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CASE REPORTS

Case report: Infant with Langerhans cell histiocytosis in the mastoid

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Abstract

Langerhans cell histiocytosis is a rare disease with an unknown etiopathogenesis; it is generally caused by monoclonal proliferation of Langerhans cells. This study presents the case of a 7-month-old infant with a disease of the mastoid bone, which is considered a special site. The diagnosis was suspected following an unsuccessful mastoiditis treatment. The interest in reporting the case arises from the various presentations of the disease, aiming to raise awareness of this possible diagnosis.

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INTRODUCTION

First described approximately 150 years ago, Langerhans cell histiocytosis (LCH) is a rare disease. It results following the monoclonal proliferation of Langerhans cells and has an unknown etiopathogenesis. LCH is hypothesized to be a neoplastic disease or an inflammatory disorder. It is important to emphasize that the disease is hypothesized to have immunological, viral, and genetic predisposing factors; however, there is no consensus regarding this in the literature[1]. It is known to primarily affect children[2], and it can affect any organ or system, with most frequent cases involving the skeleton (80%), skin (33%), and pituitary gland (25%)[3]. The clinical manifestations of LCH appear along a spectrum of diseases that may involve a single site, multiple sites in a single system, or multiple organs[3].

CASE REPORT

A 7-month-old female infant (initials M.S.B.) was admitted to a children's emergency room in Uberaba, Brazil, after being referred by another hospital. She had a swelling behind the ear since 1 month prior to presentation. The onset of the swelling was sudden, with pain and hyperemia in the retroauricular and right mastoid regions. A treatment with systemic antibiotics (amoxicillin–clavulanate and azithromycin) and a topical corticosteroid was partially successful. Ten days earlier, she was admitted to another hospital for the treatment of possible mastoiditis with oxacillin and ceftriaxone. Because there was no positive response to the treatment, she was referred to our service. On admission, in addition to the tumor, the mother reported atypical episodes of nocturnal awakenings with crying, oral pallor, cold sweats, facies, and moaning. The child was born at term through a cesarean section, and her vaccination schedule was up-to-date[4]. She resided in an urban area with proper sanitation. Her family members were healthy and included a 35-year-old mother (G1PC1A0), 31-year-old father, and 9-year-old paternal half-sister. Her grandmother and uncle died of breast and throat cancer, respectively.

On admission, her condition was noted to be generally good. Pulmonary and cardiovascular auscultation indicated no abnormalities, and the abdomen presented no changes or visceromegaly. However, head and neck examination indicated a tumor in the right retroauricular region (mastoid) draining a small amount of yellowish secretion. The patient's weight was 6.5 kg, adequate as per her age.

The hypothesis of a neoplastic lesion was formed. Serum examination and imaging indicated hypochromic microcytic anemia and high lactate dehydrogenase levels (hemoglobin, 9.8; MCV, 68.2; MHC, 21.8; and LDH, 507). Further, skull tomography was performed, followed by nuclear magnetic resonance of the skull and ears (Fig. 1). The results indicated a predominantly solid expansive lesion with well-defined margins, centered on the right mastoid, extending toward the petrous portion of the temporal bone, and measuring 4.8 × 2.76 × 5.6 cm.



Figure 1. Magnetic resonance image showing a predominantly solid lesion with heterogeneous enhancement and well-defined margins, centered on the right mastoid, extending toward the petrous portion of the temporal bone, and measuring approximately 4.8 × 2.76 × 5.6 cm

In addition, a cortical tapering of the mastoid in close contact with the ipsilateral sigmoid sinus was observed. Nevertheless, no extension to other tissues was identified, and abdominal ultrasound revealed normal findings.

Therefore, hypotheses of LCH and sarcoma were raised, and an incisional biopsy of the lesion was indicated. Immunohistochemistry results were compatible with LCH, showing positive results for CD1a and S100. Radiographs of the skull, hip, spine, and long bones were normal. She was discharged for treatment, and further staging examinations were requested. Chemotherapy was initiated 21 days after performing immunohistochemistry in accordance with the LCH-III protocol—Group 3: multifocal bone disease and "special sites"[5].

During chemotherapy, the patient received an outpatient follow-up. Two months after the biopsy, the patient was admitted due to the presence of a mastoid fistula. She was hospitalized for 31 days for hyperbaric oxygen therapy, resulting in the reduction of the lesion and subsequent complete regression. Currently, the patient is under maintenance chemotherapy without further complications. Furthermore, she is receiving the prophylactic sulfamethoxazole–trimethoprim and treatment for iron-deficiency anemia.

DISCUSSION

In most parts of the world, LCH remains a disease with an unclear etiopathogenesis or incidence, creating uncertainties regarding its treatment intensity and duration[6].

The study patient had a swelling for approximately 1 month prior to diagnostic suspicion and investigation with specific tests. Such prolonged delay in diagnosis with several medical evaluations has been described in the literature[7]. The diagnostic criteria for LCH are divided into the following: presumptive (based on clinical manifestations and laboratory and imaging tests) and definitive (confirmed by biopsy and immunohistochemistry)[7]. Biopsy is considered confirmatory if immunohistochemistry is performed and positive results are obtained for CD1a (a transmembrane protein of Langerhans cells) and if CD207 (langerin) or Birbeck granules are demonstrated on electron microscopy. In the present case, in addition to CD1a, S100 was observed; this protein is characteristic of Langerhans cells, but it does not determine diagnosis by itself[3,8].

The age of the patient at diagnosis is similar to that of the subjects of a Brazilian study in which the pediatric group was the most affected by LCH, with a predominance of infants and a median age of 2.5 years[8].

The clinical presentation of the disease is variable owing to the accumulation of dendritic cells with characteristics similar to that of epidermal Langerhans cells in various organs. The sites most often involved are the skeleton, skin, and pituitary gland. Other possibly involved organs include the liver (15%), spleen (15%), hematopoietic system (15%), and lungs (15%), lymph nodes (5%–10%), and central nervous system excluding the pituitary gland (2%–4%). The clinical course of LCH may range from a self-limiting condition to a rapidly progressive and potentially lethal disease[3]. The most common clinical manifestations at diagnosis are osteolytic lesions (69.7%), whereas the most frequently affected site is the skull (78.3%)[8]. The present case exhibited an osteolytic lesion, common in this condition; however, the mastoid is considered a special site. Special sites include orthopedic and vertebral lesions extending to soft spinal cord tissue and lesions located in functionally critical anatomical sites, e.g., eyes; ears; mouth; and temporal, mastoid, sphenoid, and zygomatic bones. These lesions may pose an immediate risk to patients because of the potential for disease progression[5].

In this sense, the current classification distinguishes between single-system disease (SS-LCH) and multisystem disease (MS-LCH). This distinction is based on the extent of the disease at diagnosis. In SS-LCH, only one organ or system is involved such as bones (a single bone or more than one bone), skin, or lymph nodes (not secondary to another lesion). In MS-LCH, two or more organs or systems are involved with or without the involvement of critical organs[5].

Adequate classification and staging consider clinical assessment and complementary examinations[5]. Complete blood count; hepatic transaminases; urine osmolality; chest, long bone, and skull X-rays; renal function; electrolytes; ferritin; coagulogram; and abdominal ultrasound are recommended[5,9,10]. These examinations were part of the evaluation of the present patient in whom only hemoglobin alteration was observed. Due to the anatomically complex structure, computed tomography was requested for diagnosis[7]. Magnetic resonance imaging of the skull was performed, as recommended, to assess the possibility of the lesion extending into the central nervous system[5]. Myelogram was not performed because it is indicated only in the presence of bicytopenia or pancytopenia[5], which were not observed in the present case. Isolated disease at a special site may warrant systemic therapy as in multisystemic diseases; this conduct was adopted for the present patient. Regardless of the involvement of critical organs, patients who respond to initial standard therapy have an excellent chance of long-term survival. The combination of prednisone and vinblastine has been shown to be an effective treatment with minimal toxicity; thus, it is considered the standard initial therapy for all patients for whom systemic therapy is indicated[5,10].

In patients with single-site diseases, the prognosis for cure reaches 100%. Response to initial treatment has been shown to be a predictor of mortality. The group of patients with complete or continuous response at the end of the first 7 weeks of treatment presented an overall survival rate of 94.4%, in contrast to the 30% observed in the non-responders group[8]. In the present patient, the response to the initial treatment was adequate; therefore, a good prognosis is expected at follow-up.

CONCLUSION

This case report aimed to highlight the importance of considering this diagnosis, particularly in the presence of bone or cutaneous lesions[11].

However, the etiopathogenesis paradigm related to LCH still remains unclear. In the presence of an inflammatory disease, proliferating cells in LCH tend to aggressively divide in response to a stimulus. In this circumstance, LCH cells remain fundamentally normal, facilitating prediction of their hyperproliferative state; the progression could then be altered with the removal of the inflammatory stimulus. By contrast, if LCH exists in a neoplastic condition, then the unrestricted proliferation of pathological Langerhans cells can result from alterations in the genes regulating cell division. In this circumstance, LCH treatment would be similar to that of cancer, and drugs targeted against the products of these altered genes would produce a substantial response, which is not observed in all cases[1].

Research is ongoing for the determination of novel treatments of LCH. In some cases of LCH, the BRAF gene has been identified on chromosome 7q34, which is associated with other neoplasms such as melanoma. For this sake, there exists a novel method for detecting BRAF V600 mutations. Thus, therapy can be modified to identify patients requiring BRAF V600 inhibitors to preserve epithelial growth factor receptor-mediated response, facilitating the selection of treatment choice[12].

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