Langerhans cell histiocytosis presented as bilateral otitis media and mastoiditis

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Langerhans cell histiocytosis (LCH) is a rare disease that may affect multiple organs. The etiology of LCH remains unclear to date. It is currently believed that clonal accumulation and proliferation of CD1a-positive Langerhans cells are causative. The term LCH or histiocytosis X refers to three separate illnesses (listed in order of increasing severity): eosinophilic granuloma, Hand-Schüller-Christian disease and Letterer-Siwe disease. A seven-month-old boy presented with history of recurrent bilateral otitis media and rash and seborrheic areas on his scalp. Two days prior, his mother noticed a small lump over the right mastoid. Lateral skull X-ray (Schüller) was evidence for lytic lesion on right temporal bone. The computerized tomography scan showed inflammatory changes with bone erosion. During surgical exploration, fragile slightly yellowish tissue with necrotic areas was found that was determined as LCH on histology. Chemotherapy was subsequently initiated. The initial presentation of LCH with bilateral ear and skull involvement is a very rare condition. The signs and symptoms of otologic histiocytosis can mimic those of acute and chronic infectious ear disease. Only a surgically obtained biopsy leads to definitive diagnosis and appropriate therapy.

Key words: eosinophilic granuloma, histiocytosis X, Langerhans cell histiocytosis, mastoiditis, mastoid granuloma, otitis media, otitis externa.
otitis media, and metastatic lesions. In the present study, a child with systemic LCH is presented, who was initially misdiagnosed and treated for non-specific otitis media. The diagnosis and the management of this relatively rare disease are discussed.

Case Report

A seven-month-old boy presented with a two-month history of recurrent bilateral otitis media and with rash and seborrheic areas on his scalp. The patient was given per os antibiotic therapy and corticosteroid ointment. Two days prior to his admission, his mother noticed a small lump over the right mastoid. On physical examination, right soft tender postauricular small swelling was noted. There was a whitish discharge from both ears and an apparent mass in the right ear canal. The patient did not have any paresis of facial nerve.

With the diagnosis otitis media, external otitis and mastoiditis, the patient underwent bilateral myringotomies under general anesthesia. There was a whitish discharge from both ear canals, while no purulent discharge was found in the middle ears. Needle aspiration from the postauricular lump was negative for the presence of purulent pus. The patient continued the therapy with intravenous antibiotics and eardrops.

Eight days later the general condition of patient showed no improvement and the lump over the right mastoid was enlarged. Lytic lesion of the temporal bone was evident on lateral skull X-ray (Schüller) (Fig. 1). The patient was re-operated immediately. After the postauricular incision was performed, a reddish and friable mass was found, which had expanded and already destroyed the mastoid bone. No purulent pus was found. Biopsy was taken from this area and the findings were characteristic for LCH. Biopsies from seborrheic areas on his scull were also positive for LCH. The computerized tomography (CT) scan of the head was typical for LCH lytic lesion over the right mastoid (2-3 cm) (Fig. 2). The rest of the workup for histiocytosis revealed hepatosplenomegaly (spleen 6-7 cm, liver 3-4 cm), anemia (Hb 6 g/dl, while upon admission 8.8 g/dl), slightly elevated SGOT (106) and SGPT (210), and albumin 33 g/L. The skeletal survey was normal. There was no diabetes insipidus. The biopsy revealed infiltration by histiocytic cell positive for CD1a and S-100 and negative for CD 45 and CD 15.

The patient was referred to the pediatric hematological oncology department for therapy and died from his disease four months later.

Discussion

Although LCH lacks the histologic appearance of a malignancy and fails to exhibit metastasis as in classic malignant disease, this benign process has the propensity to be locally aggressive, osteolytic, and recalcitrant, and to produce multiple synchronous lesions that involve multiple systems and organs.

The histologic hallmark of this disease is a proliferation of the Langerhans dendritic cell in a background of inflammatory cells with

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Fig. 1. Lateral skull X-ray (Schüller) demonstrating histiocytosis X in right temporal bone (with arrows).

Fig. 2. Computerized tomography scan showing a lytic lesion with destruction of the temporal bone on the right (asterisk).
sheets of eosinophils, as well as presence of Birbeck granule on electron microscopy. Immunohistochemical staining demonstrates positivity for CD1a and S100. The exact nature of LCH is under investigation as it has become apparent that LCH is not a true malignancy and does not behave as other malignant disorders of histiocytes. Distinct lesions are usually seen in soft tissue and bone. Bony disease was the most common finding and occurred in 79% of patients. LCH can affect almost every organ in the body. Organs involved were the lungs, spleen, liver, brain, heart, pancreas, stomach and muscle. The lesions are soft and yellow to brown with frequent areas of necrosis and hemorrhage. Microscopically, a histiocytic and eosinophilic infiltrate is seen. Giant cells may be seen, which are believed to represent fused histiocytes.

The majority of patients suffering from this disorder first present (63%) or later develop head and neck manifestations. The skull is frequently involved (42%); the temporal bone can be affected either as a solitary lesion or as part of a multisystem involvement in up to 61% of patients. When the temporal bone is involved, 30% of affected patients demonstrate bilateral disease. Manifestations of LCH may be confused with more common disorders such as chronic suppurative otitis media and acute mastoiditis, which are not responsive to medical therapy, thereby delaying the diagnosis, as observed in our case.

The cases presented demonstrate the classic postauricular swelling, which is seen in 10-30% of all patients with LCH. The ear often protrudes anteriorly, since the mass is subgaleal and lifts the entire auricle away from the temporal bone. There is frequently erosion of the bony posterior external auditory canal with sagging of the canal wall skin in such a way that the visualization of the tympanic membrane is difficult. Because the lesion infrequently involves the middle ear, the tympanic membrane is usually normal. This characteristic offers important differentiation between the lesion of LCH and acute mastoiditis, since acute mastoiditis is almost always associated with middle ear disease. Interestingly, although the facial nerve is exposed in the middle ear in 50% of all individuals, there have been only 14 reported cases of facial nerve paralysis in patients with LCH in the English literature.

Other areas of erosion include the tegmen tympani, the bony plate covering the sigmoid sinus, the squama of the temporal bone and rarely the vestibular labyrinth. The mastoid air cell system is usually destroyed when this disease involves the temporal bone. Palpation of the mass reveals soft pseudofluctuation with associated cutaneous erythema but no tenderness. Because of the propensity of this condition to erode the posterior canal wall, a secondary external otitis and stenosis may develop. Perforation of the tympanic membrane is uncommon and vestibular abnormalities are rare.

Exophthalmos results from lesions involving the orbital walls and the surrounding soft tissue reaction. The skin is a common site of involvement in more advanced LCH and the scalp is particularly apparent in this condition. A seborrheic rash with almost dandruff-like condition can result, although much more profound greasy, weeping dermatitis is also seen at times.

The flat bones of the skull, ribs, pelvis and scapula are most commonly involved. In the cranium, the frontal areas are most commonly involved and lesions may be single or multiple. The most commonly involved sites are the mandibles, especially posteriorly and along the alveolar ridges. The oral cavity can also be the site of mucosal ulcerations and stomatitis, which histologically reveal the typical histiocytic and eosinophilic infiltration. The dermatic lesions due to seborrhic dermatitis and the recurrent ear infections will raise the suspicion of LCH, while anemia, splenomegaly, hepatomegaly, and the transaminase increase indicate systemic manifestation of the disease.

The incidence of LCH is estimated to be three cases per 1,000,000 children per year - more than 50% of all cases are seen in patients under age 10 - even though recent studies have shown that approximately 30% of LCH cases occur in adults, with an incidence rate of 1.8/1,000,000. The average age of onset is 1 to 3 years, and the disease occurs more commonly in males. The natural history of this disorder is interesting because it has the potential for spontaneous resolution when the child enters adulthood.

Treatment is not specific and depends on the extent of disease at the time of diagnosis. The localized form of LCH as an isolated
bone lesion usually requires minimal treatment involving only biopsy or curettage. If the patient is asymptomatic, then a “wait and see” attitude is also possible, given the sometimes spontaneous resolution and healing of these lesions. Treatment for multifocal/multisystem LCH normally benefits from systemic therapy, which usually reduces morbidity and mortality. This is particularly true in children younger than two years of age who are at the highest risk of severe morbidity and mortality. Even so, benefits of treatment with cytotoxic agents should be weighed against long-term side effects of chemotherapy. Most common drugs used for treatment are corticosteroids, vinca alkaloids, mercaptopurine, methotrexate, and etoposide (VP16). Recent reports of successful treatment of recurrent or refractory disease with 2-chlorodeoxyadenosine (2CdA), a purine analogue, and cyclosporine, an immune modulator, offer a welcome addition to management of LCH19.

Although radiation therapy has been a traditionally viable and even popular option, it is not recommended in the head and neck secondary to significant potential side effects and does not offer control in a primary or adjuvant fashion that is acceptable. In addition, there are reports of secondary malignancy resulting from radiation treatment20.

The role of ear, nose and throat surgery in LCH is limited to diagnostic biopsy and to the treatment of localized disease (curettage, aural polypectomy). In the case of multifocal LCH, as in our patient, an invasive surgical approach is not suitable and chemotherapy should be administered. A multidisciplinary approach to LCH patients and in particular of the otolaryngologist is required to recognize LCH early, and to plan the best management of such a delicate site of disease.

REFERENCES