A previously healthy 12-year-old boy was seen with a 4-week history of a gradually worsening right frontal temporal headache. At the point of maximum discomfort, the patient had noticed a fixed soft tissue swelling for 2 weeks. Findings from physical examination revealed a 4 × 6-cm swelling of the right frontal temporal region of the head. Computed tomography and magnetic resonance imaging showed a dumbbell-shaped mass involving the right frontal soft tissue at the level of the temporalis muscle with erosion through the bone and intracranial extension (Figure 1). No intradural compression was identified. Craniotomy was performed, revealing a vascular, soft, friable tumor, which was resected. A total body bone scan and chest x-ray film revealed no additional disease. Findings from histologic examination of the tumor showed a mixture of large cells with convoluted nuclear grooves and indentations, multinucleated giant cells, and a mixed inflammatory infiltrate composed of eosinophils, neutrophils, and lymphocytes (Figure 2). An immunohistochemical S100 protein stain was performed (Figure 3). Electron microscopy demonstrated diagnostic features (Figure 4).
Eosinophilic granuloma (Langerhans Cell Histiocytosis)

Osinophilic granuloma is a localized, relatively benign form of Langerhans cell histiocytosis (LCH). Langerhans cell histiocytosis was formerly referred to as histiocytosis X; however, when it was recognized that the cells involved in histiocytosis X were phenotypically Langerhans cells, the name LCH was adopted. The term LCH does not describe one clinical entity—it encompasses a broad spectrum of clinical presentations varying from a single localized lesion to severe disseminated disease. There are 3 main types of LCH: eosinophilic granuloma, Hand-Schüller-Christian disease, and Letterer-Siówe disease. The cause and pathogenesis of LCH remains poorly understood. Langerhans cell histiocytosis is not considered to be a neoplasm; however, studies at the molecular level have shown that LCH is a clonal histiocytic proliferative disease in both the localized and systemic forms.

Langerhans cell histiocytosis can occur at any age with a peak incidence from age 1 to 4 years in an estimated 2 to 5 children per million per year. Boys are affected twice as often as girls. There is no race predilection, and LCH is a sporadic disease,1 reported in bone, skin, lymph nodes, thymus, ears, bone marrow, blood, liver, spleen, lungs, endocrine organs (except adrenals and gonads), gastrointestinal tract, and central nervous system.1-4 Bone involvement is seen with pain and swelling, sometimes accompanied by pathologic fracture. The skull is most commonly affected followed by long bones. Vertebral involvement can lead to spinal cord compression or injury. Radiographic findings typically reveal well-defined osteolytic lesions with marked periosteal reaction. Bone scan and magnetic resonance imaging are less helpful diagnostic tools than plain films. Definitive diagnosis is made by bone biopsy. Cutaneous manifestations of LCH are common in infants and may mimic seborrheic dermatitis, but LCH can produce virtually any rash, including diffuse petechiae. It may produce ulceration of the palate or gingiva or cause otitis externa and mastoiditis. Hematologic manifestations are diverse, from mild anemia to long-term disease to severe pancytopenia. Hepatosplenomegaly is common as is lymphadenopathy. Pulmonary disease can occur as part of the multisystem disease or can be isolated. Radiography reveals interstitial infiltrates, and computed tomography may show cystic nodules. Diagnosis is made by lung biopsy or bronchial washings. Diabetes insipidus is the most common endocrinopathy seen in LCH, but growth hormone deficiency can also be seen.

The diagnosis of LCH should be considered if one or more of the mentioned symptoms are noted. Initial evaluation should include complete history and physical examination, complete blood cell count, urine and serum osmolality, values for electrolytes and liver enzymes, plain radiography for bone involvement, and computed tomography for suspected brain or lung involvement, with diagnosis confirmed by biopsy. The lesions of LCH appear granulomatous and yellow-brown on gross examination. Histologic examination of the tumor shows a mixture of histiocytelike cells with convoluted nuclear grooves and indentations, multinucleated giant cells, and a mixed inflammatory infiltrate of eosinophils, neutrophils, and lymphocytes. Findings in this case revealed that many of the histiocytelike cells and some of the multinucleated giant cells were positive for the S100 protein. The LCH cells are also reactive for CD1a (a cell surface molecule) and CD11 and CD14 (not expressed by normal Langerhans cells). Diagnosis can be confirmed by electron microscopy, which demonstrates diagnostic Birbeck granules in the cytoplasm, thought to originate as invaginations of the cell membrane. The function of these granules is unknown, but their presence is pathognomonic for LCH.1,2

Prognosis depends on age at diagnosis and degree of organ involvement; it is poor in children younger than 2 years, adults older than 65 years, and patients with multisystem disease. Localized disease tends to have good prognosis with possible spontaneous remission. Treatment is controversial due to the variable clinical presentation and limited understanding of the disease. Localized disease is typically treated with resection when possible. Intralosinal steroids have been used for painful lesions or lesions involving weight-bearing bones. If these safe, effective alternatives are not possible, low-dose radiation has been used. Treatment of multisystem disease is more controversial with no clear effective treatment available. Chemotherapy and/or radiation have been used with limited success. Cyclosporin, interferon alpha, and bone marrow transplantation have been proposed as alternate therapy. In this case the lesion was completely excised with negative surgical margins. No radiation or chemotherapy was administered. The patient was discharged following surgery and is doing well at 1-year follow-up.

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