

A case of Langerhans cell histiocytosis mimicking child abuse

Şakire Başer¹, Ayşe Kaman², Işıl Zaimoğlu¹, Zeynep Gökçe Gayretli-Aydın², Türkan Aydın-Teke², Umut Kaygusuz³, Asuman Gürkan⁴, Esin Boduroğlu⁵, Yasemin Taşcı⁶, Gönül Tanır²

²Division of Pediatric Infectious Diseases, Departments of ¹Pediatrics, ³Ear, Nose and Throat Diseases, ⁴Dermatology, ⁵Pathology, ⁶Radiology, Dr Sami Ulus Maternity and Children's Training and Research Hospital, Ankara, Turkey.

E-mail: sakirebaser@gmail.com

Received: 2nd May 2016, Revised: 11th July 2016, Accepted: 17th August 2016

SUMMARY: Başer Ş, Kaman A, Zaimoğlu I, Gayretli-Aydın ZG, Aydın-Teke T, Kaygusuz U, Gürkan A, Boduroğlu E, Taşcı Y, Tanır G. A case of Langerhans cell histiocytosis mimicking child abuse. Turk J Pediatr 2016; 58: 675-678.

Langerhans cell histiocytosis is a rare non-malignant disease with clinical heterogeneity. The disease may present with various clinical findings and may imitate many other conditions. In this report we describe a 34-month-old girl who presented with chronic otitis and otorrhea, skull fracture, rash, vulvar edema, erythema and erosion in labia majors which initially suggested child abuse but the patient was diagnosed with Langerhans cell histiocytosis.

Key words: Langerhans cell histiocytosis, child abuse.

Langerhans cell histiocytosis (LCH) is a myeloid cell-based neoplasm characterized by the reactive clonal increase of Langerhans cells and consisting of the components of autoimmune inflammatory disease¹. Moreover, this disease is genetically related to BRAF-V600E gene mutation influencing the MAPK signaling pathway. Incidence rate is 8.9/million per year among children under the age of fifteen². Potential symptoms encountered in LCH diagnosis in adults and children may also be observed in numerous diseases. Differential diagnosis is based on the presentation of typical histopathological findings or CD1a positive cells³.

Tissue damage that was caused by someone else due to any reason is defined as physical abuse⁴. The awareness of conditions that simulate child abuse enables the ability to diagnose correctly. We presented a case of LCH mimicking child abuse in this report.

Case Report

A 34-month-old girl was admitted to hospital with fever, rash, ear discharge and vaginal secretion. Medical history revealed crusted rash on the scalp and intertriginous areas and ear drainage from six months of age. Systemic and topical antibiotic treatments were prescribed

several times with the diagnosis of acute otitis media and seborrheic dermatitis in other hospitals. At the age of one, laser polypectomy was performed through both of the external auditory canals. In addition to these complaints, vaginal secretion was observed for the last five months, and fever and rash were noted for the last five days. The patient, whose parents were third-degree relatives, had a one-year-old healthy sister.

On physical examination, her general condition was moderate and she was apparently agitated. Remaining data about her physical examination were as follows; body temperature 38.1 °C, respiratory rate 24/min, pulse 101/min, arterial blood pressure 100/60 mm Hg. Apparent and locally yellowish clotted plaque was seen on the scalp, and broad erythematous skin was observed beneath it. Petechial-purpuric rashes were seen on the whole trunk and extremities. Bilateral external auditory canal was obliterated with polypoid lesion and purulent discharge. Purulent discharge, vulvar edema, erythema in labia majors, and local erosion were detected on intertriginous areas on the examination of genitourinary system. Other system examinations were normal.

Routine laboratory investigations were as follows; hemoglobin (Hb) 8.9 gr/dl, white

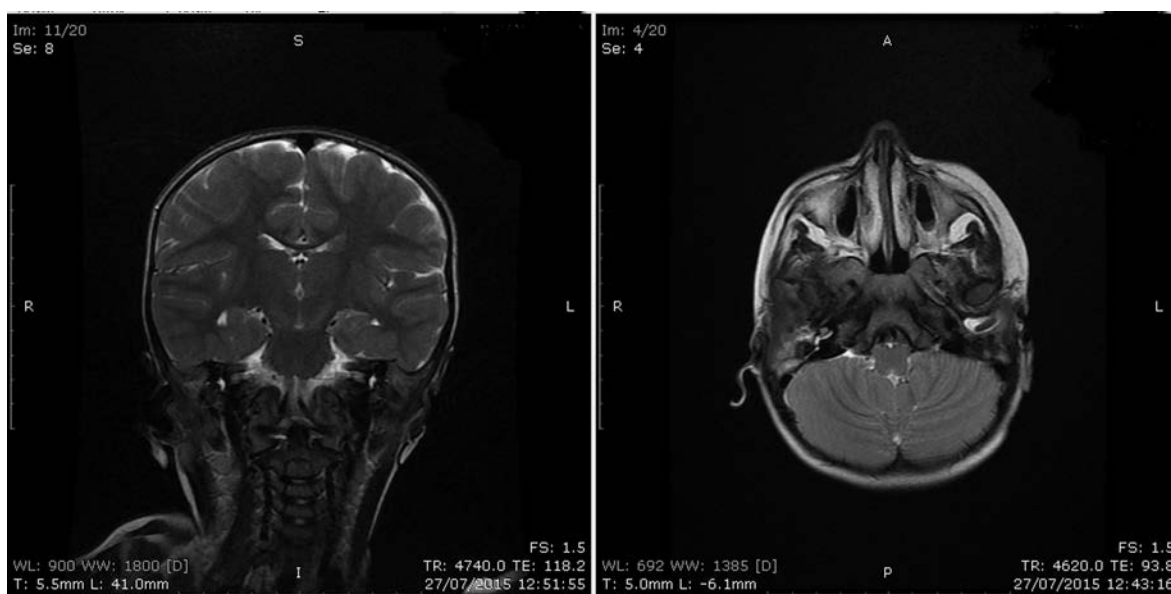


Fig. 1. Coronal T2 weighted image also demonstrates destruction of the tegmen tympani with minimal soft tissue extension to the middle cranial fossa (left). Axial and coronal T2 weighted MR images reveal fluid and soft tissue filling the mastoid air cells bilaterally, greater on the right. The soft tissue extends to the tympanic cavity bilaterally and to the subcutaneous tissue on the left. The integrity of temporal bones and the borders of the mass lesion could not be determined (right).

blood cell count (WBC) 14,900/mm³ (60% neutrophil, 30% lymphocyte, 8% monocyte, %2 eosinophil), platelet count 661,000/mm³, C-reactive protein (CRP) 174 mg/dl (0-4 mg/dl), erythrocyte sedimentation rate (ESR) 71 mm/h, aspartate aminotransferase (AST) 15 U/L (<48 U/L), alanine aminotransferase (ALT) 73 U/L (0-56 U/L), and gamma-glutamyl transpeptidase (GGT) 261 U/L (<23 U/L). Other biochemical evaluations and coagulation tests were normal. Urinalysis revealed plenty of leukocyte and urine leukocyte esterase strip were 3(+). Cerebrospinal fluid (CSF) examination was normal. Serologic tests for human immunodeficiency virus (HIV), Epstein-Barr virus (EBV), cytomegalovirus (CMV) and syphilis were all negative, and serum quantitative immunoglobulin levels were normal according to her age.

Ceftriaxone was empirically commenced for the suspicions of urinary tract infection and chronic vulvitis. Cultures of blood and CSF were resulted as negative. Temporal computed tomography (CT) scan revealed numerous fractures in right temporal and bilateral mastoid bone. Cranial CT was performed due to suspicion of child abuse and no cerebral hemorrhage or contusion were revealed. Abdominal ultrasonography (USG) showed

heterogeneity of liver and these findings were interpreted as a lesion that might develop depending on contusion, infiltrative disease or infectious process. Whole body direct bone survey graphics were normal.

A diagnosis of physical child abuse was suspected because of the bilateral fracture in temporal CT, the abdomen USG image that compatible with the liver contusion and purulent genital discharge, vulvar edema, erythema in labia majors and the local erosion that was detected on the examination of genitourinary system. Further social history of family was questioned by social workers.

Contrast-enhanced temporal magnetic resonance imaging (MRI) revealed soft tissue intensities in both of the squamous and mastoid parts of temporal bone, surrounding the external auditory canal and extending to the tympanic cavity. Diffuse contrasting was observed in the meningeal structures at the levels of both temporal lobes (Fig. 1). Histiocytosis X was firstly considered in the differential diagnosis. Histopathological analysis of the biopsy specimen taken from the lesions on the scalp and axillary area demonstrated an infiltration developing in a way of filling the upper dermis under the epidermis, having the diffuse developmental

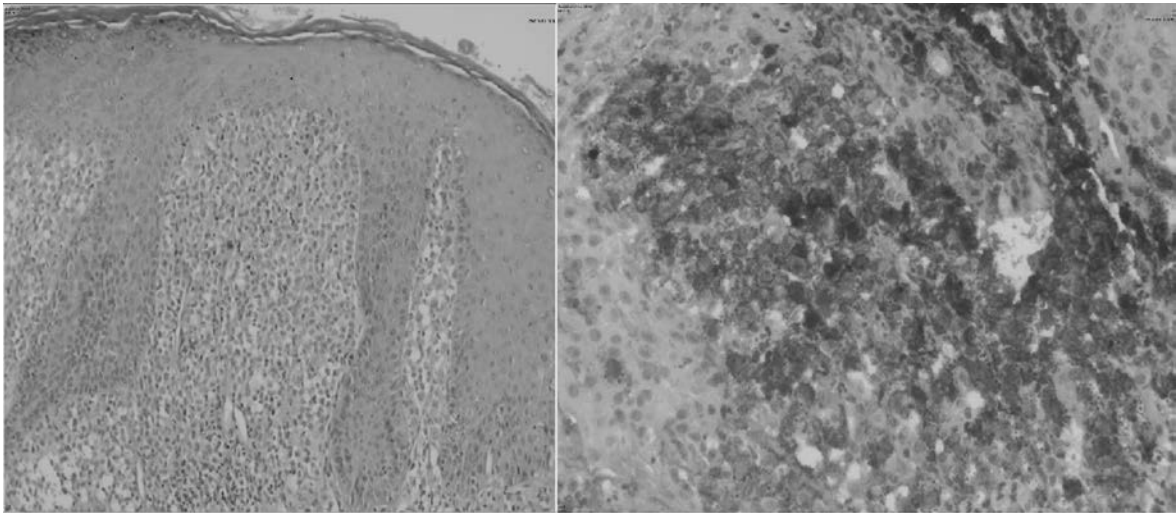


Fig. 2. Diffuse growth of the tumor filling the upper dermis HEx100 (left). CD1a and S-100, that they were locally positive with CD34, and adjacent cells were stained with CD68 strong positive staining cytoplasm of neoplastic cells, CD1a,x200 (right).

pattern that extending to the lower dermis, and consisting of atypical cells with big vesicular anisocoric nucleus, small nucleolus, and large eosinophilic cytoplasm (Fig. 2). Giant cell formation was not recorded. The patient was diagnosed as LCH according to these findings. In the bone scintigraphy taken for staging the disease, focally increased activity involvement was recorded on the area complying with the adjacency of left temporal bone-sphenoid bone, and the distribution of activities was measured to be at the desired level and symmetry in the lines of epiphysis and for other bones in the body. Bone marrow aspiration revealed no involvement. The treatment protocol with vinblastine and prednisone was administered to the patient. She has been on follow-up for eight months uneventfully, her MRI findings returned to normal.

Discussion

Langerhans cell histiocytosis has been defined as a heterogeneous clinical condition occurring with the clonal proliferation of bone marrow-based dendritic cells of the epidermis⁵. The disease may involve any organ or tissue. Although the involvements of skeletal system and skin are the most commonly seen, parenchymal organs, lymph nodes, and central nervous system may also be involved⁶. Nowadays, LCH classification is made by taking into account the number of affected areas (single or multi-systemic and

local or multifocal) and involvement of the risk organs. Bone marrow, liver, and spleen involvement are considered as high stage disease². Ear involvement and rash related to the skin involvements that are commonly seen in this disease were present in our patient whose complaints started when she was six months old. The patient was evaluated as having systemic form as expected for that age group. The involvement of eyes and endocrine system which may be observed in the systemic form was not present in our patient. Similar to this case, the cases with chronic otitis and otorrhea depending on the temporal bone were reported, previously^{7,8}.

Although the physical examination findings are numerous in child abuse, ecchymosis, bite marks, fractures, injuries in internal organs, and head trauma are the most commonly reported findings⁹. Skull fractures may be present due to accidents as well as the child abuse. Especially more than one complicated skull fracture and compression fractures are the indications increasing the probability of child abuse¹⁰. In the present case, child abuse was included in the differential diagnosis due to the bilateral fracture in temporal CT and the ultrasonographic images that were compatible with the liver contusion. A study that included 25 pediatric LCH patients reported that, LCH imaging findings are not specific, they might be similar to the infection, inflammation or neoplastic diseases, and they might even imitate

the traumas not related to accidents ¹¹.

Skin findings of LCH may also vary to some extent. The differential diagnosis should include especially seborrheic dermatitis, psoriasis, atopic dermatitis and scabies. Acrodermatitis enteropathica, 'blueberry muffin' type rash, and molluscum contagiosum were reported as the findings that might be rarely confused with LCH ¹²⁻¹⁴. Recurrent skin findings of our patient had been evaluated as seborrheic dermatitis, and the treatment was administered according to this diagnosis. Petechial rash is a rare symptom seen in LCH ¹³. In this case, the probability of child abuse was considered due to the presence of distinct vulvar, labial edema and laceration, her unfavorable general hygienic condition, and the detection of the images compatible with fracture and contusion. Since the detection of vulvar lesions in the age group of children is a highly stimulant factor in terms of child abuse, professional social service evaluation was made. It was reported that, a 4-year-old patient with bilateral vulvar vesicular lesions and surrounding erythema, who developed diabetes insipidus during the follow-up, was diagnosed as vulvar LCH with central nervous system involvement¹⁵.

Langerhans cell histiocytosis is diagnosed through the clinical, radiological findings and histological and immunophenotyping analysis of the biopsy taken from the lesion or involved organ if any in systemic involvement¹⁶. The present case had temporal MRI findings compatible with histiocytosis X, bilateral external auditory canal obliteration, hepatic, vulvar and skin involvement. For this reason, systemic form of LCH was considered and diagnosis was confirmed by means of typical histopathological findings on biopsy.

When the cases of child abuse are early noticed, the abused children can be saved from chronic abuse or death. For this reason, detailed medical history and analyses of physical examination findings are quite significant for the early diagnosis of child abuse. LCH may present with various clinical findings and may imitate many other conditions. LCH should be considered in cases of chronic otitis and otorrhea that are resistant to the medical treatment, and ear involvement may result with formation of polyps and also the disease should be kept in mind in young children who had complaints

similar to the findings of child abuse.

REFERENCES

1. Zinn DJ, Chakraborty R, Allen CE. Langerhans Cell Histiocytosis: Emerging Insights and Clinical Implications. *Oncology (Wiliston Park)* 2016; 30: 122-132.
2. Lee JW, Shin HY, Kang HJ, et al. Clinical characteristics and treatment outcome of Langerhans cell histiocytosis: 22 years' experience of 154 patients at a single center. *Pediatr Hematol Oncol* 2014; 31: 293-302.
3. Monsereenusorn C, Rodriguez-Galindo C. Clinical Characteristics and Treatment of Langerhans Cell Histiocytosis. *Hematol Oncol Clin North Am* 2015; 29: 853-873.
4. Beyaztaş YF, Oral R, Butun C, Beyaztaş A, Buyukkayhan D. Fiziksel çocuk istismarı: Dört vakanın sunumu. *Cocuk Sağlığı ve Hastalıkları Dergisi* 2009; 52: 75-80.
5. Hussein MR. Skin-limited Langerhans' cell histiocytosis in children. *Cancer Invest* 2009; 27: 504-511.
6. Weitzman S, Egeler M. Histiocytic disorders of children and adults: introduction to the problem, overview, historical perspective and epidemiology. In: Weitzman S, Egeler M (eds). *Histiocytic Disorders of Children and Adults* (1st ed). Cambridge: W.B. Saunders, 2005; 1-13.
7. Kleinjung T, Woenckhaus M, Bachthaler M, et al. Langerhans' cell histiocytosis with bilateral temporal bone involvement. *Am J Otolaryngol* 2003; 24: 265-270.
8. Postovsky S, Daitzchman M, Dale A, et al. Unusual presentation of mastoid eosinophilic granuloma in a young patient. *Pediatr Hematol Oncol* 2001; 18: 283-289.
9. Koc F, Halıcıoğlu O, Akşit S. Which findings may suggest physical abuse? *J Pediatr Res* 2014; 1: 1-5.
10. Hobbs CJ. Skull fracture and the diagnosis of abuse. *Arch Dis Child* 1984; 59: 246-252.
11. Fitzgerald NE, MacClain KL. Imaging characteristics of hemophagocytic lymphohistiocytosis. *Pediatr Radiol* 2003; 33: 392-401.
12. Huang JT, Mantagos J, Kapoor R, Schmidt B, Maguiness S. Langerhans cell histiocytosis mimicking molluscum contagiosum. *J Am Acad Dermatol* 2012; 67:117-118.
13. Shaffer MP, Walling HW, Stone MS. Langerhans cell histiocytosis presenting as blueberry muffin baby. *J Am Acad Dermatol* 2005; 53: 143-146.
14. Papa CA, Pride HB, Tyler WB, Turkewitz D. Langerhans cell histiocytosis mimicking child abuse. *J Am Acad Dermatol* 1997; 37: 1002-1004.
15. Roche E, Pandya N, Munthali L, Atra A. Genital ulceration in a 4 year old-- a case of safeguarding? From social services to pathology. *BMJ Case Rep* 2012; 21: 2012.
16. Donadieu J, Chalard F, Jeziorski E. Medical management of langerhans cell histiocytosis from diagnosis to treatment. *Expert Opin Pharmacother* 2012; 13: 1309-1322.