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Case Report

Late-Onset Langerhans Cell Histiocytosis Presenting with Seizures and Bilateral Temporal Involvement

Özge Öcek, Hasan Kuş, Pınar Ortan

Department of Neurology, Izmir University of Health Sciences, Bozyaka Education and Research Hospital, İzmir, Turkey

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Corresponding author: Özge Öcek, e-mail: ozge_giray@yahoo.com

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Abstract

Langerhans cell histiocytosis is known as a rare childhood disease. In this case, we wanted to share our patient's experience whose first symptom was an epileptic seizure, which attracted attention at an advanced age and revealed bilateral temporal lobe involvement. Our case was a 51-year-old male, who had been having seizures with focal onset, autonomic characteristics, impaired awareness, and occasionally secondary generalized seizures for 5 years, was admitted due to an increase in the frequency of seizures over the past 6 months. The patient was diagnosed with Langerhans cell histiocytosis as a result of pathological examination of the bronchoalveolar lavage. In cranial magnetic resonance imaging, bilateral temporal regions are hyperintense on T2 and Fluid Attenuated Inversion Recovery (FLAIR)-weighted images and hypointense and partially enhanced contrast on T1-weighted images. Additionally, central involvement of Langerhans cell histiocytosis was supported by hyperintensity in the optic chiasm, pituitary gland, and around the third ventricle on T2 and FLAIR-weighted images. Electroencephalography showed sharp slow wave activity in the left anterior temporal region. After controlling our patient's seizures, we referred him to the oncology and hematology departments to regulate his treatment for primary disease. It should be noted that in late-onset Langerhans cell histiocytosis, epileptic seizures may occur as the first symptom rarely, due to secondary involvement of the central nervous system.

Keywords: Epileptic seizure, Langerhans cell histiocytosis, MRI

INTRODUCTION

Langerhans cell histiocytosis (LCH) can be defined as a group of diseases characterized by the atypical histiocytes that accumulate and damage locally or widely in the different parts of the body, such as the skin, bones, lungs, lymph nodes, mucocutaneous tissues, and endocrine organs.[1] Although the cause is not yet understood, it has been shown to be a clonal disease of childhood. The primary form is seen in early infants and is usually fatal. Its secondary form may occur due to infection or malignancy.[1,2] Adulthood onset and presentation with epilepsy of LCH are exceptional.[2-5] Radiologically, osteolytic lesions can be observed in the sphenoidal, orbital, ethmoidal, and temporal bones. Endocrinological disorders may occur with the involvement of hypothalamic–pituitary axis (HPA), while the formation of a mass lesion in the brain and invasion of the brain stem may be seen rarely.[6] In this article, we wanted to present our case of LCH whose first symptom was epileptic seizure and revealed bilateral temporal lobe and brain stem involvement accompanied by clinical and radiological findings.

CASE PRESENTATION

A 51-year-old male was admitted to our clinic due to increase in the seizure frequency in September 2021. From his history, it was learned that the patient had been having epileptic seizures since 2016; however, the frequency, severity, and durations of the seizures increased in the last 6 months. It was understood that awareness was impaired during the seizures, which had focal onset, autonomic features, and generalized secondary seizures from time to time. He was under treatment with levetiracetam 2000 mg/day and lacosamide 200 mg/day. Additionally, he had been diagnosed with hypothyroidism, erectile dysfunction, and diabetes insipidus since 2018. It was determined that when the patient had respiratory distress 6 months ago, he was diagnosed with LCH due to findings in thoracic computed tomography (CT) and bronchoalveolar lavage which was taken along with bronchoscopy; however, treatment was not commenced yet (Figure 1). On physical examination, purulent, ulcerated lesions were observed on the surface of the skin in both axillary regions and on the back of the right auricle (Figure 2). Neurological examination was normal. In the electroencephalography (EEG), sharp slow wave activity was observed in the left anteriotemporal region and the phase reversal was detected at the F7 electrode (Figure 3). Brain CT was normal. Cranial magnetic resonance imaging (MRI) revealed lesions in the bilateral temporal (parahippocampal) regions that were hyperintense on T2- and FLAIR-weighted images, hypointense on T1-weighted images, and enhanced contrast partially (Figure 4). Additionally, hyperintense nodular lesions in the brain stem and hyperintensity on the optic chiasm, around the third ventricle, in the pituitary gland on T2-weighted images were observed. Routine laboratory tests were within normal range. The lumbar punction could not be performed because it was not accepted by the patient. Autoimmune and paraneoplastic antibody tests from serum were negative. Clindamycin and tetrodotoxin were recommended for skin lesions. The frequency of the epileptic seizures of the patient was reduced when the dose of lacosamide was increased to 400 mg/day. The patient was scheduled to be given

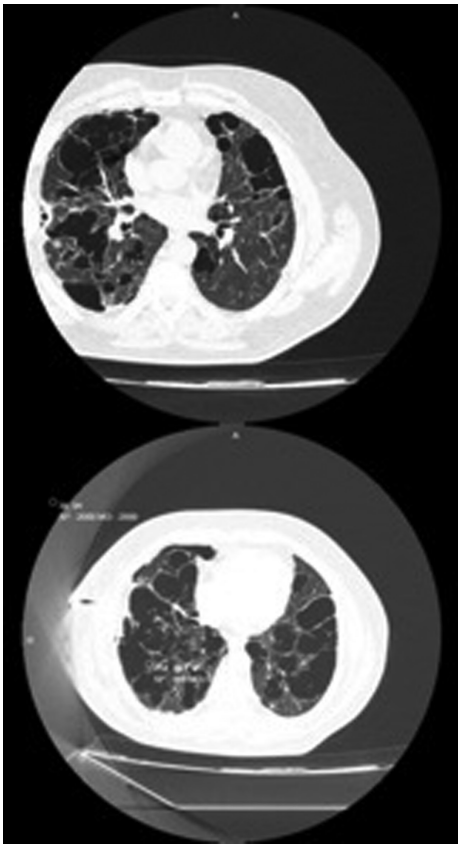

Figure 1. Diffuse thin-walled air cysts (compatible with Langerhans cell histiocytosis) are observed in both the lungs on thoracic CT. CT, computed tomography.

chemotherapy and monitored together by hematology and oncology departments.

DISCUSSION

Neurological involvement of LCH has been described as 2 main forms: tumoral lesions and degenerative lesions. Both forms of involvement can be found in the same patient. In the pathogenesis, tumoral lesions are dominated by histiocytic infiltration, while neurodegenerative LCH is characterized by demyelination, neuronal loss, and gliosis.[7] Neurological symptoms may occur due to direct pressure of tumoral lesions and invasion of neural structures during the neurodegenerative process. Central nervous system involvement is reported in the range of 6%-30% in LCH, which mostly accompany with multiorgan invasion and osteolytic lesions in skull.[1,3,8] It may present with various

MAIN POINTS

- Langerhans cell histiocytosis (LCH) is a rare type of malignancy in adulthood and has the potential to involve the central nervous system.
- It is remarkable that our case of LCH presented with epileptic seizures.
- Our case's magnetic resonance imaging revealed bilateral temporal lobe, brain stem, optic chiasm, hyperintensity around the third ventricle, and the pituitary gland involvement.
- It is important to make a rapid differential diagnosis following seizure control.
- The necessity of a multidisciplinary approach should be kept in mind.

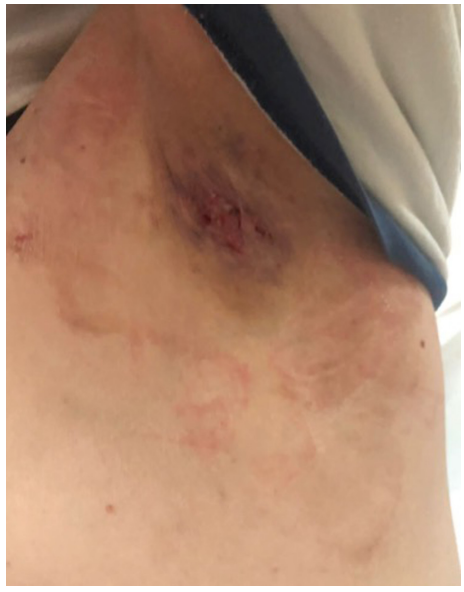

Figure 2. A necrotic, purulent-catarrhal nodular lesion with edges measuring 10 × 15 mm in the area of the left armpit.

neurological clinical findings such as most frequently headache, irritability, change in consciousness, neck stiffness, nausea, vomiting, epileptic seizures, aphasia, proptosis, cranial nerve paralysis (especially optic, oculomotor, and trigeminal nerves), and hemiplegia.[1,2]

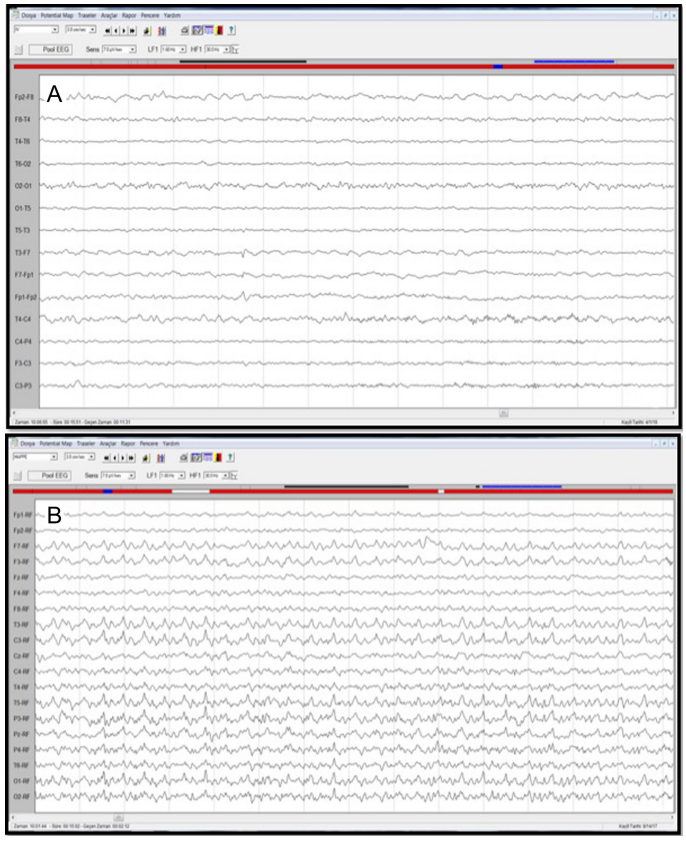

Figure 3. Waking EEG. Isolated sharp wave activity of low amplitude in the left anterior temporal region, bipolar and monopolar (A,B). EEG, electroencephalography.

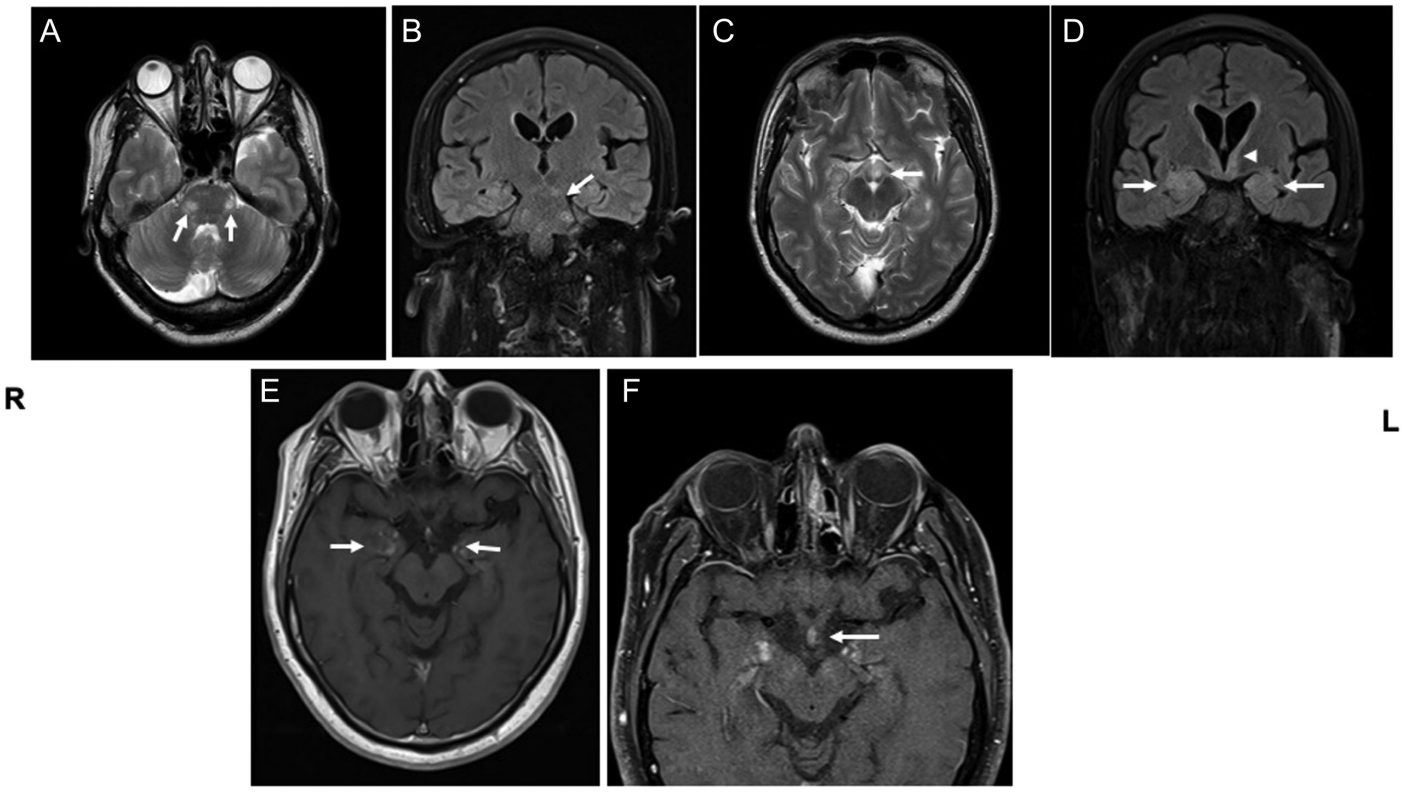

Figure 4. Cranial MRI examination. Nodular hyperintensity is observed in T2- and FLAIR-weighted sections of the Pons (A,B) in the pituitary gland and hyperintensity in T2- and FLAIR-weighted sections around the third ventricle (C, D). Hyperintense lesions are observed in the T2 and FLAIR-weighted sections in the medial of both temporal lobes (D). In contrast-weighted T1-weighted sections, nodular contrast is noted in both hemispheres in the medial temporal lobe (E) Slight contrasting is noted in the optic chiasm (F). MRI, magnetic resonance imaging.

Epileptic seizures can be seen in 9.4% of cases with the involvement of the temporal and hippocampal regions.[1] In the literature, Kim et al[9] reported a case with 3 cm mass lesion involving the right frontal lobe, presented with generalized tonic-clonic type seizure. After surgery and chemotherapy, the patient had no neurologic deficit or seizure attack. In our case, due to involvement in both parahypocampal regions, focal onset, bilateral tonic-clonic epileptic seizure was the first symptom. Because that our patient did not have surgical indication, we had difficulties in providing seizure control.

In brain CT, lesions may have lower density than gray matter and lytic lesions can be detected in the bone window.[10] On cranial MRI, lesions can be observed as nodules, which are hyperintense or isointense on T1-weighted images compared to gray matter and hyperintense on T2-weighted images, in supratentorial areas, and more rarely, it can be observed in the basal ganglia, dentate nuclei of the cerebellum, along the leptomeningeal area, HPA, or in the brain stem.[1,4,5] It may also be accompanied by fragmentary contrast enhancement on the optic chiasm.[4-6] While brain CT of our patient was normal, T2-weighted images of the cranial MRI showed the presence of symmetrical, hyperintense lesions, which have nodular enhancement pattern, in the bilateral temporal regions, additionally hyperintensity in the optic chiasma, pituitary gland, and around the third ventricle on flair and T2-weighted images supported central involvement of LCH.

Prayer et al[11] stated that LCH most frequently involves the HPA in the intracranial region and its clinical manifestation was diabetes insipidus. They also showed that intracranial extra-axial lesions can be found in 76.7% in HPA, 2% in meninges, 28% in pineal gland as cystic appearance, and 6% in choroid plexus. They reported that leukoencephalopathy-like appearance as intracranial intra-axial involvement in%36, enlarged Virchow–Robin cavities in 70%, gray matter changes were seen in the cerebellar dentate nucleus in 40%, and the basal ganglia in 26%. Also, they found that cerebral atrophy was found in 8% of the cases. Furthermore, brain stem involvement, which is associated with a poor prognosis, is less common.[11] In our patient's history, the diagnosis of hypothyroidism and diabetes insipidus were secondary to hypopituitarism which was due to the involvement of HPA. It was interesting that our patient had brain stem and optic chiasm lesions, but no neurological examination findings had been detected.

On the other hand, lobar involvement of LCH is quite rare.[12] Liang et al[13] declined 16 cases of brain parenchymal LCH with imaging data in the PubMed literature from 1990 to May 2021. The mean age was 31 years (95% CI: 21.5-41.2). The lesions were mostly located in the frontotemporal lobe (14 cases), particularly in the frontal lobe. Our patient's age was advanced and he had bilateral involvement of the temporal lobe and epileptic seizure presentation is also noteworthy.

Langerhan's cell histiocytosis patients, who had isolated CNS involvement, can be followed up asymptomatically for a long period regardless of the lesion localization. It is recommended to monitor for extracranial involvement every 6 months during follow-up.[14] Long-term survival is shorter in patients with a predominance of the neurodegenerative

process, as in our case, than in patients with symptomatic tumoral lesions.[7] The mortality of systemic LCH patients without treatment is quite high. When the remission is achieved with early diagnosis, chemotherapy and immunosuppressive therapy, administration of hematopoietic stem cell transplantation can prolong survival.[6,8]

In conclusion, it should be noted that epileptic seizure may be the first symptom of malignancies. Langerhans cell histiocytosis is a rare type of malignancy in adulthood and has the potential to involve the brain parenchyma; however, its diagnosis is extremely challenging. The necessity of a multidisciplinary approach should be kept in mind after making a rapid differential diagnosis following seizure control.

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Declaration of Interests: The authors have no conflicts of interest to declare.

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