Langerhans cell histiocytosis (LCH). Case series

Eduardo Nehemías Chún Ajxup M.D.
Iveth Sarahí Amador Rosa M.D.
Estuardo Emmanuel Ruiz Gramajo M.D.
Marvin Adolfo Santizo Gramajo M.D.
José Carlos Echeverría Solís M.D.

Quetzaltenango, Guatemala

Case Report

Plastic Surgery

OPEN ACCESS

Background: Langerhans cell histiocytosis (LCH) is a rare clonal neoplasm characterized by the proliferation of dendritic cells resembling Langerhans cells. Clinical presentations range from isolated osseous lesions to multisystemic disease involving risk organs. To present and analyze clinical cases of LCH, highlighting the role of radiological findings in differential diagnosis and clinical classification. Pediatric patients with cranial and long bone lesions, described. Imaging studies revealed lytic lesions with cortical erosion and soft-tissue infiltration. Definitive diagnosis was achieved through biopsy and immunohistochemistry (CD1a, langerin, S100). Radiology is essential for early detection and diagnostic orientation, although findings are not pathognomonic. The integration of imaging with clinical and pathological data allows differentiation of LCH from other pediatric entities and supports appropriate therapeutic management. LCH remains a diagnostic challenge due to its rarity and diverse manifestations. The dissemination of case reports contributes to expanding medical knowledge and emphasizes the importance of radiology in clinical practice.

Keywords: Langerhans cell histiocytosis; radiology; bone lesions.

Langerhans cell histiocytosis (LCH) is a rare clonal neoplasm characterized by the proliferation of dendritic cells with a phenotype similar to Langerhans cells. Its incidence is estimated at 2–5 cases per million children annually, although it can occur at any age. Somatic mutations in the MAPK pathway, particularly BRAF V600E, explain its neoplastic behavior and the wide clinical heterogeneity observed.

Clinical manifestations vary according to the number of organs involved. Unifocal forms often present as painful osseous lesions, especially in the skull and long bones, whereas multisystemic disease may affect the liver, spleen, bone marrow, or lungs, with a poorer prognosis. In this context, radiology plays a pivotal role in early detection and classification. Radiographs and computed tomography typically reveal lytic lesions with cortical erosion and extension into soft tissues. Magnetic resonance imaging provides superior assessment of meningeal or intracranial involvement. In pulmonary disease, high-resolution CT demonstrates reticulonodular patterns and bilateral cystic changes, which are highly suggestive but not pathognomonic.

Definitive diagnosis requires biopsy and immunohistochemistry, with markers such as CD1a, langerin, and S100. Nevertheless, recognition of imaging features is essential for guiding the differential diagnosis against other pediatric bone or pulmonary lesions, ensuring timely classification and appropriate therapeutic decisions. Given its rarity and diverse presentations, LCH remains a diagnostic and therapeutic challenge, underscoring the importance of case reports and series that expand current knowledge and highlight the radiological perspective in clinical practice.

Case 1

A 2-year-old male patient was admitted to the Pediatric Emergency Department, due to gingival bleeding of approximately 12 hours duration, with no history of trauma. His mother reported unquantified fever, irritability, generalized jaundice, and seropurulent discharge from the left ear. Physical examination revealed pallor, desquamative lesions on the scalp, temporal, occipital, and bilateral inguinal lymphadenopathy, as well as palpable hepatosplenomegaly. Vital signs were stable and whitin normal range and laboratory studies showed severe anemia (Hb 5.3 g/dL, Hct 16.5%), leukocytosis, and thrombocytosis. Peripheral smear demonstrated microcytic hypochromic anemia, and coagulation times were prolonged. Skin biopsy revealed atypical histiocytes and acantholysis, while lymph node biopsy demonstrated loss of architecture with extensive infiltration by large atypical histiocytic cells. The clinical and histopathological findings were compatib le with multisystem Langerhans cell histiocytosis.

Case 2

A 2-year-old male patient with no significant medical history presented with a clinical course spanning several months, initially characterized by swelling in the right parietal region. Imaging studies revealed multiple osteolytic cranial lesions as described therefore; consequently, he underwent a right craniectomy with placement of prosthetic material and a biopsy was performed. Histopathological and immunohistochemical analyses showed findings consistent with Langerhans cell

From the Radiology Department at Hospital Regional de Occidente, Quetzaltenango, Guatemala. Received on August 19, 2026. Accepted on August 25, 2026. Published on August 27, 2026.

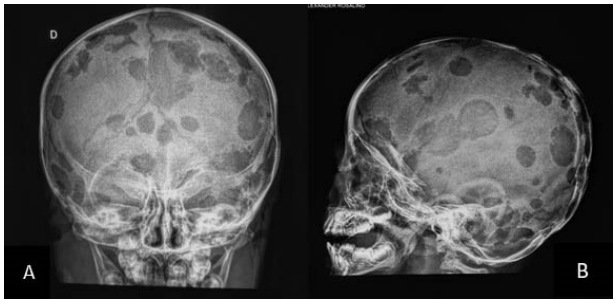

Figure 1. The following anteroposterior (A) and lateral (B) skull radiographs show multiple osteolytic lesions diffusely distributed throughout the cranial vault; these present well-defined sclerotic margins without periosteal reaction, giving them a "punched-out" appearance.

histiocytosis (LCH). A diagnosis of multisystem LCH was subsequently established after hepatic involvement was identified during the disease staging workup. This case involves multisystem LCH with cranial bone and hepatic involvement; the patient is undergoing chemotherapy and is being monitored clinically and radiologically to assess therapeutic response and the progression of previously identified lesions, alongside periodic monitoring of hepatic and hematological function during treatment.

Case 3

A 5-year-old boy, with no relevant medical history, presented with a four-month history of bone pain and swelling involving the right side of the skull. Initially, he developed a painful mass in the right parietal region and subsequently another palpable lesion in the right frontal region. He had no fever, weight loss, visual disturbances, or neurological symptoms. Physical examination revealed two firm, tender prominences without significant skin changes. Computed tomography and conventional x-ray of the skull demonstrated two well-defined osteolytic lesions involving the right frontal and parietal bones, with focal extension into the extracranial soft tissues and no evidence of intracranial involvement. Radiologic evaluation of the remaining skeleton showed no relevant additional lesions, and staging studies

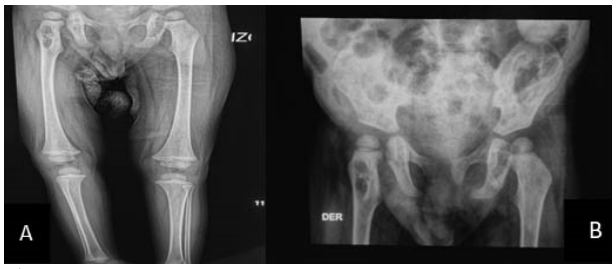

Figure 2. The following anteroposterior radiographs of both lower limbs (A) and the pelvis (B) show multiple unilocular osteolytic lesions with well-defined, sclerotic margins and no periosteal reaction, diffusely distributed throughout both iliac bones and the metaphysis of the right femur.

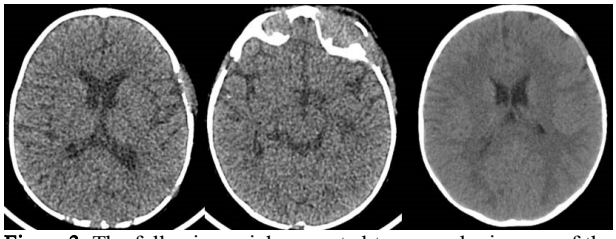

Figure 3. The following axial computed tomography images of the brain reveal multiple osteolytic, punched-out lesions lacking a sclerotic rim, with full-thickness bone destruction involving all bones of the skull.

revealed no visceral involvement. Biopsy of one lesion demonstrated an infiltrate of Langerhans cells with numerous eosinophils. Immunohistochemistry was positive for CD1a, S100, and langerin. Because multiple lesions were confined exclusively to the skull, the diagnosis of multifocal monostotic cranial Langerhans cell histiocytosis was established.

Discussion

Langerhans cell histiocytosis (LCH) is a rare clonal proliferative disorder of dendritic cells characterized by activation of the mitogen-activated protein kinase (MAPK) pathway, most commonly through BRAF V600E and MAP2K1 mutations. Although historically considered an inflammatory disease, current evidence supports its classification as an inflammatory myeloid neoplasm. Skeletal involvement represents the most common manifestation of single-system disease, accounting for nearly 80% of pediatric cases and a substantial proportion of adult presentations. Nevertheless, isolated osseous LCH remains uncommon in adults and frequently poses a diagnostic challenge because of its nonspecific clinical and radiological appearance.

The radiological manifestations of osseous LCH are highly variable and largely depend on the

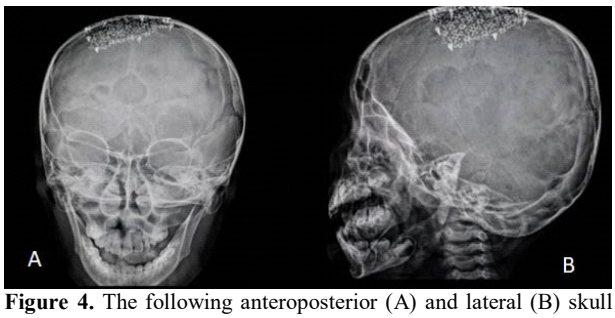

Figure 4. The following anteroposterior (A) and lateral (B) skull radiographs reveal multiple osteolytic lesions diffusely distributed throughout the cranial vault; these present well-defined sclerotic margins without periosteal reaction, giving them a "punched-out" appearance. Additionally, in the right parietal region, there is evidence of a cranioplasty with prosthetic material in proper position, showing no findings suggestive of periosteal reaction.

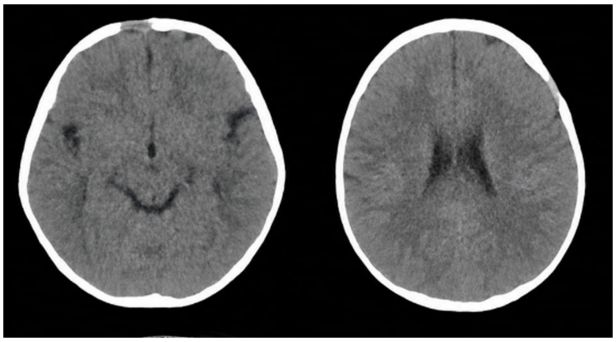

Figure 5. The following non-contrast axial CT images reveal a well-defined, beveled-edge lytic lesion in the frontal region measuring 2.1 x 1.3 cm; another lesion with similar characteristics is also observed in the left frontoparietal region adjacent to the coronal suture, measuring 2.8 x 1.5 cm. These findings represent lytic lesions consistent with Langerhans cell histiocytosis.

anatomical location, stage of disease, degree of cortical destruction, and associated soft tissue involvement. Consequently, imaging findings often overlap with those of infectious, inflammatory, and neoplastic conditions, making histopathological confirmation essential.

Conventional radiography remains the initial imaging modality for evaluating suspected bone lesions. The classic radiographic appearance consists of a sharply marginated osteolytic lesion without internal mineralized matrix. Depending on lesion chronicity, the margins may range from well-defined to permeative, and cortical thinning or destruction may be present. Characteristic findings have been described in specific locations, including beveled-edge calvarial lesions caused by asymmetric destruction of the inner and outer tables, vertebra plana resulting from complete collapse of the vertebral body with preservation of adjacent intervertebral discs, and floating teeth secondary to alveolar bone destruction in mandibular involvement. Although these imaging features are suggestive, they are not pathognomonic.

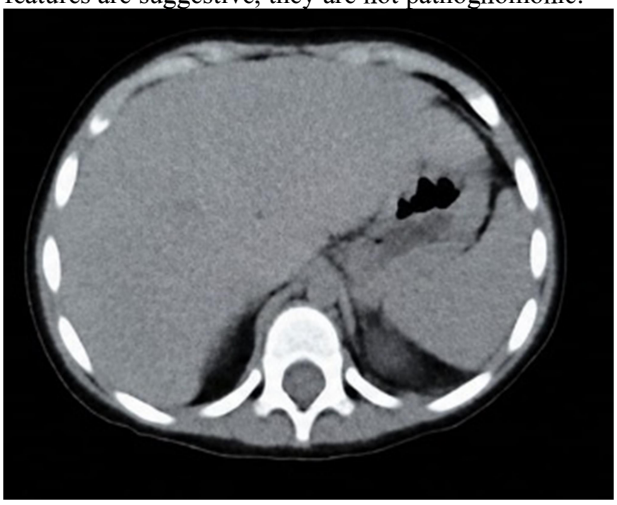

Figure 6. The following axial computed tomography images show a liver of normal shape and density, with no evidence of masses or intrahepatic bile duct dilation. The liver is enlarged, with the right lobe measuring 9.8 cm, consistent with hepatomegaly.

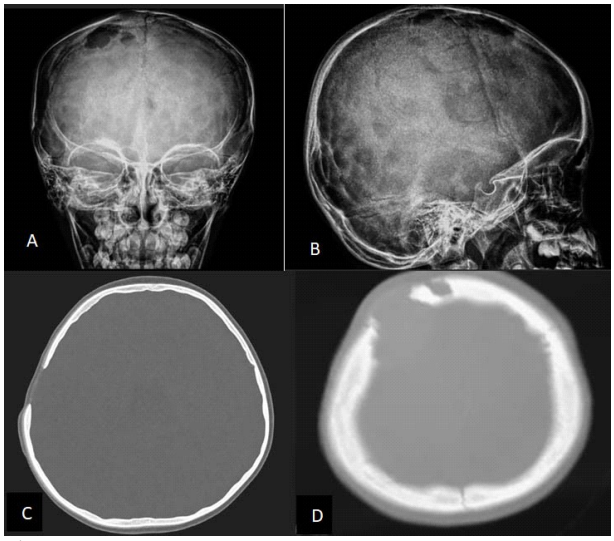

Figure 7. A decrease in calvarial bone density is observed in these AP (A) and lateral (B) views, with multiple radiolucent osteolytic lesions showing relatively well-defined margins; some exhibit a geographic appearance and multifocal distribution, predominantly in the parietal and frontal regions. Sames as see in TC axial views (C, D), the lesions involve the structure of the cranial table, with areas of apparent cortical discontinuity. The osteolytic lesions of the cranial vault are more clearly identified on the lateral view (B), with some presenting a "punched-out" appearance. No evident pattern of aggressive periosteal reaction is observed. Cranial sutures are identifiable and show no significant displacement.

Computed tomography (CT) provides superior spatial resolution for evaluating cortical integrity, trabecular architecture, and the extent of osseous destruction. CT is particularly valuable for lesions involving complex anatomical regions such as the skull base, facial bones, spine, pelvis, and ribs. Typical findings include geographic lytic defects with cortical breakthrough, endosteal scalloping, and occasional periosteal reaction. Multiplanar reconstructions facilitate assessment of cortical breach and adjacent soft tissue extension while providing essential information for biopsy planning and surgical management. In anatomically challenging locations, CT also allows accurate evaluation of neurovascular relationships and potential complications.

Magnetic resonance imaging (MRI) represents the most sensitive modality for evaluating bone marrow infiltration and extraosseous disease extension. The signal characteristics of LCH lesions are relatively consistent, typically demonstrating low-to-intermediate signal intensity on T1-weighted sequences and intermediate-to-high signal intensity on T2-weighted and STIR images due to replacement of normal fatty marrow by cellular inflammatory tissue. Following intravenous gadolinium administration, lesions usually exhibit intense and relatively homogeneous enhancement, reflecting their rich vascular supply and inflammatory cellularity. MRI is particularly useful for detecting adjacent soft tissue masses, muscle involvement, neurovascular

compression, and epidural extension in spinal lesions. Diffusion-weighted imaging may reveal restricted diffusion secondary to increased cellular density, although overlap with malignant tumors limits its diagnostic specificity.

Whole-body imaging has become increasingly important in the evaluation of patients with LCH. ^18F-fluorodeoxyglucose positron emission tomography/computed tomography (^18F-FDG PET/CT) has emerged as an essential imaging modality for staging, identification of clinically occult lesions, assessment of multisystem involvement, and monitoring therapeutic response. Compared with conventional skeletal surveys, PET/CT demonstrates greater sensitivity for detecting metabolically active lesions and may alter clinical staging by identifying additional sites of disease. Furthermore, decreasing FDG uptake after therapy has been shown to correlate with treatment response and disease remission, making PET/CT an increasingly valuable tool during follow-up.

Despite these advances, no imaging modality alone can establish a definitive diagnosis of osseous LCH. The radiological differential diagnosis is broad and varies according to patient age and lesion location. In pediatric patients, considerations include osteomyelitis, Ewing sarcoma, aneurysmal bone cyst, osteoblastoma, and metastatic neuroblastoma, whereas in adults metastatic disease, lymphoma, plasmacytoma, multiple myeloma, giant cell tumor, and primary malignant bone tumors become increasingly relevant. Therefore, correlation between clinical presentation, imaging findings, and histopathological examination remains indispensable.

Histopathological confirmation continues to represent the diagnostic gold standard. Microscopically, lesions are composed of characteristic Langerhans cells with abundant eosinophilic cytoplasm and nuclei displaying longitudinal grooves, admixed with numerous eosinophils and variable inflammatory infiltrates. Immunohistochemical positivity for CD1a, Langerin (CD207), and S100 protein confirms the diagnosis, while molecular testing may identify activating mutations within the MAPK pathway, particularly in patients considered for targeted therapies.

Management strategies are determined by disease extent, lesion location, symptoms, and multisystem involvement. Solitary osseous lesions may be managed successfully with curettage, limited surgical excision, intralesional corticosteroid injection, or careful observation in selected patients because spontaneous regression has been reported. Conversely, multifocal skeletal disease and multisystem involvement frequently require systemic therapy. More recently, molecular characterization has led to the introduction of BRAF and MEK inhibitors, which have demonstrated encouraging results in refractory or recurrent disease harboring activating MAPK pathway mutations.

The two patients presented in this report illustrate the diagnostic challenges associated with isolated osseous LCH. In both cases, imaging initially suggested a broad spectrum of differential diagnoses because of the nonspecific appearance of the osteolytic lesions. Nevertheless, careful multimodality evaluation enabled accurate characterization of lesion morphology, cortical involvement, marrow replacement, and adjacent soft tissue extension, facilitating appropriate biopsy planning and definitive diagnosis. These cases further emphasize the complementary roles of radiography, CT, MRI, and histopathology in establishing the diagnosis and guiding patient management.

From a radiological perspective, awareness of LCH is essential because early recognition may substantially influence clinical decision-making. Although imaging findings are rarely pathognomonic, the combination of a solitary lytic lesion, cortical destruction without aggressive periosteal reaction, marrow replacement on MRI, avid contrast enhancement, and the absence of a mineralized matrix should prompt consideration of LCH within the differential diagnosis, particularly in younger patients. Familiarity with these imaging characteristics may reduce diagnostic delays, avoid unnecessary extensive surgical procedures, and facilitate timely multidisciplinary management.

Conclusion

Langerhans cell histiocytosis remains a diagnostic and therapeutic challenge due to its rarity and broad clinical spectrum. Radiology plays a pivotal role, enabling the detection of lytic bone lesions with cortical erosion, soft-tissue extension, and, in pulmonary cases, reticulonodular patterns and bilateral cystic changes. Although these findings are not pathognomonic, they guide the differential diagnosis against other pediatric conditions and support accurate clinical classification. Definitive diagnosis requires biopsy and immunohistochemistry; however, the early integration of imaging findings facilitates timely management and multidisciplinary care. The publication of case reports and series remains crucial to expand current knowledge of this disease and to strengthen evidence-based medical practice.

Conflicts of interests

The authors declare that there are no financial, personal, or institutional conflicts of interest that could have influence the work reported in this manuscript.

Acknowledgements

We thank the Hospital Regional de Occidente for its support of the Radiology Department, providing the necessary supplies and equipment for the prompt diagnosis of patients.

References

1. Sato A, Kobayashi M, Yusa N, Ogawa M, Shimizu E, Kawamata T, et al. Clinical and prognostic features of Langerhans cell histiocytosis in adults. Cancer Sci. 2023;114(9):3687-3697. doi:10.1111/cas.15879.
2. Javadi T, Hill C, McLemore ML, Oskouei S, Bahrami A. Adult-onset Langerhans cell histiocytosis of bone: A case series highlighting a rare entity. Ann Diagn Pathol. 2023;66:152171. doi:10.1016/j.anndiagpath.2023.152171.
3. Han HX, Chang L, Lang M, Lin H, Li J, Duan MH, et al. Clinical characteristics, genomic profiling and outcomes of single system multifocal Langerhans cell histiocytosis in adults with bone involvement. Blood Cancer J. 2023;13(1):135. doi:10.1038/s41408-023-00913-8.
4. Goyal G, Acosta-Medina AA, Abeykoon JP, Dai C, Ravindran A, Vassallo R, et al. Long-term outcomes among adults with Langerhans cell histiocytosis. Blood Adv. 2023;7(21):6568-6578. doi:10.1182/bloodadvances.2023010706.

Iveth Saraí Amador Rosa
Radiology Department
Hospital Regional de Occidente
Quetzaltenango, Guatemala