A childhood secondary headache case associated with Langerhans cell histiocytosis

Langerhans hücreli histiyositoz ile ilişkili bir çocukluk çağı sekonder baş ağrısı vakası

Abstract

Neurological involvement is very rare in patients with a diagnosis of Langerhans Cell Histiocytosis (LCH). During the course of the disease, headache can also be seen in addition to systemic effects. A 6 years old girl was admitted to the hospital with only a headache without any systemic symptoms and was diagnosed with LCH. Magnetic resonance imaging showed a solid mass extending from the sphenoid bone corpus to the left great wing of the sphenoid, left orbital apex, left posterior ethmoid cells, left cavernous sinus, and dural space. The correct decision for neuroimaging in patients with headaches is very important in terms of mortality and morbidity. We wanted to share our patient's case who was diagnosed with LCH by presenting only with headache without any other systemic finding, to remind that LCH may be a secondary cause of headache.

Keywords: Headache; histopathology; langerhans cell histiocytosis; neuroimaging; pediatrics

Öz

Langerhans hücreli histiyositoz (LHH) tanılı hastalarda nörolojik tutulum oldukça nadirdir. Hastalığın seyri sırasında sistemik etkilere ek olarak baş ağrısı da görülebilir. 6 yaşında kız hasta herhangi bir sistemik semptomu olmaksızın sadece baş ağrısı şikayeti ile hastaneye başvurdu ve LHH tanısı aldı. Manyetik rezonans görüntülemede, sfenoid kemik korpusundan sfenoid kemiğin sol büyük kanadına, sol orbital apekse, sol posterior etmoid hücrelere, sol kavernöz sinüse ve dural boşluğa uzanan katı bir kitle olduğu tespit edildi. Baş ağrısı olan hastalarda nörogörüntüleme için doğru karar verilmesi mortalite ve morbidite açısından çok önemlidir. LHH' nin sekonder bir baş ağrısı nedeni olabileceğinin göz ardı edilmemesi için başka bir sistemik bulgusu olmayan sadece baş ağrısı ile başvuran ve LHH tanısı konulan olgumuzu sunmaktayız.

Anahtar Sözcükler: Başağrısı; histopatoloji; langerhans hücreli histiyositoz; nörogörüntüleme; pediatri

Yasemin Baranoglu Kilinc[1], Aysegul Danis[2], Siddika Halicioglu[3]

[1] Division of Pediatrics, Izzet Baysal State Hospital

[2] Department of Pediatric Neurology, Izzet Baysal Research and Training Hospital, Bolu Abant Izzet Baysal University

[3] Department of Radiology, Faculty of Medicine, Bolu Abant Izzet Baysal University

Received/*Geliş* : 19.01.2023
Accepted/*Kabul*: 02.03.2023

DOI: 10.21673/anadoluklin.1239361

Corresponding author/*Yazışma yazarı*
Yasemin Baranoglu Kilinc
Izzet Baysal State Hospital, Division of Pediatrics, Bolu, Turkey.
E-mail: yaseminbaranoglu@hotmail.com

ORCID
Yasemin B. Kilinc: 0000-0002-1795-5677
Aysegul Danis: 0000-0003-0962-2116
Siddika Halicioglu: 0000-0001-7091-5650

INTRODUCTION

Although secondary headache is rare in childhood, underlying diseases can cause mortality and morbidity, so the diagnosis should be made quickly. Histiocytosis is a rare disease in adult and child individuals, described by acervation of cells of mono-nuclear immune system in a variety of body structures. Although brain and spinal cord involvement is more common in Langerhans cell histiocytosis (LCH), Erdheim-Chester, and Rosai-Dorfman-Destombes disorders subtypes of histiocytosis, it is still rare (1). It was previously reported that children with LCH rarely complain of headaches with common symptoms such as painful bone lesions, pruritus, rash, fever, lymphadenopathy, cytopenias, loss of appetite, weight loss, irritability, and behavioral changes (1). However, there is no child case was diagnosed with LCH by presenting with the complaint of headaches without any of the other symptoms reported. In this case report, we aimed to share a pediatric patient who applied with only headache and was diagnosed with LCH based on examination, neuroimaging, and histopathology findings.

CASE

A six-year-old female patient, who was previously healthy, was admitted to our clinic with a headache. She had no additional systemic complaints. Her pain was in the frontal region, starting 1-2 hours after falling asleep at night and waking her up for a month, but the pain was not accompanied by nausea, vomiting, photophobia, or phonophobia. There was no weight loss, fever, or night sweats. She had no vision problems that she could describe. There was no malignancy and primary headache in her family history.

Her systemic examination was normal, except for minimal laps in the submental and submandibular areas and the presence of alopecia areata 1.5x1.5 cm in diameter on the scalp. In the fundus examination, the left optic disc borders were evaluated as faint. Complete blood count, liver and kidney function tests, electrolytes, lactate dehydrogenase level, and thyroid function tests were normal. Her sedimentation was high (25 mm/h (N:0-10)). Contrast-enhanced cranial Magnetic Resonance Imaging (MRI) was performed urgently due to secondary headache caused by sleep and blurred left optic disc margins. MRI showed a solid mass extending from the sphenoid bone corpus to the left great wing of the sphenoid, left orbital apex, left posterior ethmoid cells, left cavernous sinus, and dural space. Left internal carotid artery and optic nerve were observed in this mass. After intravenous (iv) contrast agent injection, significant homogeneous enhancement and the presence of a dural tail were observed. In the diffusion MRI examination, diffusion restriction was observed in the defined solid mass (Figure 1). In the low-dose brain computed tomography (CT) scan performed with the prediagnosis of LCH in order to suspect bone destruction seen on MRI and to investigate the presence of other destroyed lesions in the calvarial bones (Figure 2), the mass described on MRI was observed as hyperdense, there was significant destruction in the bone structures and minimal sclerosis was observed in the vicinity. Since lytic lesions in bone structures were observed in brain CT examination, skull base and meningeal involvement of LCH were considered in the differential diagnosis. With the results of cranial CT and MRI, the patient was referred to biopsy for a definitive diagnosis. As a result of the biopsy, the diagnosis of LCH was confirmed, and she was transferred to the oncology department for follow-up and treatment.

DISCUSSION

Cranial nerve system involvement in LCH includes mass lesions of the hypothalamic-pituitary axis, choroid plexus, brain, cerebellum, or MRI signal abnormalities of the cerebellum, pons, and basal ganglia. Central (neurogenic) diabetes insipidus is the most common endocrine manifestation in LCH and may result in disruption of the hypothalamic-pituitary axis from the posterior pituitary gland, resulting in disruption of antidiuretic hormone secretion (2). Half of the patients with central diabetes insipidus develop a deficiency of anterior pituitary hormones. During the disease, hypothalamic dysfunction may develop too due to non-endocrine causes such as eating disorders, obesity, and sleep disorders (3).

Headaches in patients with LCH may be due to all these endocrine/non-endocrine causes as well as to the neurological involvement of the disease. We asked

Table 1. Cases diagnosed with LCH with neurological involvement in the literature

Case		Symptoms			Neuroimaging features	Reference
A	G	Headache	Other CNS symptom	Add on systemic symptom		
6 y	F	+	-	-	CT: Hyperdense mass, bone destruction, and sclerosis in adjacent bones MRI: T1 hyperintense, T2 isointense soft tissue mass in the left retroorbital area in the left retroorbital area, the verges can not be individuated with sphenoid bone	Our case
8 y	M	+	-Left temporal pain	-Slight exophthalmos -Conjunctival hemorrhage in the left eye	CT: Soft tissue mass in the left temporal fossa, a large bone defect, containing region of larger wing of left sphenoid bone, left lateral orbit and posterior wall of the left maxillary sinus MRI: Heterogeneously contrast augmenting mass near left temporal pole of patient, abrading to left orbit and maxillary sinus	(6)
39 y	F	-	-Dizziness -Balance disorders	-Oropharynx and oral cavity ulceration -Hepatomegaly with innumerable simple biliary cysts	CT: bilateral maxillary sinus repletion and a peripheral osteosclerosis of the encircle bone walls MRI: hyperintense nodular signal at T2 FLAIR weighted images lateral to the right pons, at the level of the left middle cerebellar peduncle and at the left mesencephalon.	(7)
8 y	M	-	- Ataxia - Mild developmental delay -Hyperreflexia	-Generalized rash -Multiple bone lesions	CT: Bony devastation in cranium MRI: Symmetric high-intensity marks in the cerebellum and dentate nuclei, thickered pituitary stem	(8)
8 y	M	-	-Ataxia -Mild developmental delay	-Otorrhea -Auricular canal polyp -Swellings at the retroauricular regions	CT: Bony devastation in cranium MRI: Symmetric high intensity in the dentate nuclei areas of the cerebellum on T2-weighted and FLAIR images	
4 y	M	-	-Ataxia -Mild developmental delay	-Skin rash -Fever -Hepatomegaly -Lymphadenopathy	CT: Bony devastation in cranium MRI: High signal at cerebral white substance, basal nuclei, hypothalamus, midbrain, pons, bilateral dentate nuclei, and thickered pituitary stem	
28 y	M	+	-Dizziness -Tinnitus -Papilledema -Seizures	-Femur lesion	CT: Blank sella MRI: Infiltration of the leptomeninges and ependyma, and perineural involvement of the left trigeminal nerve, and excluded a primary brain tumor	(9)
45	M	+	-Generalized weakness	-Malaise	CT: A large hyperdense field middled on the right cerebellar tonsil leading to a mild pressing fourth ventricle	(10)

A: Age; CNS: Central nervous system, CT: Computed tomography, G: Gender, F: Female, LCH: Langerhans cell histiocytosis, M: Male, MRI: Magnetic resonance imaging, (+): Present, (-): Absent

to share our case who was diagnosed with LCH by presenting only with headache (without any other systemic finding) to remind that LCH may be a secondary cause of headache.

In the neurological involvement of LCH and other histiocytosis, non-parenchymal regions are mostly affected (dura, base of skull, etc.). Actual infiltration of brain tissue is infrequent and occurs in merely 5% of adult and child individuals. However, neurological symptoms are seen in 10-25% of LCH cases (2).

In patients with neurological involvement, hypothalamic-pituitary-adrenal (HPA) axis is seen in 20% of patients and is one of the most frequently infiltrated sites. HPA infiltration is existing clinically as diabetes insipidus and in a number of conditions where anterior pituitary hormones are deficient. In adult individuals, diabetes insipidus may develop months or even years before the diagnosis of LCH (4).

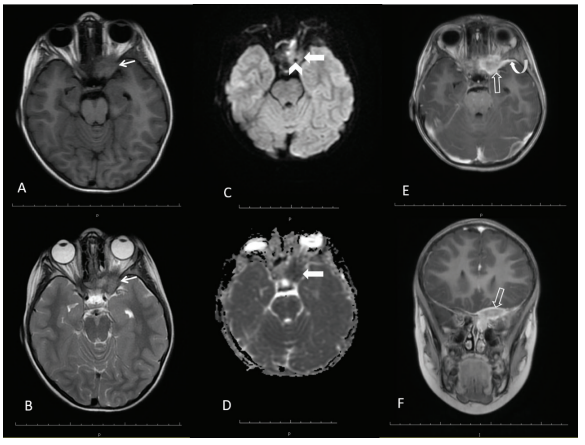

Figure 1. The images of magnetic resonance imaging examination. In the magnetic resonance imaging examination, a T1W hyperintense (A), T2W isointense (B) soft tissue mass marked with a white thin arrow was observed in the left retroorbital area in the left retroorbital area, whose borders could not be distinguished with the sphenoid bone. On diffusion-weighted images, hyperintense was observed in the trace sequence (C), and diffusion restriction was observed in the lesion marked with a white thick arrow on the ADC map (D). In addition, signalless internal carotid artery marked with a white arrowhead within the mass is observed in C. On the postcontrast axial (E) and coronal (F) T1W images, homogeneous enhancement was observed in the mass marked with a white blank arrow and the dural tail marked with a curved white arrow in E.

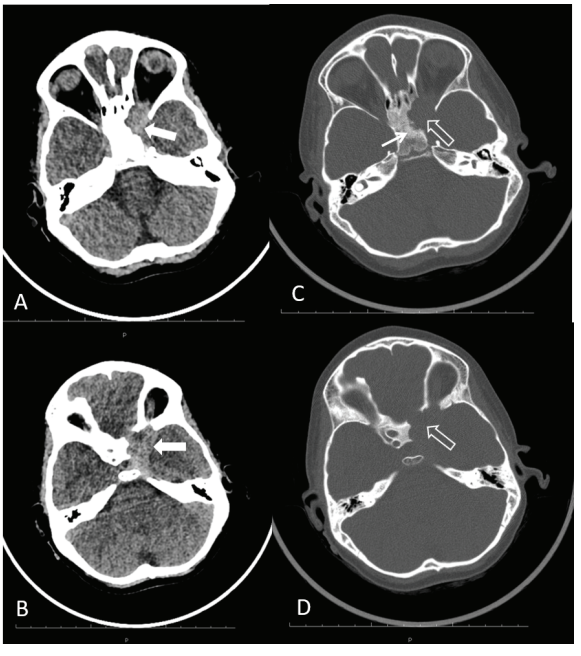

Figure 2. The images of low-dose nonenhanced computed tomography scan. In low-dose nonenhanced computed tomography, a hyperdense mass was observed at the level of the retroorbital-cavernous sinus in the axial brain parenchyma window (A, B). In the bony window bone destruction marked with a light white arrow and sclerosis in adjacent bones marked with a thin white arrow were observed (C, D).

Other neurologic disease areas include pachymeninges, pineal gland, choroid plexus, and brain parenchyma. Parenchymal lesions are characteristically observed in the posterior fossa, which consists of brain stem and cerebellar peduncles.

It was reported that the greatest clinical problems in patients with clinical or MRI evidence of central nervous system CNS involvement are observed in the areas of verbal intelligence, attention, memory and learning (2, 5).

Clinical symptoms in patients with LCH depend on CNS involvement and type. Cases diagnosed with LCH with neurological involvement in the literature are shared in Table 1.

Rare tumoral lesions in meninges and choroid plexus can cause headache, seizure, and focal symptoms by increasing intracranial pressure and hydrocephalus (2). LCH-associated neurodegenerative lesions have a highly variable clinical picture. Although many patients have MRI changes typical of neurodegeneration, they show no neurological symptoms.

CONCLUSION

According to our literature review results, our patient is the only *pediatric* patient who was diagnosed with LCH by applying to the hospital with only a headache. Although LCH is a very rare diagnosis in children presenting with headaches, it should be included in the differential diagnosis of patients with secondary headaches.

Conflict-of-interest and financial disclosure

The authors declare that they have no conflict of interest to disclose. The authors also declare that they did not receive any financial support for the study.

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