

Case report

Langerhans cell histiocytosis in children: a case report and brief review of the literature



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Abstract

Langerhans cell histiocytosis (LCH), formerly known as histiocytosis X, is a non-malignant disease involving clonal proliferation of Langerhans cells. It is an orphan disease affecting mainly the child and the young adult. Its etiology is still unknown, and its clinical spectrum is quite wide. Systemic treatment incorporating steroids and cytostatic drugs for at least one year has improved prognosis of multisystem LCH and represents the current standard of care. We report the case of a multifocal bone LCH in a 2-year-old girl affecting the frontal and parietal bones, associated with emphysematous bulla. The diagnosis was confirmed with histological examination. The evolution was favorable after treatment. Based on this observation, we will make a brief review of the literature to present the clinical, histological, radiological, therapeutic and evolutionary aspects of this orphan disease.

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Introduction

Langerhans cell histiocytosis (LCH) is a rare group of disorders whose etiologies are incompletely characterized and understood. Formerly known as histiocytosis X, the disease has a wide spectrum of clinical presentations, ranging from isolated disease with spontaneous resolution to life-threatening multisystem disease [1]. We report the case of a 2-year-old girl who presented a LCH initially affecting the frontal and parietal bones, and secondarily caused emphysematous bulla.

Patient and observation

A 2-year-old girl was admitted in the department of hematology and pediatric oncology with a symptomatology of rounded frontal swelling, measuring 3 cm in diameter that was progressively increasing for 3 months (Figure 1 A, Figure 1 B). She had a good overall physical condition, particularly normal height and weight regarding her age, no bone pain, no changes in activity level, and no fever. Radiological explorations consisted of a medical ultrasound of the formation, revealing a nodule of the frontal soft tissues, with an osteolytic lesion related to the frontal bone. The cerebral computed tomography (CT) scan showed the presence of a well-defined oval tissue formation in the frontal bone, enhanced after injection of contrast agent, measuring 16.6 x 12.6 mm lysing the opposite bone (Figure 2A). It is associated with a second localization in the left parietal bone, with the same characteristics as the frontal one, measuring 16.1 x 11.3 mm (Figure 2 B). The thoracic CT scan revealed the presence of two subpleural emphysematous bulla located in the right Fowler. A biopsy of the frontal formation was performed, showing bone and fibrous tissues containing a polymorphic cellular infiltrate made of mononucleate histiocytic elements.

Some nuclei were kidney-shaped, others were convoluted and grooved. This infiltrate was also made of neutrophils and especially of eosinophilic polynuclear cells and lymphocytes. The immunohistochemical study revealed that histiocytic cells diffusely express the CD1a, and focally express the CD68 and PS100. In the same operative time as the biopsy, a myelogram was performed thinking of a possible metastatic neuroblastoma that showed an inflammatory marrow. Work-up of extension consisted of a bone scintigraphy, which showed the absence of a clear scintigraphic sign in favor of distant bone localization. We followed the LCH treatment guidelines (LCH-III protocol) established by the Histiocyte Society (HS). It consisted of an initial 6-week course of therapy with vinblastine (6 mg/m²) and prednisone (40 mg/m²). An assessment at the end of this initial course was performed with a CT scan than showed the persistence of both lytic bone lesions with a net regression of the tissue component. A second course of treatment with vinblastine and prednisone was then undertaken. The assessment made with another CT scan concluded in an almost total regression of the frontal and parietal bone lesions (Figure 3), while the emphysematous bulla were persistent. Maintenance therapy consisted of pulses of vinblastine and prednisone every 3 weeks and daily continuous 6-mercaptopurine for a total treatment duration of 12 months.

Discussion

Histiocytoses are rare disorders characterized by the accumulation of cells derived from dendritic cells or macrophages. The first classification of histiocytosis, published in 1987 by the working group of the HS, consisted of 3 categories: langerhans cell (LC) or non-LC-related, and malignant histiocytoses (MH). A new classification has been elaborated based on histology, phenotype, molecular alterations, and clinical and imaging characteristics, dividing

the histiocytoses into 5 groups resumed in Table 1 [2]. Among histiocytic disorders, LCH is the most common one, affecting an estimated 4 to 5 per million children 0 to 15 years of age each year. The median age of diagnosis is 3.5 years, and the highest incidence rate is observed before 1 year of age, with a decreased incidence observed thereafter [1]. Although major advances have increased our understanding of LCH, its pathophysiology remains unknown and may be the result of either an aberrant autoimmune response or a neoplastic process [1,3]. The most commonly affected organs are: bone (80%), skin (33%), pituitary (25%), liver (15%), spleen (15%), hematopoietic system (15%), lungs (15%), lymph nodes (5-10%), and the central nervous system excluding the pituitary (2-4%) [3]. Systemic signs, such as fever, lethargy, and weight loss, may be noted in patients with either single-system or multisystem disease. Bone involvement is mostly unifocal and most commonly presents as a soft tissue mass presenting with swelling or pain [1], as it was the case in our patient, whose presenting symptom was a soft tissue mass with no pain however. Any bone may be involved, excluding the hands and feet. Radiographically, LCH typically mimics multiple myeloma, presenting as either single or multiple osteolytic lesions; however, in contrast to multiple myeloma, LCH lesions may be accompanied by a periosteal reaction [1]. Skin is the second most frequently involved organ system after bone, lesions may be either circumscribed or spread 77 and there may be either single or multiple lesions [1]. Risk organs include the hematologic system, the spleen and the liver [3]. The lung had been considered for many decades as a risk organ, but in the absence of involvement of other risk organs, lung disease is only in exceptional cases the ultimate cause of death. This usually occurs through "mechanical complications" such as an uncontrolled pneumothorax, or as a late event due to chronic emphysematous changes [3]. The emphysematous bulla were present in our patient from the first CT scan and stayed the same with no clinical expression throughout the evolution of the disease. Many treatments for multisystem LCH, from minimal therapy to intensive chemotherapy, have been tried.

However, a randomized trial of treatment made of Vinblastine and etoposide, associated with one dose of corticosteroids, were equally effective treatments for multisystem LCH, but patients who did not respond within 6 weeks were at increased risk for treatment failure and would require different therapy [4]. These evidences have been used to establish the HS evaluation and treatment guidelines that currently represent the standard of treatment. Our patient had a treatment consisting of an initial 6-week course of therapy with vinblastine and prednisone, and the response after the first 6 weeks was a net regression of the tissue component, confirming the results of the study. Regarding the prognosis, for patients older than 2 years at the time of diagnosis, a 10-year survival rate of 97% has been reported; for those younger than 2 years, the rate is 77% [5]. Patients with multisystem disease have an overall survival rate of approximately 71% at 10 years. When at-risk organ systems (spleen, liver, bone marrow, lungs) are involved, 10-year survival decreases to approximately 50% [5].

Conclusion

LCH is a rare entity with various and non-specific clinical presentations. It usually affects bones, but other organs can be involved. The diagnosis of LCH is based on histological and immunophenotypic examination of lesional tissue. Uni or multifocal bone involvement is often of good prognosis. The treatment is controversial, involving chemotherapy and corticotherapy.

Competing interests

The authors declare no competing interests.

Authors' contributions

Zakaria El Ouali: conceptualization, data curation, investigation, writing, original draft; Nisrine Khoubila: data curation, supervision, validation, writing, review & editing; Siham Cherkaoui, Mohamed Rachid, Mouna Lamchahab, Meryem Qachouh, Abdellah Madani, Asmaa Quessar; supervision. All the authors have read and agreed to the final manuscript.

Table and figures

Table 1: histiocytoses classification showing the 5 groups of diseases

Figure 1: pictures of the frontal swelling in front (A) and side views (B)

Figure 2: initial CT scan images showing the frontal (A) and parietal (B) formations, with the cranial reconstruction (C)

Figure 3: photography of the child's face after treatment

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Group	Diseases
Langerhans (L)	Langerhans cell histiocytosis Erdheime-Chester disease/extracutaneous juvenile xanthogranuloma Indeterminate cell histiocytosis
Cutaneous and mucocutaneous (C)	Juvenile xanthogranuloma Adult xanthogranuloma Solitary reticulohistiocytoma Benign cephalic histiocytosis Generalized eruptive histiocytosis Progressive nodular histiocytosis Xanthoma disseminatum Cutaneous Rosaie-Dorfman disease Necrobiotic xanthogranuloma Multicentric reticulohistiocytosis Cutaneous histiocytoses not otherwise specified
Malignant (M)	Histiocytic sarcoma Indeterminate cell sarcoma Langerhans cell sarcoma Follicular dendritic cell sarcoma
Rosaie-Dorfman disease (R)	Rosaie-Dorfman disease Noncutaneous, non-LCH not otherwise specified
Hemophagocytic lymphohistiocytosis and macrophage activation syndrome (H)	Hemophagocytic lymphohistiocytosis/macrophage activation syndrome



Figure 1: pictures of the frontal swelling in front (A) and side views(B)

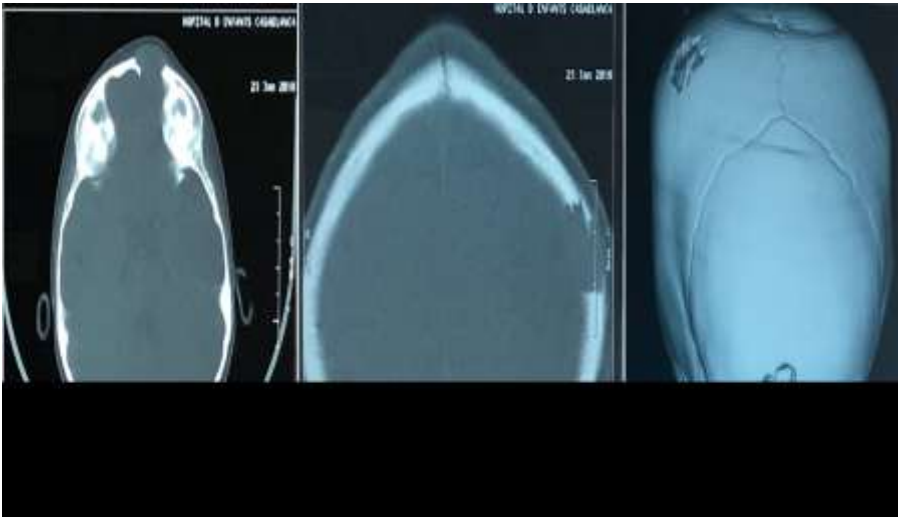


Figure 2: initial CT scan images showing the frontal (A) and parietal (B) formations, with the cranial reconstruction (C)



Figure 3: photography of the child's face after treatment