 case reports in the literature describing RDD in patients with SLE. We describe a patient with SLE and antiphospholipid antibody syndrome who had lacrimal gland, orbital, nodal, and extranodal involvement with RDD.

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CASE REPORT

A 37-year-old African American man with a history of SLE [arthritis, neutropenia, positive antinuclear antibodies (ANA), positive anticardiolipin antibodies (aCL)] and stroke developed a tender lump over his right upper eyelid. He denied diplopia or decreased vision. Review of systems was unremarkable. On examination, there was a firm immobile mass present superomedially along the trochlea of the right upper eyelid. There was no fluctuance. Extraocular motility was full without evidence of proptosis. The lacrimal glands were symmetric, and examination of the conjunctiva and cul-de-sac was normal. Vision was 20/20 in each eye. The anterior segment and funduscopic examination were normal.

Magnetic resonance imaging (MRI) of the orbits revealed an enhancing lobulated soft tissue mass seen symmetrically in the preseptal areas bilaterally, inseparable from the lacrimal glands. The soft tissue was hypointense on T2-weighted images. The globes, optic nerves, and extraocular muscles were normal bilaterally. He underwent right orbitotomy with excision of the mass.

Microscopic examination of the tissue revealed infiltration of connective tissue by dense chronic mixed inflammatory infiltrate of plasma cells, T and B lymphocytes, and large pale histiocytes (Figure 1). The histiocytes had clear abundant cytoplasm and contained intracytoplasmic lymphocytes or plasma cells (emperipolesis) (Figure 2). Immunohistochemically, the large histiocytes were positive for S-100 (Figure 2) and negative for CD1A. These findings were consistent with extranodal RDD.

The nodular lesion on the right upper eyelid resolved spontaneously. The patient underwent whole body computer tomographic (CT) scan to look for lymphadenopathy. CT scan showed multiple soft tissue masses within the subcutaneous fat about the pelvic inlet. A 9 mm soft tissue nodule was seen within the retroperitoneum on the right. Mild axillary, inferior mesenteric, and iliac lymphadenopathy with mild splenomegaly were also noted. These findings were thought to be related to the RDD. Followup CT scans revealed spontaneous resolution of the nodal and extranodal lesions.

DISCUSSION

RDD was first described in 1969¹ and recently reviewed in 1990⁵. It usually presents as painless massive cervical lymphadenopathy, but mediastinal, axillary, and inguinal nodes can also be involved². Extranodal disease is seen in 28% of cases⁶. The commonest extranodal manifestation is in the

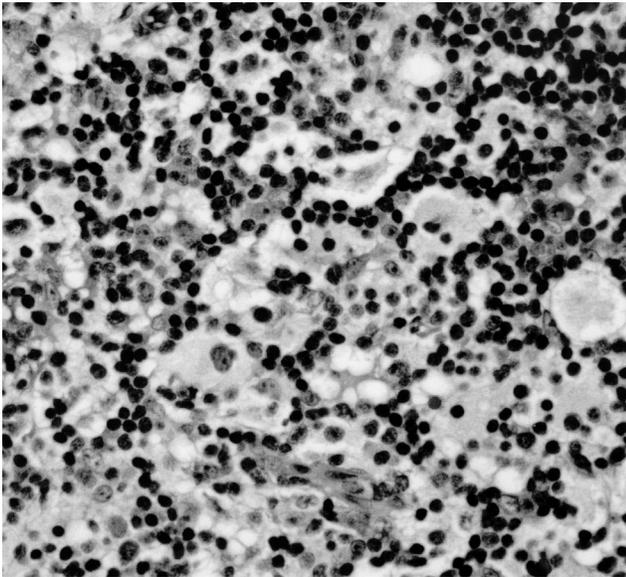


Figure 1. Orbital mass biopsy showing dense mixed inflammatory infiltrate with large pale histiocytes, plasma cells, and lymphocytes (hematoxylin-eosin, original magnification $\times 400$).

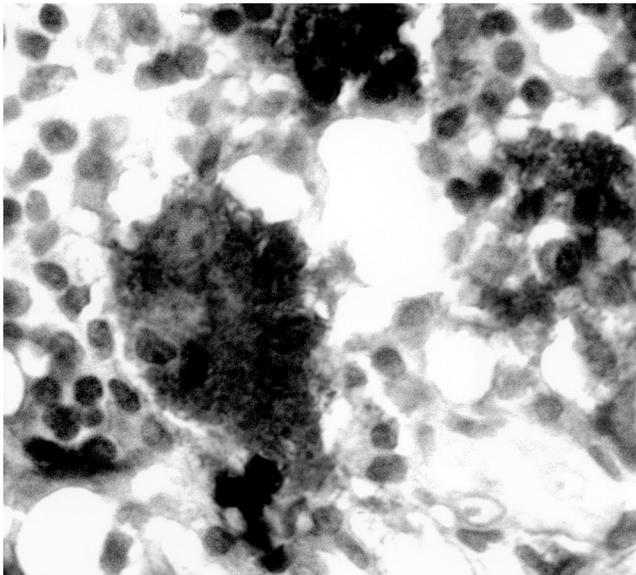


Figure 2. Emperipolesis with histiocytes staining positive for S100 stain (immunohistochemical stain, original magnification $\times 1000$).

head and neck area in about 22% of cases^{5,6}. The orbit or eyelid is involved in 10% of cases^{7,8}. Male to female ratio is equal.

The pathologic finding of RDD is proliferation of distinctive histiocytic cells that show emperipolesis in the background of a mixed inflammatory infiltrate, consisting of plasma cells and lymphocytes. This leads to the effacement of the involved organ architecture, with eventual formation of fibrous bands. The histiocytes express S100 protein that along with emperipolesis is characteristic of RDD⁹.

Juskevicius, *et al* reported a 48-year-old man with SLE

and persistent enlargement of the right parotid gland. He underwent excisional biopsy of the right parotid gland. The histologic examination was consistent with RDD. After 2 year followup, he had exacerbations and remissions of the swelling of his submandibular and parotid salivary gland and also developed lacrimal gland enlargement⁹.

Petschner, *et al* described a case of a 59-year-old woman with polyarthralgias, myalgias, photosensitivity, polyserositis, and cervical, axillary and inguinal lymphadenopathy. She had ANA, low complements, and IgM aCL. A diagnosis of SLE was entertained. She responded poorly to methotrexate, azathioprine, and corticosteroids. She had trilinear cytopenia without hemolysis. Bone marrow biopsy showed marked hypercellularity and polyclonal plasmacytosis. MRI of abdomen revealed a retroperitoneal mass and histology was consistent with Rosai-Dorfman sinus histiocytosis. She was treated with high dose steroids, intravenous immunoglobulin, splenectomy, and courses of cyclophosphamide, without improvement. Then anti-CD20 monoclonal antibody (rituximab) was tried, and she had dramatic improvement of symptoms¹⁰.

Drosos, *et al* have described a patient with primary Sjögren's syndrome who developed excessive lymphadenopathy and splenomegaly, diagnosed to be RDD.

RDD generally has a clinical course characterized by exacerbations and remissions. It undergoes complete remission in most patients^{3,5}. However, a subset of patients who had immunologic abnormalities at or before presentation can have a less favorable prognosis and a higher mortality rate³. Treatment is reserved for special circumstances, like tracheal or epidural compression or invasion of other vital structures. Local excision or radiotherapy is helpful in selected patients¹¹.

Lymphadenopathy is a common clinical manifestation of SLE. It can be generalized or regional in distribution. The differential diagnosis involves either reactive hyperplasia or lymphoma. But lupus lymphadenitis can simulate Castleman's disease or Kikuchi's lymphadenitis¹².

Castleman's disease or angiofollicular lymph node hyperplasia is a rare disease with unknown etiology. It can present as local or multicentric lymphadenopathy. Constitutional symptoms may be absent. Multicentric lymphadenopathy with other clinical symptoms can mimic SLE¹³.

Kikuchi's disease or histiocytic necrotizing lymphadenitis is a self-limited disease of young women with unknown cause, which can mimic SLE. Signs and symptoms include cervical adenopathy, fever, weight loss, and a prodrome of upper respiratory tract infection. Laboratory findings are generally normal. Diagnosis is based on characteristic histologic findings in the biopsy¹³.

Thus, lymphadenopathy in SLE should be evaluated cautiously. Biopsy is the key to rule out malignancy and confirm the diagnosis. With only a few case reports in the

literature, it is very difficult to ascertain the association between SLE and RDD. Whether the association is a coincidence or has a pathological relationship remains to be determined.

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