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Langerhans cell histiocytosis located in the spheno-orbital bone and the pons: illustrative case

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BACKGROUND This is a case of aggressive Langerhans cell histiocytosis (LCH) with an atypical intracranial location.

OBSERVATIONS In this report, the authors present the diagnosis and treatment of a 12-year-old male patient diagnosed with LCH. The patient was admitted to the emergency department with left-sided facial palsy, and a solid lesion with mass effect in the pons was found. A biopsy was performed via suboccipital craniotomy, and the diagnosis was LCH. A chemotherapy regimen was started since the LCH sample was the resistant type. The patient showed improvement in his neurological deficit following treatment.

LESSONS This rare localized and aggressive case's diagnosis process and treatment choices may apply to future cases.

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KEYWORDS Langerhans cell histiocytosis; brainstem; pons; neurosurgery; pediatric oncology

Histiocytic disorders are rare and characterized by the accumulation of macrophages, dendritic cells, or monocyte-derived cells in various tissues in patients. Langerhans cell histiocytosis (LCH) was classified as a class 1 histiocytosis disease in 1997 by the World Health Organization. It was later classified as group L (Langerhans) in the classification of the Histiocyte Society in 2016.[1]

Intracranial invasion in LCH presents with system involvements other than those of a stand-alone intracranial lesion. The lesions in the central nervous system (CNS) usually appear late. The median interval has been shown as 5–20 years after diagnosis.[2] Intracranial lesions can be detected after the development of a clinical condition such as diabetes insipidus or epilepsy or during image-based screening in patients with primary LCH.

In LCH, cranial changes include the following: 1) lesions of the craniofacial bone and skull base with or without soft tissue extension; 2) intracranial, extra-axial changes (hypothalamic-pituitary region, meninges, circumventricular organs); 3) intracranial, intra-axial changes (white matter and gray matter); and 4) cerebral atrophy.[3] In this article, we present a case of systemic LCH disease with the rare involvement of the pons.

Illustrative Case

A 12-year-old male patient underwent an operation for a mass in the mandible when he was 2 years old. His pathology was compatible with LCH. Positron emission tomography–computed tomography (PET-CT) showed multiple bone lesions (mandible, left femur, and left frontotemporal bones) and multiple lymph nodules at that time. The pediatric oncology department initiated an induction chemotherapy regimen with prednisolone and vinblastine (for 6 weeks) and then continued with a maintenance regimen for 52 weeks. The first chemotherapy treatment was completed in November 2013. Eleven months after completion of the treatment, the patient presented with cervical swelling, and a biopsy sample was taken. His pathology was consistent with LCH. Recurrence was considered, and scanning led to the discovery of a new occipital bone lesion. Another chemotherapy regimen was started for the recurrent disease, including prednisolone, vincristine, and cytarabine, between October

ABBREVIATIONS CNS = central nervous system; LCH = Langerhans cell histiocytosis; MRI = magnetic resonance imaging; PCR = polymerase chain reaction; PET-CT = positron emission tomography–computed tomography; RT = radiotherapy.

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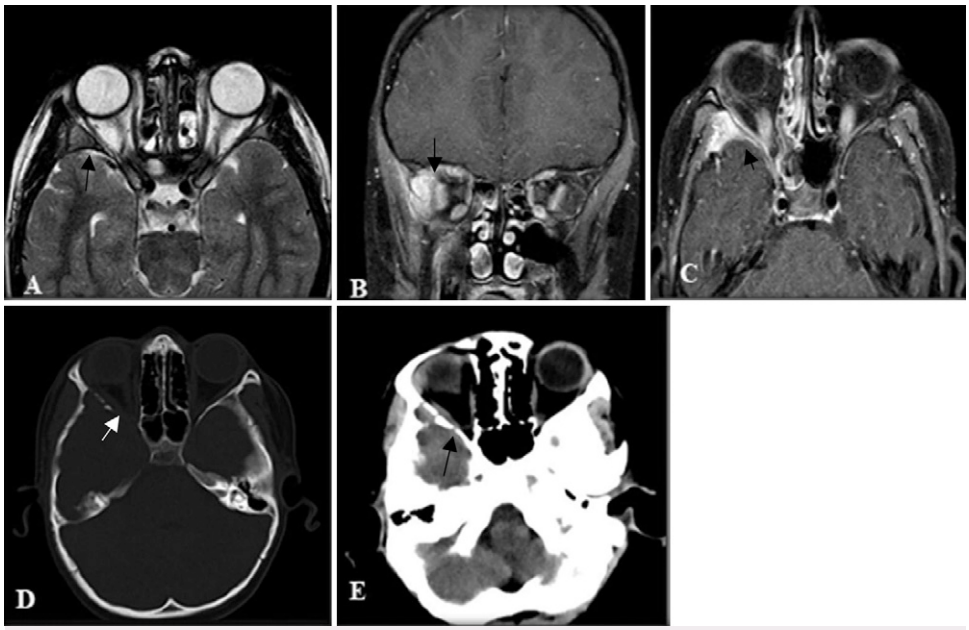

FIG. 1. Axial T2-weighted hyperintense magnetic resonance (MR) image of a 22 × 16-mm–diameter LCH mass that breaches the orbital wall and destroys the sphenoid wing extending into the extraconal region (**A**). Coronal (**B**) and axial (**C**) T1-weighted contrast-enhancing MR images of the mass. Computed tomography shows the intraorbital extension of the mass and its destruction of bone structures (*arrows*, **D and E**).

2014 and August 2015. Three months after treatment, PET-CT scans showed that there were metabolic decreases in the lesions. Between August 2015 and September 2021, no additional lesions were identified during the follow-up.

In September 2021, a right-sided, dense, homogeneous, contrast-enhancing mass with a diameter of 22 × 16 mm was detected in the lateral orbital wall and was destroying the sphenoid bone (Fig. 1). A lesion with a diameter of 5 mm in the right half of the pons, which was hyperintense on T2-weighted magnetic resonance imaging (MRI), was also found without contrast enhancement. There were also hyperintense appearances of both dentate nuclei on T2-weighted MRI sequences (Fig. 2).

Neurological examination was normal. The patient underwent surgery for the spheno-orbital localized lesion. However, it was decided not to operate for the pontin lesion because of its eloquent location and a lack of symptoms. S100, CD68, and langerin were positive in the immunohistochemical staining, and polymerase chain reaction (PCR) detected a *BRAF V600E* mutation. The pathological diagnosis was again LCH. This was the patient's second recurrence. According to a new protocol for LCH in 2021, the pediatric oncology department decided to start chemotherapy. Since the last recurrence was 6 years earlier, the same chemotherapy regimen was started. The patient received chemotherapy between December 2021 and February 2022. Three months after treatment, the patient presented to the emergency service with complaints of spasms and weakness in the left half of the face. Left-sided facial paralysis was noticed alongside lateral gaze palsy on the same side. MRI showed the growth and an increase in contrast enhancement of the mass in the pons (Fig. 3). The lesion was hyperintense in both T1- and T2-weighted sequences and enhanced homogeneously with gadolinium.

To diagnose the pontine lesion correctly, it was decided to conduct a biopsy. During the operation, gray-purple tumor tissue was seen adjacent to the facial colliculus on the fourth ventricle floor. The biopsy was taken using neuro-navigation under cranial nerve neuromonitoring. There was no additional neurological deficit postoperatively.

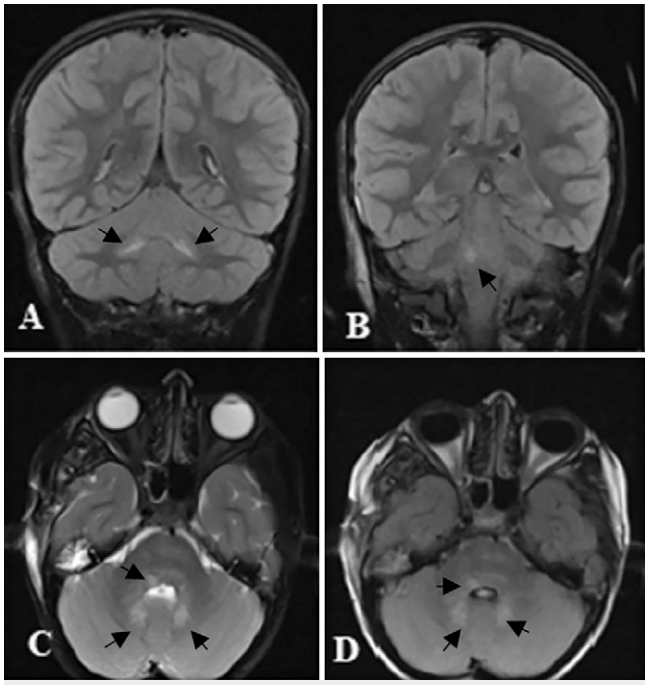

FIG. 2. Bilateral dentate nucleus (**A, C, and D**) and right-sided pons (**B and C**) involvement that appears hyperintense on T2-weighted and fluid-attenuated inversion recovery magnetic resonance imaging (MRI) examinations but do not enhance contrast (*black arrows*).

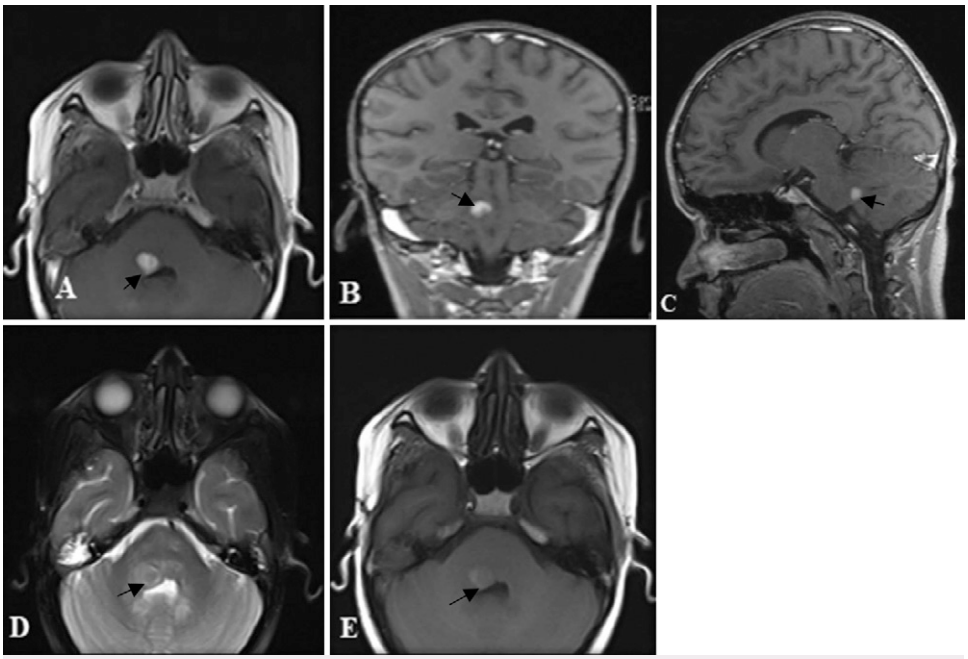

FIG. 3. MR images of a progressive pontomedullary joint lesion, which started to enhance on follow-up and had mass effect (*black arrows*, **A–C**). Axial T2-weighted (**D**) and T1-weighted (**E**) MRI of the lesion.

Microscopic evaluation revealed histiocytic cells with oval nuclei, amphophilic cytoplasm, reactive gliosis, and periventricular lymphocytic infiltration. Immunohistochemical staining showed S100 positivity, while langerin and CD1a were negative (Fig. 4). However, with the detection of a *BRAF V600E* mutation on PCR, the pathology result was interpreted as LCH. An isolated recurrence was considered, and cytarabine was started.

After the first chemotherapy session, the patient's clinical status dramatically recovered, and his sixth and seventh cranial nerve palsies were resolved. However, there was no significant difference in lesion sizes in the control MRI (Fig. 5).

Patient Informed Consent

The necessary patient informed consent was obtained in this study.

Discussion

Typical imaging features of cranial LCH areas are destructive lesions involving bone, isodense on computed tomography, isointense on T1-weighted MRI, isointense to hyperintense on T2-weighted images, and diffuse and homogeneous enhancement on postcontrast MRI.[2,4] From a clinical perspective, the main symptoms are diabetes insipidus, headaches, seizures, ataxias, balance disorders, nausea, vomiting, and visual disturbances, according to the location of the lesions.

Contrast-enhancing solid lesions have been observed in the parietal, temporal, frontal, and occipital lobes in order of frequency.[3,5–7] Lesions on the brainstem or cerebellum are rare, as they are generally seen in late stages of the disease and present as resistant cases.[2] Lesions developing in these areas are usually T2 hyperintense with mass effect, showing microvascular or patch-like contrast enhancement. However, only 2 lesions occupying solid spaces in the pons were identified in the literature, and few lesions with punctate contrast enhancement were observed.[5,8–10]

Observations

Our case is the third located in the pons causing mass effect. In the other 2 cases in the literature, the diagnosis was also made after newly developed neurological symptoms in patients previously diagnosed with LCH. Cagli et al.[5] operated on their patient for a temporally located lesion. They followed the lesion located in the pons. After enlargement of the lesion on follow-up, they decided on Gamma Knife treatment. A complete cure was achieved after treatment.

In the case reported by Vourtsi et al.,[10] a patient with a known diagnosis of LCH was also diagnosed with a contrast-enhancing lesion in the pons and temporal bone after the patient had experienced vision and hearing problems. Conventional radiotherapy (RT) was administered to the patient with a diagnosis of LCH because of his medical history and radiological features. During follow-up, complete regression of the lesion and improvement in the patient's clinical status were observed.

Grois et al.[8] also reported a case of LCH with punctate contrast enhancement in the pons. In this case, the patient was administered chemotherapy because of a previous diagnosis of LCH with skin involvement. Brain RT was given because his skull had also been affected. The patient developed visual symptoms in the follow-up period. The patient's imaging showed diffuse lesions in the cerebral cortex and cerebellum and a punctate contrast-enhancing lesion in the pons. The patient underwent biopsy operations twice on the brain lesions. The intracranial biopsy result was compatible with normal parenchyma. In addition, the skull sample presented LCH compatibility; hence, conventional RT was given again, and the chemotherapy regimen was changed. The patient died of pneumonia.[2]

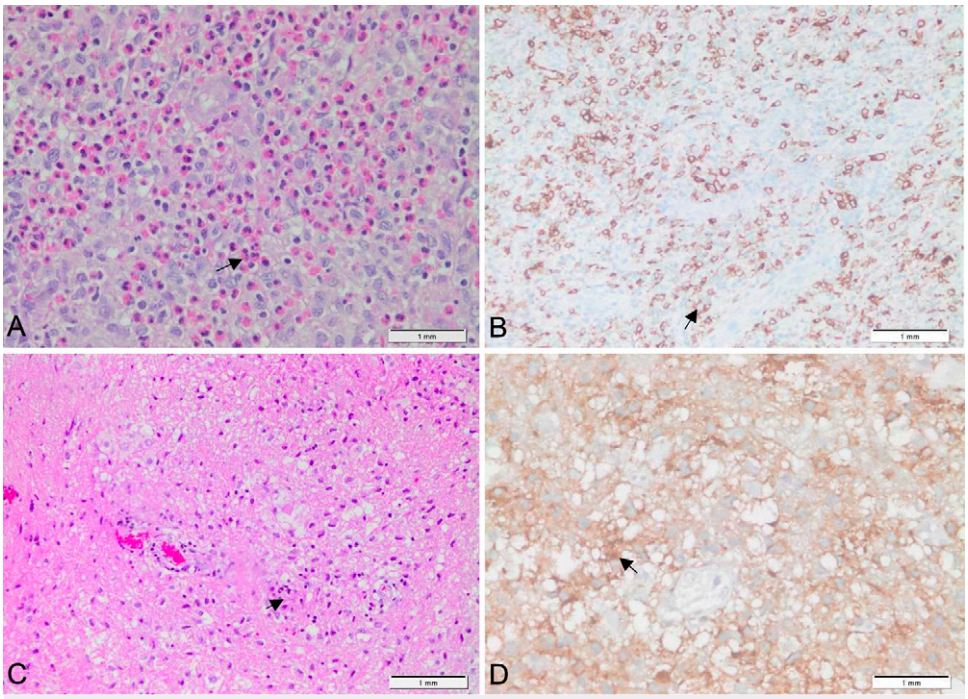

FIG. 4. Microscopic appearance of the tumor showing Langerhans cells having oval nuclei and groove formation in the eosinophil-rich inflammatory background (hematoxylin and eosin [H&E] stain, x200, **A**). Immunohistochemical staining of Langerhans cells (langerin stain, x400, **B**). Scattered histiocytic cells have oval nuclei and rare lymphocytic cells in the background of reactive gliosis (H&E stain, x400, **C**) and immunohistochemical staining of histiocytic cells (*black arrows*, CD163 stain, x400, **D**).

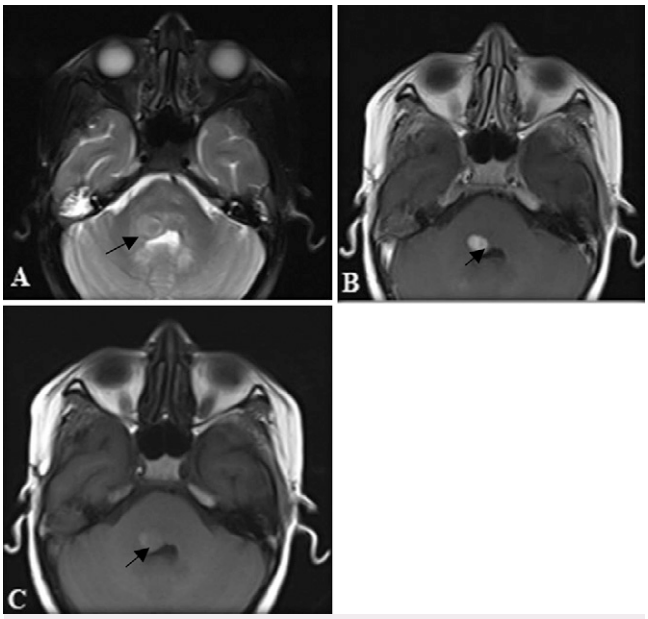

FIG. 5. Axial T2-weighted (**A**), contrast-enhanced T1-weighted (**B**), and T1-weighted (**C**) MR images obtained 1 month postoperatively. There was no significant size difference in the mass (*black arrows*) in the images, but a minimal decrease in the edema was observed in the multisectional examinations. In addition, clinical improvement was observed in the patient.

In addition, in the radiological studies of intracranial involvement of LCH, Prayer et al.[9] reported that there were cases of LCH with microvascular and patch-like lesions in the pons. However, radiological features, clinical courses, and treatment options were not specified.

Lessons

Our case is an example of LCH with a very aggressive course characterized by intracranial involvement and progression under treatment. The pontine lesion detected in the previous MRI was monitored, and surgery was not performed because of the eloquent location, lack of clinical findings, and contrast enhancement. After the patient was admitted to the emergency department with a cranial nerve palsy (left facial and abducens paralysis) and enlargement and contrast enhancement of the pontine lesion, an intervention was decided as necessary. Differential diagnoses of the lesion included lymphoma, pontine glioma, metastasis, and tuberculoma; therefore, a diagnostic biopsy was performed. The histopathological investigation was once again consistent with LCH. Treatment was continued with another systemic chemotherapy regimen.

Since treatment planning is mostly case based, a precise protocol is not available. In the literature, surgical excision plus chemotherapy is considered the most effective treatment option.[2,6] In our case, only a biopsy was performed, not total resection, because of the risk of permanent neurological deficits. The patient has benefited from his current regimen, and all neurological findings have improved.

No treatment is standardized for CNS LCH but includes surgery, chemotherapy, RT, or various combinations. The treatments

are utilized based on the location of the lesion, its morphological features, and systemic involvement. In the literature, the success rates of current treatments are between 52% and 100%, with the highest success rates being shown with surgery plus chemotherapy (100%) and surgery-only (88%) options.[2,8,9] These results emphasize that surgical treatment is the most important treatment option.

Radiotherapy is primarily used in patients with multiple intracranial involvement, for whom surgery is not an option, or in patients with postoperative residuals. Chemotherapy is planned as a combined treatment with surgery and is more prominent in cases with systemic involvement. In addition, Cagli et al.[5] succeeded with Gamma Knife treatment in a patient similar to the present case. In our case, Gamma Knife surgery was also an option, and it could be applied based on further follow-ups.

Intracranial involvement in LCH is not uncommon, but pontine lesions are very rare, with specific findings and risks. They are more frequently encountered in diseases with longer durations. A patient with long-tract and cranial nerve findings should be suspected to have a pontine lesion. Diagnosed cases must be treated aggressively to eliminate any dangerous potential complications. Surgery may be an option for treatment, particularly when there is suspicion about the diagnosis. Nevertheless, the essential treatment modalities are chemotherapy and RT in pontine lesions of LCH.

References

1. Emile JF, Abla O, Fraitag S, et al. Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. *Blood.* 2016;127(22):2672–2681.
2. Gersey ZC, Zheng I, Bregy A, et al. Intracranial Langerhans cell histiocytosis: a review. *Interdisciplinary Neurosurgery.* 2020;21: 100729.
3. Saatci I, Baskan O, Haliloglu M, Aydingoz U. Cerebellar and basal ganglion involvement in Langerhans cell histiocytosis. *Neuroradiology.* 1999;41(6):443–446.
4. Leenknegt B, et al. Craniofacial and intracranial Langerhans cell histiocytosis. *J Belge Radiol.* 2020;104(1):57, 1–2.
5. Cagli S, Oktar N, Demirtas E. Langerhans' cell histiocytosis of the temporal lobe and pons. *Br J Neurosurg.* 2004;18(2):174–180.
6. Rodríguez-Pereira C, Borrás-Moreno JM, Pesudo-Martínez JV, Vera-Román JM. Cerebral solitary Langerhans cell histiocytosis: report of two cases and review of the literature. *Br J Neurosurg.* 2005;19(2):192–197.
7. Luna LP, Drier A, Aygun N, et al. MRI features of intra-axial histiocytic brain mass lesions. *Clin Radiol.* 2021;76(2):159.e19–159.e28.
8. Grois N, Fahrner B, Arceci RJ, et al. Central nervous system disease in Langerhans cell histiocytosis. *J Pediatr.* 2010;156(6): 873–881.e1.
9. Prayer D, Grois N, Prosch H, Gadner H, Barkovich AJ. MR imaging presentation of intracranial disease associated with Langerhans cell histiocytosis. *AJNR Am J Neuroradiol.* 2004;25(5):880–891.
10. Vourtsi A, Papadopoulos A, Moulopoulos LA, Xenellis J, Vlahos L. Langerhans cell histiocytosis with involvement of the pons: case report. *Neuroradiology.* 1998;40(3):161–163.

Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Cekic, Karagoz, Sakar, Senay, Bozkurt, Dagcinar. Acquisition of data: Cekic, Senay, Akar, Bozkurt. Analysis and interpretation of data: Cekic, Senay, Bozkurt. Drafting of the article: Cekic, Bozkurt, Dagcinar. Critically revising the article: Cekic, Karagoz, Sakar, Dagcinar. Reviewed submitted version of the manuscript: Karagoz, Sakar. Approved the final version of the manuscript on behalf of all authors: Cekic. Administrative/technical/material support: Cekic, Karagoz, Senay, Bozkurt, Dagcinar. Study supervision: Cekic, Karagoz, Sakar.

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