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Case Report

Calvarial Langerhans cell histiocytosis in an Adult: Typical imaging findings in an atypical age group

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ABSTRACT

Langerhans Cell Histiocytosis (LCH) is a rare disorder characterized by neoplastic proliferation of Langerhans-type dendritic cells. LCH is most frequently encountered in the pediatric populations, and involvement of the skeletal system is a common manifestation. Herein, we report a case of LCH presented as an isolated skull lesion in a 66-year-old patient. This presentation has never been reported in the literature at this advanced age and suggests that, despite being exceptionally rare, clinicians should consider LCH in the differential diagnosis of skull lesions in the elderly with classical radiological appearance.

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Introduction

Langerhans Cell Histiocytosis (LCH) is the most common histiocytic disorder (a group of diseases affecting the macrophages and dendritic cells). Based on the number of lesions and the systems involved, LCH could present as a unifocal or localized pathological process, or a multifocal disease affecting an individual or multiple organ systems. The clinical presentation is variable and highly dependent on the severity and number of organs involved and might range from a self-limited condition to a life-threatening fatal disease. Although clinical man-

ifestations and radiological features suggest an LCH diagnosis, histopathologic; and immunohistochemical examination confirm the final diagnosis.

LCH is most frequently encountered in the pediatric population. The majority of adulthood cases present before the age of 50 with cases presenting after this age being an exception. In light of this, we report, to our knowledge, the first case of LCH presented as isolated skull lesion with classic computed tomography (CT) and magnetic resonance imaging (MRI) features in a 66-year-old patient with further histopathological confirmation.

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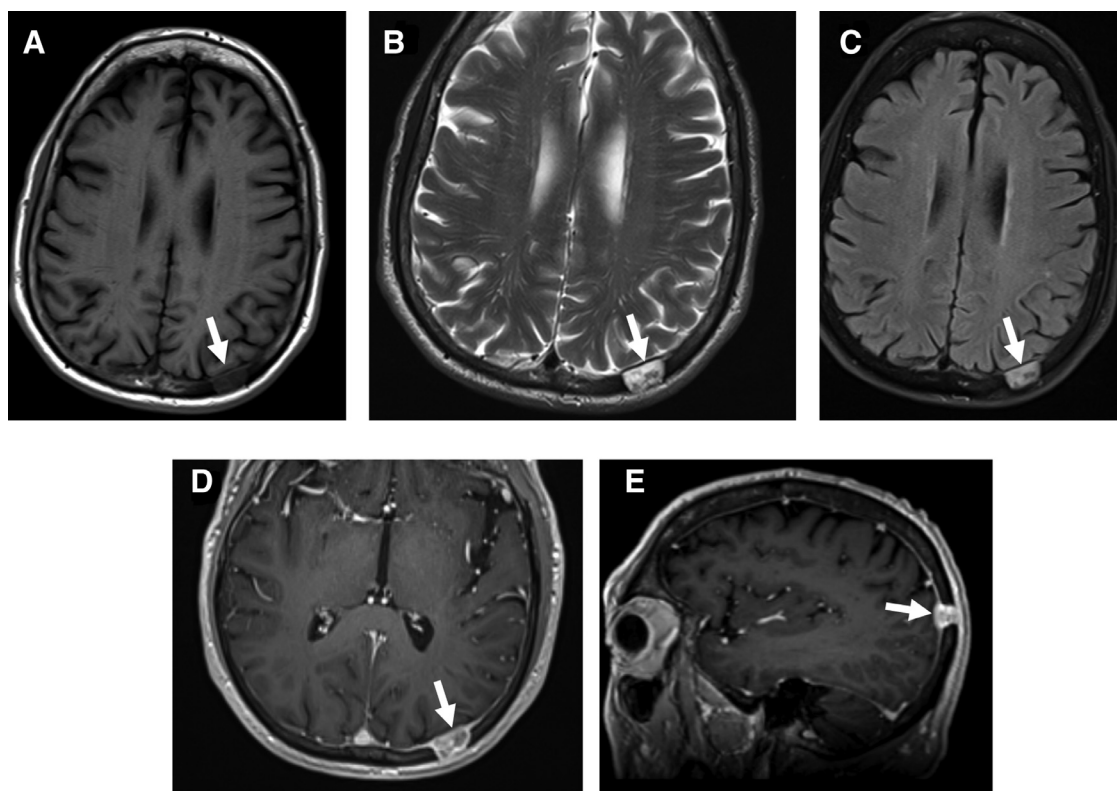


Fig. 1 – MRI at the time of presentation demonstrating the calvarial lesion breaching the inner and outer table to involve the scalp and dura. (A) Axial T1 shows a left parietal bone T1-isointense lesion; (B,C) Axial T2 (B), and FLAIR (C) images show that the lesion is heterogeneously hyperintense; (D,E) postcontrast (gadoterate meglumine) axial (D) and parasagittal (E) demonstrate homogenous enhancement within the lesion that breaches both calvarial tables and involves the dura (white arrows) and overlying soft tissues.

Case presentation

A 66-year-old male presented to his primary care physician complaining of recent focal left parietal pain encountered on palpation. Physical exam revealed an abnormal soft tissue mass in this region. Brain MRI from 8 years prior was normal. Given the new findings, a repeat MRI study was obtained.

Brain MRI demonstrated a focal T2 hyperintense enhancing lesion breaching the inner and outer calvarial tables with extension to and involvement of the underlying dura (Fig. 1). A subsequently obtained CT demonstrated a lytic lesion with unequal erosion of the inner and outer tables of the parietal bone and a sequestered fragment within the lesion (Fig. 2). Given the appearance and age, the differential diagnosis included metastasis, plasmacytoma, and lymphoma. While these findings are very suggestive of LCH, this diagnosis was never entertained given the patient's age. All further laboratory work was negative, and surgical excision of the lesion was performed.

Hematoxylin-and-eosin-stained sections of the lesion show a piece of skull with a lytic center involved by extensive fibrosis and a mixed infiltrate, including eosinophils, many putative benign reactive lymphocytes, and smaller numbers of larger cells with moderate-to-abundant eosinophilic cyto-

plasm and grooved lobulated nuclei. The larger eosinophilic cells with grooved nuclei are strongly positive for CD163, S100 protein, and CD1a. BRAF (p.V600E) is negative by immunohistochemistry (Fig. 3). The final diagnosis is LCH.

Given the unusual diagnosis of LCH, the patient was referred to medical oncology. Staging 18-Fluorodeoxyglucose/CT and postoperative radiographs revealed no residual disease or distant metastasis (Fig. 4). In addition, BRAF testing was negative. Given gross total resection of the isolated calvarial disease and lack of BRAF mutation, no further treatment was suggested and observation was recommended.

Discussion

LCH is a rare neoplastic disorder of proliferation of Langerhans-type myeloid dendritic cells that can affect individual or multiple organs. This rare disease predominantly affects the pediatric population [1]. The disease is even less common in adults with an annual incidence of 1-2 cases per million [2]. The International Registry of the Histiocyte Society case series of 274 adult patients with LCH, the largest to date, estimates the mean age of onset in adults at diagnosis is 35 years in females and 33 years in males (with standard

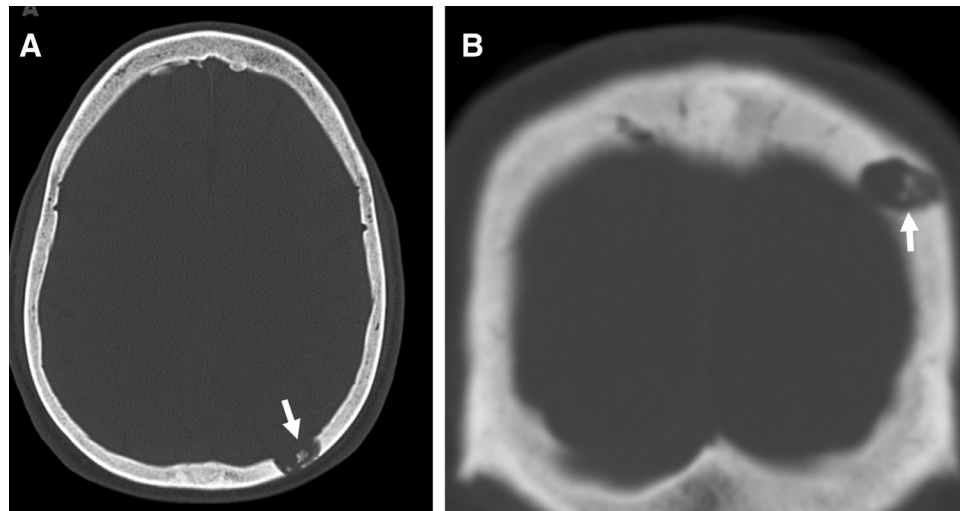


Fig. 2 – Noncontrast enhanced bone window CT demonstrates a lytic lesion within the left parietal bone; (A) Axial bone window image shows unequal involvement of the inner and outer calvarial tables with a bony sequestrum; (B) coronal bone window image shows an associated bony sequestrum within the lesion.

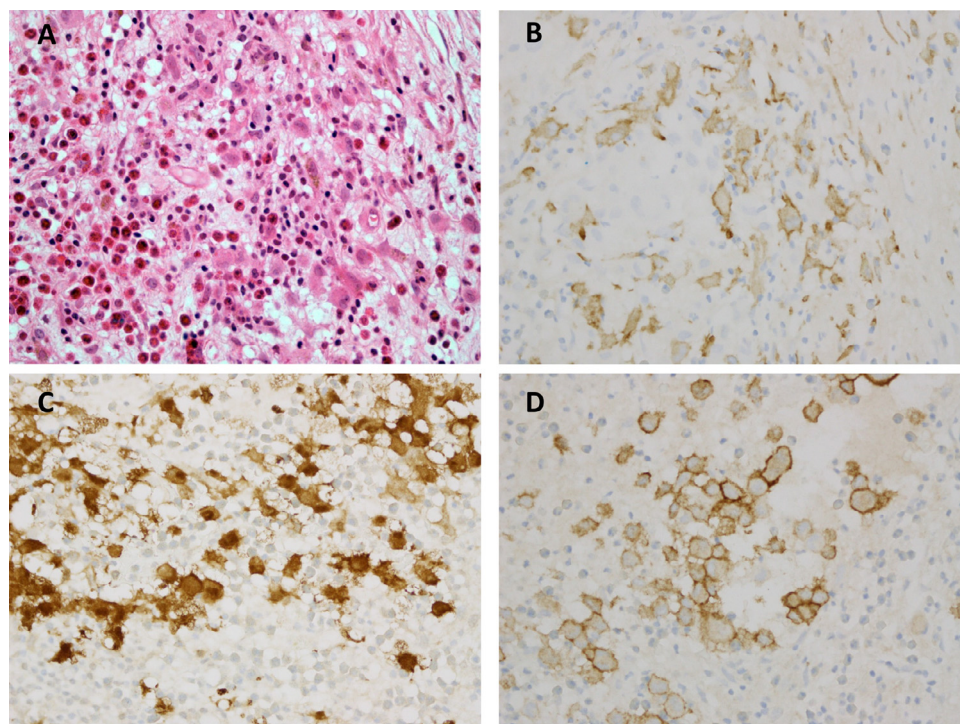


Fig. 3 – Hematoxylin and eosin-stained section (A) and immunohistochemistry for CD163 (B), S100 (C), and CD1a (D) confirms the diagnosis of LCH.

deviation of 14 and 15 years, respectively), suggesting that presentation above the age of 50 is an exception [3]. However, the true incidence of the disease in patients above 50 years remains unknown.

Solitary organ system involvement of the disease in adults is estimated to be present in fewer than 50% of patients [3,4]. After lungs, the skeletal system is the second most commonly involved solitary organ; however, an isolated calvarial lesion

is exceedingly rare and to our knowledge has not been reported in the radiology literature in patients older than 90 years. Chiong et al reported a case of isolated skull LCH in a 41-year-old and reviewed the literature, detecting only 4 similar cases with the oldest being 56-years-old [5].

The pathophysiology of LCH is still unclear with an ongoing debate regarding its etiology. One theory suggests that LCH is a neoplastic disease based on the observation that a high

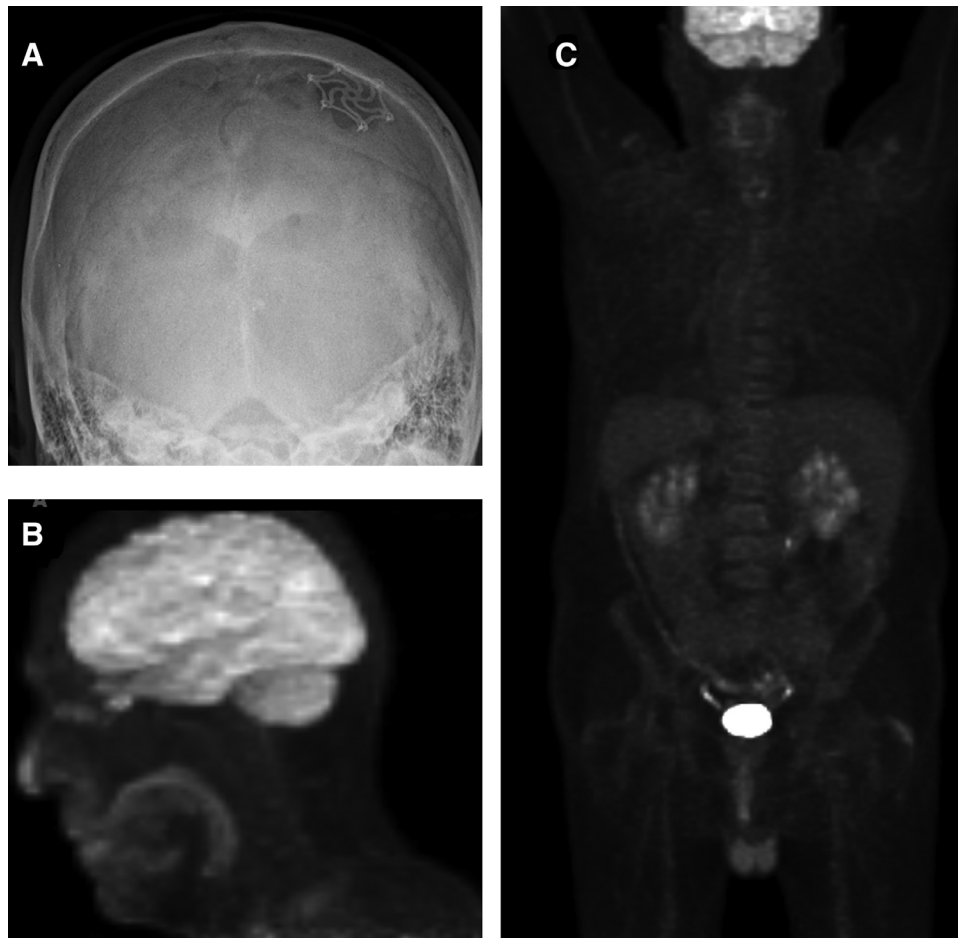


Fig. 4 – Postoperative radiographs and PET/CT demonstrate no residual disease. (A) A radiographic posterior-anterior view shows postoperative changes without local recurrence; (B,C) PET, Minimum intensity projections (MIP), shows no residual disease in the calvarium (B, left sagittal MIP projection) or additional sites of disease (C, whole body frontal projection).

percent of LCH lesions are positive for oncogenic BRAF V600E mutation [6]. Alternatively, other studies argue that LCH is a disease of immune dysfunction and that LCH lesions develop secondary to genetic alterations resulting in increased recruitment and activation of immune cells (regulatory T lymphocytes, eosinophils, and plasma cells) [7,8].

Radiological findings of osseous LCH can sometimes mimic other benign or malignant tumors as well as infections [9]. Our case demonstrated typical CT and MRI imaging findings of osseous LCH as the CT showed unequal involvement of the inner and outer tables, consistent with a beveled-edge lesion. Furthermore, the lytic lesion contained a fragment of intact bone, sometimes referred to as “button sequestrum” in LCH skull lesions. The MRI also demonstrated heterogeneous but mostly hyperintense T2 and Fluid-attenuated inversion recovery (FLAIR) signal, diffuse enhancement, and extension/involvement of the underlying dura, features that are all considered typical for LCH skull lesion. Unlike lesions involving other bones, LCH skull lesions are characterized by lack of periosteal reaction, which was also observed in our case [10]. Additionally, a common central nervous system (CNS) manifestation of LCH is infiltration of the posterior pituitary gland

(radiologically appreciated as loss of the normal posterior pituitary bright spot and thickening of the pituitary stalk), but this radiological sign was not present in our patient. Despite the classical imaging findings, the diagnosis remained elusive, given the exceptional age group and was only achieved with tissue sampling. Our case suggests that, while exceptionally rare, LCH can be included in the differential diagnosis of isolated skull lesions in adults if the imaging features are classical.

In adults, the most common differential diagnoses of a solitary solid lesion breaching the cortex includes lymphoma, single metastatic lesion, and plasmacytoma; whereas the differential of multiple skull lesions includes multiple metastases, multiple myeloma, leukemia, and lymphoma. Besides the characteristic radiological appearance of LCH lesions described above, LCH can be distinguished from other differential diagnoses by histologic and immunohistochemical examination. Classically, LCH histologic findings are characterized as a clonal cellular proliferation of mononuclear cells with an interspersed inflammatory component, characteristically eosinophils. By immunohistochemistry, LCH cells are positive for CD1a, and S100 and negative for CD21 and CD35.

The choice of treatment for skull LCH depends on the number of lesions (unifocal vs multifocal disease), and the involvement of extra-skeletal systems. Watchful observation or surgical excisions are usually performed for solitary skull lesions. Other therapeutic options, including local radiotherapy and systemic chemotherapy, could be utilized in cases of more extensive disease. In our case, the staging 18-Fluorodeoxyglucose/CT and postoperative radiographs revealed no residual disease or distant metastasis. Therefore, no further systemic treatment was indicated.

Conclusions

Although extremely rare, clinicians should consider LCH in the differential diagnosis of isolated skull lesions in the elderly with classical radiological appearance. In our patient, CT and MR imaging showed a solitary beveled-edge lytic lesion of the left parietal bone with T2/FLAIR signal hyperintensity and diffuse enhancement. Histology and immunohistochemistry confirmed LCH diagnosis, and in the absence of other lesions, surgical excision was a sufficient therapeutic measure.

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