A 10-YEAR-OLD Iraqi child presented with a bilateral exophthalmos (Figure 1). An ophthalmologist had partially stitched up his eyelids to avoid subluxation of the globes. Exophthalmos began at age 3 years and was diagnosed as pseudotumor orbitae. Attempted control of progressive proptosis with steroid therapy had been unsuccessful. Health status was otherwise normal. Erythrocyte sedimentation rate and serum immunoglobulin levels were elevated. A cranial magnetic resonance imaging scan showed abnormal tissue completely occupying the orbital spaces (Figure 2), the sphenoidal and maxillar sinuses, the right retrostyloid space, and slightly infiltrating the anterior fossa up to the sella. Chest x-ray films, radionucleotide bone scan, and bone marrow aspirate showed no abnormalities. An orbital tissue biopsy specimen showed sheets of large, pale, eosinophilic polygonal histiocytic cells with large vesicular nuclei and small nucleoli; occasional multinucleated histiocytes and spindle-shaped histiocytes were also present. No intact lymphoid cells were detected in the cytoplasm of large histiocytes (ie, no emperipolesis), mitosis was rare, and small lymphocytes and plasma cells were frequently scattered through the lesion as single cells and also arranged in clusters (Figure 3, left). By immunohistochemistry the histiocytic cells stained positive for S100 protein (Figure 3, right) and CD68, but negative for CD1a (not shown); a presumptive diagnosis of Rosai-Dorfman disease of soft tissue was made. Diagnosis of multifocal Rosai-Dorfman disease of the soft tissue was then confirmed with a biopsy specimen of an asymptomatic, mildly enlarged submaxillar lymph node. At histological examination, the lymph node architecture was preserved and the sinuses were distended by distinctive large histiocytes with abundant pale cytoplasm, often filled with apparently intact lymphocytes (emperipolesis). By immunohistochemistry the histiocytic cells stained positive for S100 protein and CD68, but negative for CD1a (not shown). These cells showed the same phenotype observed in orbital tissue (Figure 3). Sixteen weeks of chemotherapy (vinblastine, 6 mg/m² per week), gave poor results. Further chemotherapy with mercaptopurine (60 mg/m² per day) and methotrexate (12 mg/m² per week) for another 16 weeks also gave poor results.
Diagnosis and Discussion

Multifocal Rosai-Dorfman Disease of Soft Tissue

Figure 1. Severe exophthalmos.

Figure 2. Abnormal tissue completely occupying the orbital spaces, slightly infiltrating the anterior fossa up to the sella.

Figure 3. Orbital tissue. Left, Sheets of large, pale to eosinophilic polygonal histiocytic cells with large vesicular nuclei and small nucleoli; occasional multinucleated histiocytes and spindle-shaped histiocytes were also present (hematoxylin-eosin, original magnification ×150). Right, The histiocytic cells stained positive for S100 protein (alkaline phosphatase anti–alkaline phosphatase, original magnification ×150).

Rosai-Dorfman disease (RDD) is an uncommon proliferative disorder of histiocytes that was first described in 1969.1

Generally, RDD is characterized by massive lymphadenopathy (frequently accompanied by anemia), increased erythrocyte sedimentation rate, and elevated levels of serum immunoglobulins. Histologically, this condition is characterized by a proliferation of large pale cells that show striking lymphocytophagocytosis (emperipolesis) and immunoreactivity for S100 protein.2 However, it has only recently been described as a distinct entity in soft tissue, with pernicious locally recurrent lesions.3,4

The disease is often not recognized in the soft tissue.3,5 Emperipolesis can be less conspicuous and proliferating histiocytes are spindled, associated with collagen deposition, and arranged in a vague storiform pattern with scattered lymphoplasmacytic aggregates. Lymph node involvement can be present or not.3

These features lead to a variety of misdiagnoses, including benign inflammatory and fibrohistiocytic lesions, lymphoma, and malignant fibrous histiocytoma.3

Rosai-Dorfman disease of the soft tissue occurs more often in older patients than does nodal RDD.3 Areas involved can include face, leg, arm, shoulder, abdomen, groin, buttock, back, retroperitoneum, orbit, and chest wall.3,5

Optimal therapy has not been established.6 Knowing that RDD of soft tissue mimics fibrous and inflammatory lesions of soft tissue is important for prompt diagnosis and selection of the most appropriate therapy.

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