

Multisystem Langerhans Cell Histiocytosis Presenting with Spontaneous Pneumothorax and Osteolytic Lesions: A Case Report

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Case Report

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Abstract

Langerhans cell histiocytosis (LCH) is a rare myeloid neoplasm characterized by a highly heterogeneous clinical presentation, ranging from localized osseous lesions to multisystem disease involving high-risk organs. We report the case of a two-year-old girl who presented with persistent fever, dyspnea, and irritability. Initial chest radiography demonstrated a diffuse bilateral reticulonodular pulmonary pattern. During hospitalization, she developed a spontaneous right-sided pneumothorax associated with complete right lung atelectasis. Chest computed tomography revealed multiple bilateral pulmonary cystic lesions, while radiographs of the skull and long bones demonstrated multiple well-defined osteolytic lesions without periosteal reaction. The diagnosis of Langerhans cell histiocytosis was confirmed by histopathological examination. Despite intensive supportive management, the patient died seven days after admission because of severe pulmonary involvement. This case highlights the pivotal role of diagnostic imaging in the early recognition of multisystem LCH and underscores the importance of considering this entity in pediatric patients presenting with cystic lung disease accompanied by lytic bone lesions, as prompt diagnosis may facilitate appropriate management and improve clinical outcomes.

Introduction

Langerhans cell histiocytosis (LCH) is a rare myeloid neoplasm characterized by the clonal proliferation and accumulation of abnormal dendritic cells expressing the immunophenotypic markers of epidermal Langerhans cells. Originally described under several distinct entities, including Letterer-Siwe disease, Hand-Schüller-Christian syndrome, and eosinophilic granuloma of bone, these disorders were unified by Alfred Lichtenstein in the mid-20th century under the term Histiocytosis X, recognizing their shared pathological hallmark of atypical histiocytes accompanied by a dense inflammatory infiltrate.

LCH is diagnosed predominantly during early childhood, with an estimated incidence of four to eight cases per million children annually, reaching its highest frequency between one and three years of age. Although considerably less common in adults, the disease follows a different clinical course in this population, most often presenting as isolated pulmonary involvement that is strongly associated with cigarette smoking.

The clinical spectrum of LCH is remarkably broad, ranging from solitary, self-limited osteolytic lesions to aggressive multisystem disease involving high-risk organs such as the bone marrow, liver, and spleen. Recognizing this clinical heterogeneity, together with the underlying molecular mechanisms, is essential for establishing an accurate diagnosis through immunohistochemical confirmation, including CD1a and langerin (CD207) expression, and for guiding current therapeutic strategies, which range from conventional chemotherapy to targeted therapies directed against the MAPK signaling pathway.

Case Presentation

A two-year-old girl was brought to Hospital Regional de Occidente San Juan de Dios with a five-day history of persistent fever, dyspnea, and irritability. On admission, she weighed 12 kg and measured 82 cm in height. Her vital signs included a temperature of 37.5°C, a respiratory rate of 35 breaths per minute, a heart rate of 140 beats per minute, a blood pressure of 90/80 mmHg, and an oxygen saturation of 45% on room air. Physical examination revealed a critically ill, lethargic child with absent breath sounds over the right hemithorax and crackles and wheezing throughout the left hemithorax.

Initial laboratory investigations revealed a white blood cell count of $10.28 \times 10^3/\mu\text{L}$ with neutrophil predominance (61%), a hemoglobin level of 9.5 g/dL, a hematocrit of 31.8%, and a platelet count of $277 \times 10^3/\mu\text{L}$.

As part of the initial diagnostic workup, a chest radiograph was obtained, demonstrating a diffuse bilateral reticulonodular pattern (Fig. 1).

Owing to progressive clinical deterioration, follow-up chest radiography was performed and revealed a spontaneous right-sided pneumothorax associated with complete right lung atelectasis (Fig. 2).

Subsequent chest computed tomography confirmed these findings and further demonstrated multiple bilateral air-filled cystic lesions throughout both lungs (Fig. 3).

Given the coexistence of cystic lung disease and spontaneous pneumothorax in a pediatric patient, the diagnostic evaluation was expanded to include radiographs of the skull and long bones. These studies demonstrated multiple well-defined, rounded osteolytic lesions without periosteal reaction involving the skull and long bones (Figures 4 and 5), findings highly suggestive of Langerhans cell histiocytosis.

The diagnosis was subsequently supported by cytopathological examination of a bronchial lavage specimen, which demonstrated chronic granulomatous inflammation and positive S100 immunostaining. The patient required admission to the intensive care unit because of severe respiratory compromise, where she underwent mechanical ventilation and placement of a chest tube for the management of the pneumothorax. Despite aggressive supportive care, her clinical condition continued to deteriorate, and she died seven days after hospital admission because of extensive pulmonary involvement.

Discussion

Langerhans cell histiocytosis (LCH) is a rare myeloid neoplasm that predominantly affects children and exhibits a highly heterogeneous clinical presentation. Disease manifestations range from isolated, self-limited lesions to aggressive multisystem involvement affecting high-risk organs. This clinical variability often delays diagnosis, particularly when pulmonary manifestations predominate.

Several case series have shown that multisystem LCH in pediatric patients may present with pulmonary involvement, osteolytic bone lesions, and, less commonly, spontaneous pneumothorax secondary to rupture of pulmonary cysts. Our patient exhibited all of these features, including diffuse cystic lung

disease, a spontaneous right-sided pneumothorax, and multiple osteolytic lesions involving the skull and long bones. This constellation of imaging findings strongly suggested the diagnosis before histopathological confirmation. In contrast to isolated pulmonary LCH, which occurs predominantly in adult smokers, pulmonary disease in children is usually part of multisystem involvement and is associated with a more aggressive clinical course, particularly when high-risk organs are affected.

Current evidence indicates that LCH is driven by constitutive activation of the mitogen-activated protein kinase (MAPK/ERK) signaling pathway in myeloid precursor cells. Approximately 50%–60% of patients harbor the BRAF V600E mutation, whereas mutations involving MAP2K1, BRAF insertions or deletions, and other components of the MAPK pathway account for most remaining cases. Although LCH is now classified as a myeloid neoplasm, the abundant inflammatory infiltrate observed within lesions explains many of its clinical and pathological features. Neoplastic cells constitute only a minority of the lesion but promote recruitment of eosinophils, lymphocytes, and macrophages through the release of pro-inflammatory cytokines, leading to tissue destruction and osteolytic bone lesions.

Bone involvement remains the most common manifestation of LCH and typically presents as well-defined osteolytic lesions affecting the skull, long bones, ribs, pelvis, and vertebrae. Pulmonary involvement, although uncommon in children, is characterized radiologically by bilateral nodules and cysts that may progress to spontaneous pneumothorax following cyst rupture. Recognition of this imaging pattern is particularly important because the coexistence of diffuse cystic lung disease and multifocal osteolytic lesions considerably narrows the differential diagnosis and should prompt consideration of LCH.

Management depends on the extent of disease at presentation. Solitary bone lesions are often self-limited and may be treated with curettage, intralesional corticosteroids, or observation, whereas multisystem disease generally requires systemic chemotherapy. Current Histiocyte Society protocols recommend vinblastine combined with prednisone as first-line therapy for multisystem LCH. Unfortunately, despite intensive care support, mechanical ventilation, and chest tube placement for management of the pneumothorax, our patient experienced progressive respiratory failure and died seven days after admission, underscoring the poor prognosis associated with severe pulmonary involvement in pediatric multisystem disease.

This case emphasizes the pivotal role of diagnostic imaging in the early recognition of multisystem LCH. The combination of diffuse bilateral pulmonary cysts, spontaneous pneumothorax, and multiple osteolytic lesions represents a characteristic radiologic pattern that should immediately raise suspicion for this diagnosis. Early recognition of these findings may expedite histopathological confirmation, facilitate timely initiation of appropriate therapy, and potentially improve clinical outcomes.

Declarations

Consent

Written informed consent was obtained from the patient's legal guardian for publication of this anonymized case report and the accompanying clinical and radiological images. All identifying information has been omitted to preserve patient confidentiality.

Disclosures

Human subjects: This case report was conducted using anonymized clinical information obtained during routine medical care. According to institutional policy, the use of de-identified clinical data for academic and research purposes is permitted through the general informed consent signed at the time of hospital admission.

Conflicts of interest: The authors have declared that no competing interests exist.

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References

1. Astigarraga I, García-Obregón S, Pérez-Martínez A, Gutiérrez-Carrasco I, Santa-María V, Rodríguez-Vigil Iturrate C et al (2022) Histiocitosis de células de Langerhans. *An Pediatr (Barc)*. ;97(2): 130.e1-130.e7. 10.1016/j.anpedi.2022.05.002
2. National Cancer Institute Langerhans Cell Histiocytosis Treatment (PDQ®)–Health Professional Version [Internet]. Bethesda (MD): National Cancer Institute; 2010 [cited 2026 Aug 25]. Available from: <https://www.cancer.gov/types/langerhans/hp/langerhans-treatment-pdq>
3. Medina MÁ, Meyer W, Echeverri C, Builes N (2021) *Biomédica* 41(3):396–402. 10.7705/biomedica.5430. Histiocitosis de células de Langerhans: reporte de caso y revisión de la literatura
4. Tillotson CV, Reynolds SB, Patel BC Langerhans Cell Histiocytosis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 [cited 2026 Aug 25]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK430885/>
5. Emile JF, Ablu O, Fraitag S, Horne A, Haroche J, Donadieu J et al (2016) Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. *Blood* 127(22):2672–2681. 10.1182/blood-2016-01-690636
6. Fu Z, Li H, Arslan ME, Ells PF, Lee H (2021) Hepatic Langerhans cell histiocytosis: a review. *World J Clin Oncol* 12(5):335–341. 10.5306/wjco. v12.i5.335

Figures



Figure 1

chest radiograph demonstrating a diffuse bilateral reticulonodular pulmonary pattern

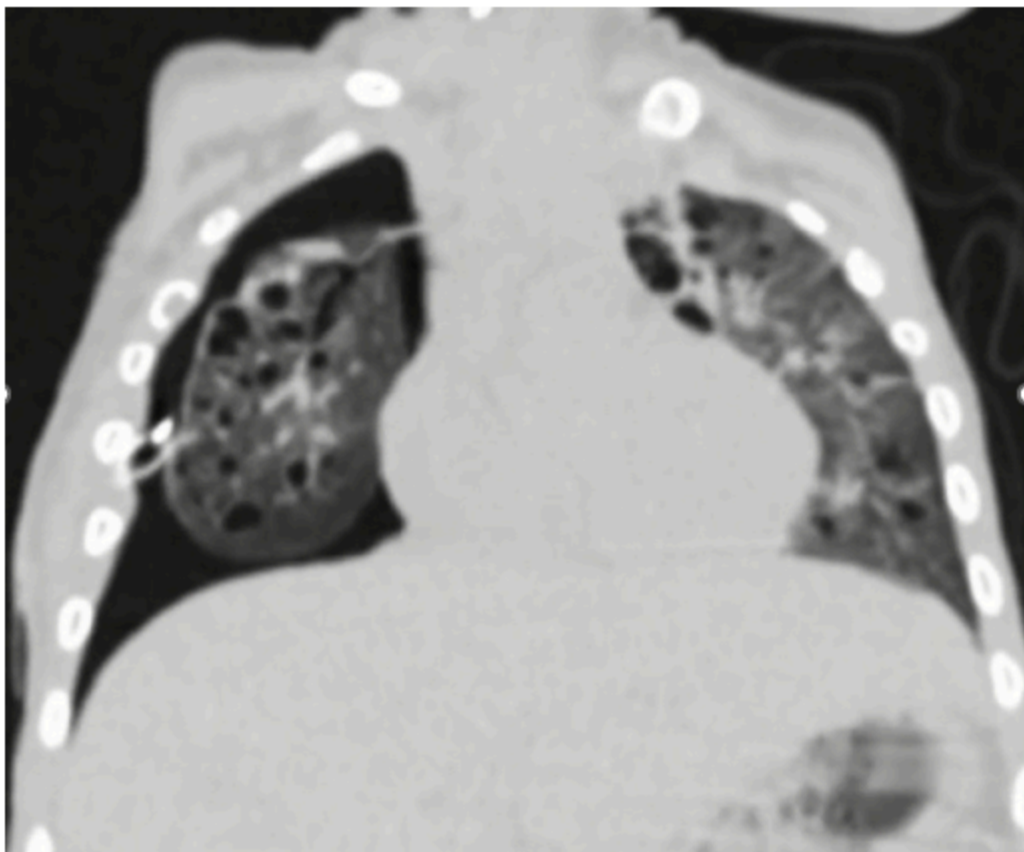


Figure 2

follow-up chest radiograph showing a right-sided spontaneous pneumothorax with complete right lung atelectasis.

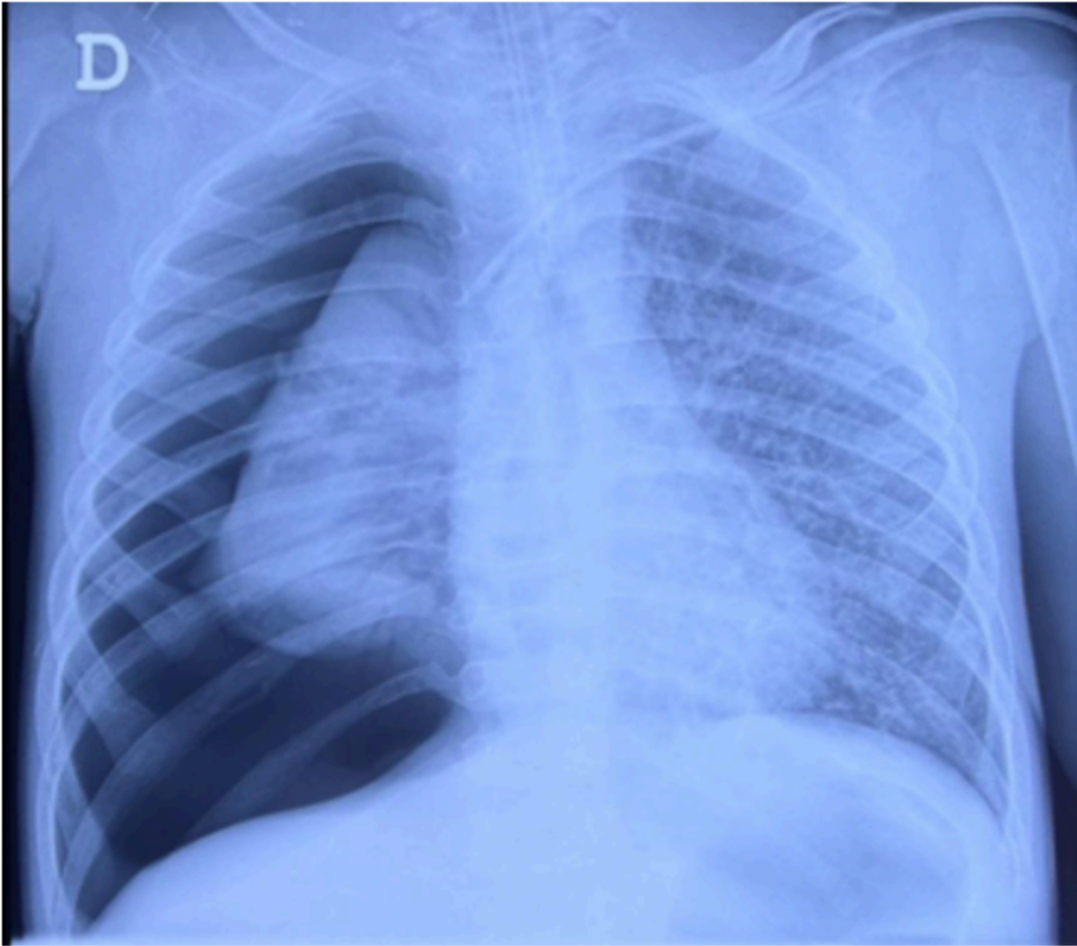


Figure 3

coronal chest CT demonstrating multiple bilateral thin-walled pulmonary cysts, associated with a right-sided pneumothorax and complete right lung atelectasis

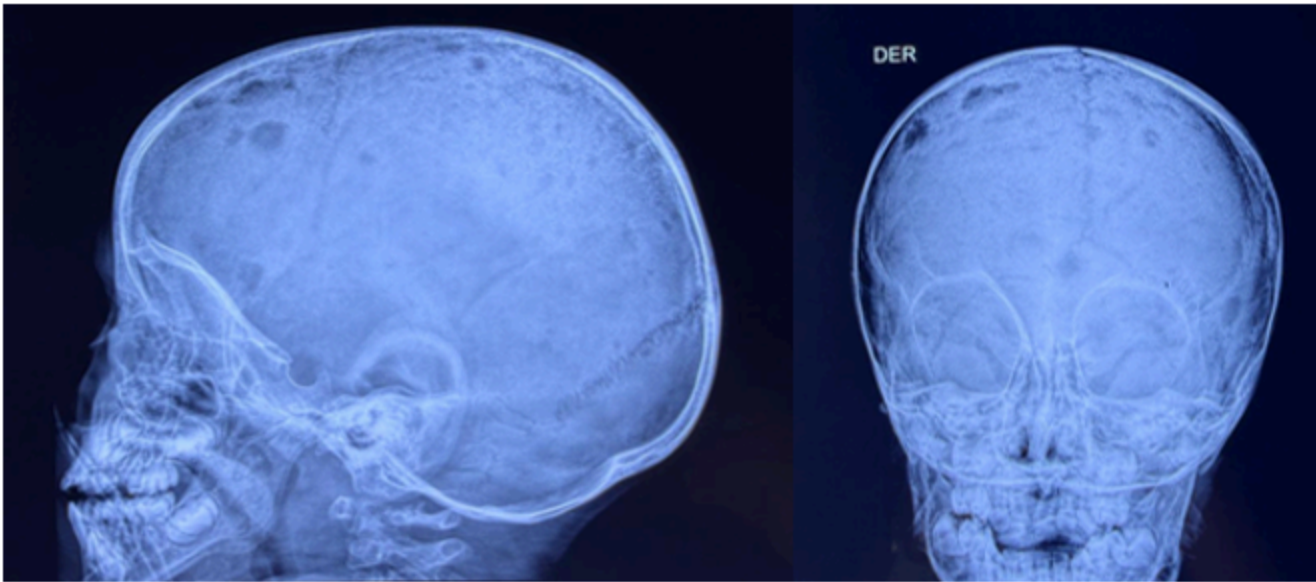


Figure 4

skull radiographs demonstrating multiple well-defined osteolytic lesions without periosteal reaction.

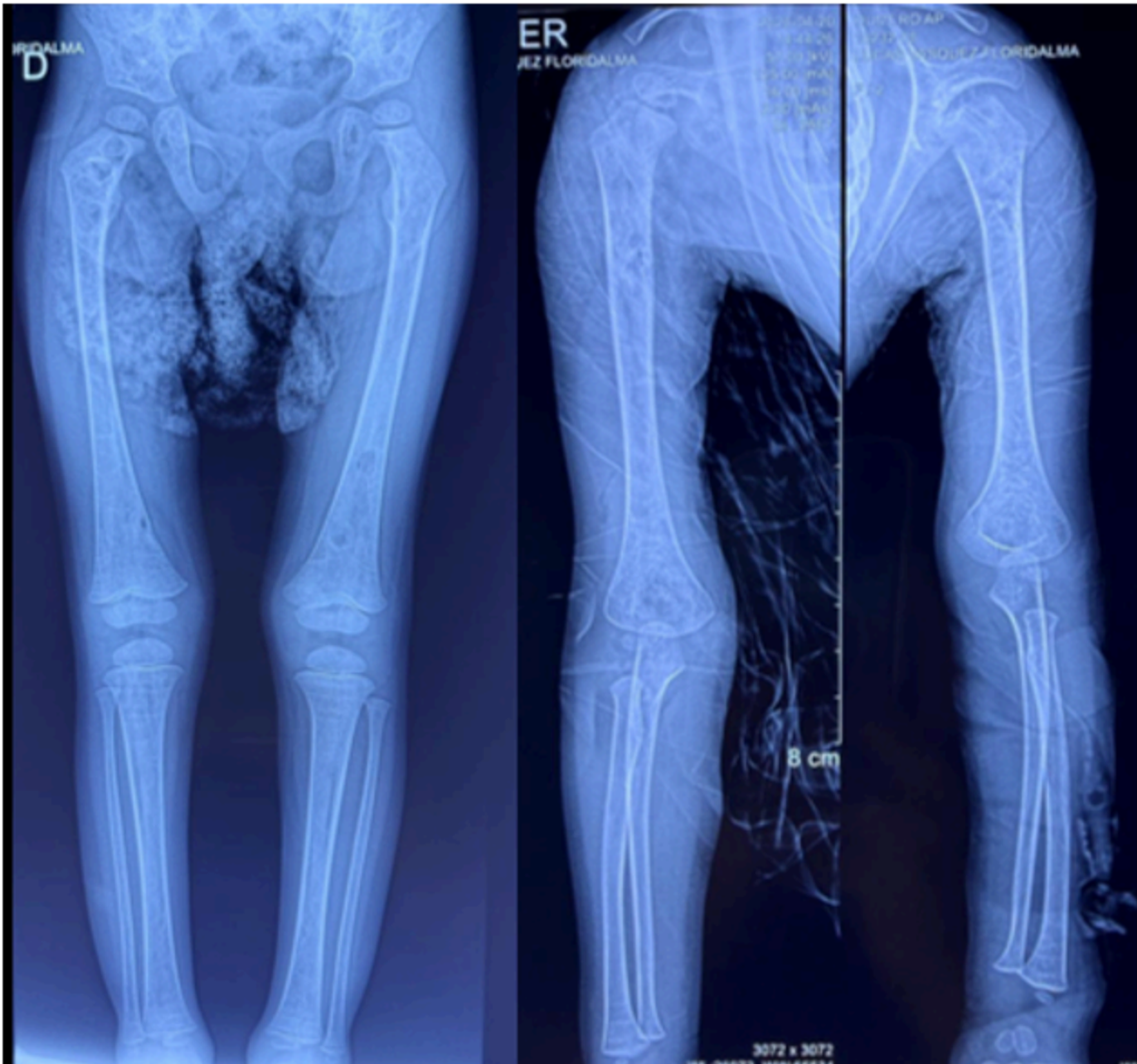


Figure 5

long-bone radiographs demonstrating multiple well-defined osteolytic lesions without periosteal reaction.