Case Report
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Langerhans Cell Histiocytosis in a Three-Year-Old Girl in Bosnia and Herzegovina

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Abstract

Objective. To present a rare disease, and to point out that clinical manifestations treated for a long period of time without an adequate response to therapy may be a manifestation of a rare disease. **Case report.** We present the case of a 3-year-old girl who had been drinking a large amount of water for the previous ten days with frequent urination, and who experienced the worsening of symptoms of scalp dermatitis that had been treated for a year without success. Physical examination revealed a maculopapular rash on the scalp, neck and both ear shells, and exophthalmos of the right eye with periorbital edema. Magnetic resonance imaging of the orbits showed extensive lesions of the skull bones. Further diagnostic evaluation revealed similar lesions in other bone structures. Biopsy of the affected region, microscopic and immunohistochemical analysis led to diagnosis of Langerhans cell histiocytosis. **Conclusion**. Langerhans cell histiocytosis mostly occurs in the first three years of life. The incidence is 4-5 patients per million children under 15 years of life. The clinical presentation is highly variable, and can range from isolated, self-healing skin and bone lesions to life-threatening multisystem diseases. Due to the diverse clinical picture, that is often unrecognized, these patients are often referred to other specialists, resulting in the treatment of individual symptoms rather than the underlying disease.

Key Words: Langerhans-Cell ▪ Child ▪ Dermatitis ▪ Exophthalmos ▪ Rare Disease.

Introduction

Histiocytoses are a rare and heterogeneous group of diseases characterized by pathological accumulation and multiplication of cells of the monocyte-macrophage system in tissues. The World Health Organization divides histiocyte diseases into dendritic cell diseases, macrophages, and histiocyte malignancies. The Langerhans cell (LC) is a bone marrow-derived mononuclear cell, belonging to the dendritic cell family. Factors that play a role in the etiology and pathophysiology are: infections (especially viral), immune system cell dysfunction, neoplastic mechanisms, genetic factors, race/ethnicity, and a combination of these causes (1, 2). We present a case of a rare disease from initial symptoms to diagnosis.

Case Presentation

A three-year-old girl had been brought to the pediatrician in primary health care. For the previous ten days she had been drinking a large amount of water which was accompanied by frequent urination. Her scalp dermatitis had been treated unsuccessfully for the previous year, and the symptoms were deteriorating. At the physical examination there were changes on the scalp, neck and both ear shells, in the form of erythema, papules and crusts, with odor (Figure 1). There was evident proptosis of the right eye, with periorbital edema and divergent strabismus. The general condition of the child was good. Laboratory results were normal, except for mild anemia (Hgb 10.3g/dl, Hct 32%, MCV 60 fl). Due to suspicion of a retrobulbar tumor mass an ophthalmologist was consulted and rec-

ommended urgent magnetic resonance imaging (MRI) of the orbit.

Examination of the child's medical records indicated that child was born healthy. At the age of two, changes began on her scalp and she was referred to a dermatologist. The dermatologist treated her under the diagnoses of Seborrheic dermatitis, Eczematous dermatitis and Tinea capitis, but the lesions persisted.

Two months after the scalp lesions appeared, she presented for an examination with a petechial rash. Laboratory results showed thrombocytopenia (PLT 70×10^9/L). She was examined by a hemato-oncologist, treated on an outpatient basis with vitamin C, and her platelet count returned to normal within 7 days. She had not been examined by a pediatrician in the previous six months, but she visited a dermatologist in a private practice. MRI of the orbit showed extensive lesions of the skull bones, corresponding to the lesions usually seen with Langerhans cell histiocytosis (Figure 2).

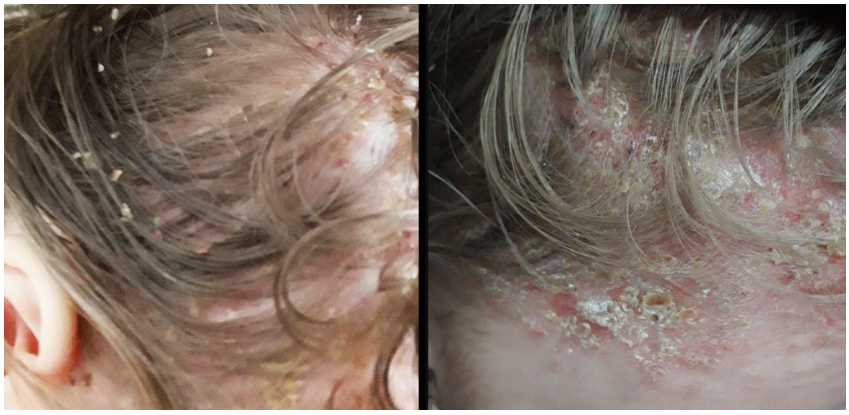

Figure 1. Scalp skin involvement.

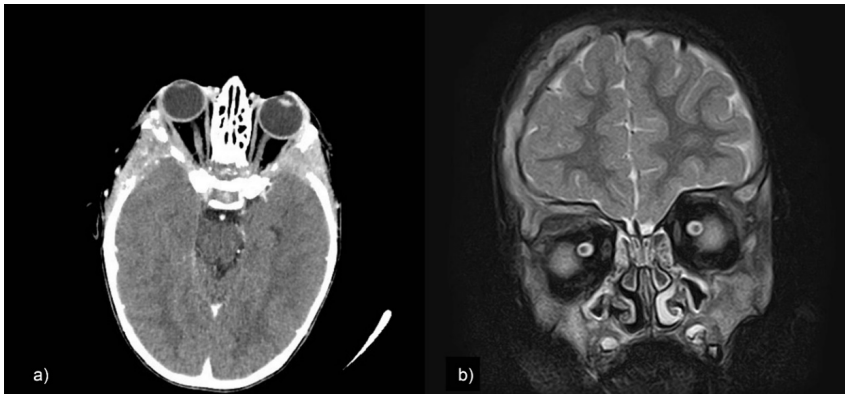

Figure 2. a) CE-CT axial scan revealed the presence of osteolytic lesions in the skull, causing right-side proptosisb; b) Coronal T2w MRI scan indicates the involvement of the right orbital roof, along with the rest of the frontal bone with isointense osteolytic lesions.

The diagnostic evaluation continued in the hemato-oncology department. Osteolytic lesions were also found on the bones of the pelvis, femur and humerus (Figure 3).

After femoral bone biopsy, the pathohistological, microscopic and immunohistochemical findings confirmed the diagnosis of Langerhans cell histiocytosis. Chemotherapy started according to the protocol.

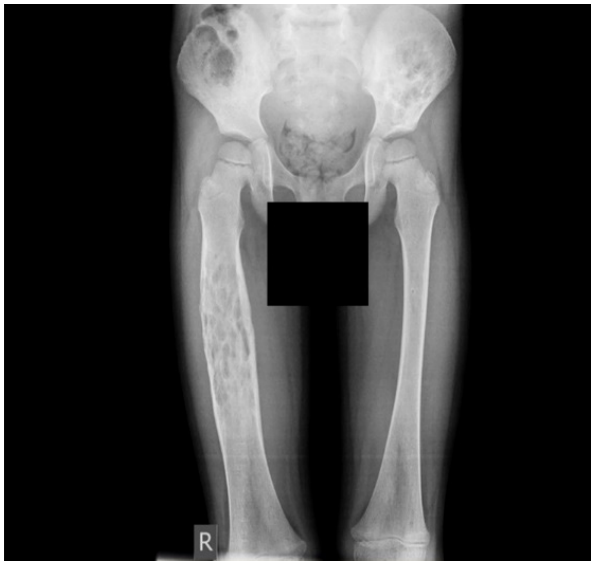

Figure 3. X-ray representation of the osteolytic lesions in the left iliac bone and metaphysis of the right femur.

Discussion

Langerhans cell histiocytosis (LCH) can occur at any age, but the incidence is highest in the first three years of life. The current classification differentiates between the single system disease (SS-LCH) and the multisystem disease (MS-LCH). MS-LCH is defined as the involvement of two or more organs or organ systems. The following organ systems are classified as risk organs, and their involvement indicates a worse prognosis: the spleen, liver, hematopoietic system, and lungs. SS-LCH includes the involvement of one of the following systems (unifocal or multifocal involvement): bones, skin, lymph node, lungs, central nervous system or other (thyroid, thymus) (3-5). The most commonly affected organ in LCH is bone, where changes are present in 80% of cases (61% in the skull). It manifests as a tumor mass, sometimes accompanied by pain and swelling (6, 7). The time from the onset of bone lesion symptoms to the diagnosis of LCH varies, ranging from 1.5 to 4 months, according to a study in Japan. However, there are cases where the changes lasted more than 6 months (8, 9).

Skin lesions occur in 40% of cases, and they are the first manifestation of the disease in 80% of patients. They have different clinical manifestations, from varicella-like changes, seborrheic eczema, or macular rash. The time from the appearance of clinical symptoms of skin lesions to diagnostic biopsy is at least 3 months, in some cases more than 2 years. The final LCH diagnosis is based on histological and immunophenotypic examination of the tissue. Treatment depends on the severity of the disease and the number of organs affected (10, 11, 5).

Conclusion

The aim of this paper is to present LCH as a rare disease, and to indicate the time needed from the initial symptoms to the establishment of the final diagnosis through review of other studies. The clinical presentation is highly variable and can range from isolated, self-healing skin and bone lesions, to a life-threatening multisystem disease. Due to the diversity of the clinical features in this disease, patients are often referred to other specialists (dermatologist, orthopedist, ear, nose and throat specialist or pediatric dentist), which results in the treatment of individual symptoms rather than the underlying disease. Cooperation among specialties is important for early establishment of the correct diagnosis. The prognosis is better in older children in whom the disease is limited to the skin and bones, while children with an affected liver, spleen and bone marrow have a poorer prognosis. Making the right diagnosis in a short period of time is a significant challenge for physicians, and considerably influences the prognosis of the disease and the quality of life of the patient.

What Is Already Known on This Topic:

LCH is a rare disease, with unexplained etiology and unpredictable clinical course. It is most often manifested by changes in the bones and skin, in the form of a single systemic disease. In young children, skin changes often progress to the multisystem form. Patients with unifocal disease generally have a good prognosis. Patients with multifocal LCH have a variable prognosis, depending on how quickly the disease continues to progress and the patient's response to treatment.

What This Study Adds:

Only a few cases of LCH in children have been described in BH, but more detailed studies on this disease have not been published. We present the first case of a three-year-old girl where the disease began with changes on the skin, but the diagnosis was set after a multifocal form had developed, with exophthalmos, diabetes insipidus, infiltration of the skull bones, and lesions in other bone structures. From this case we see that bone changes require radiological evaluation. The clinical presentation of LCH with skin lesions should lead to a straightforward diagnosis. A biopsy of a typical skin lesion would be the way to confirm the clinical suspicion and avoid delay in management. For physicians in primary health care it is very important to have information about rare cases in order to be able to establish a diagnosis more quickly and ensure a better prognosis for the patient.

Conflicts of Interest: We declare that we have no conflict of interest.

Authors' Contributions: Conception and design: ALB and MLK; Acquisition, analysis and interpretation of data: DB and MLK; Drafting the article: MLK; Revising it critically for important intellectual content: ALB, AK, DB and MLK; Approved final version of the manuscript: ALB, AK, DB and MLK.

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