Clin. Lab. 2026;72:XXX-XXX

CASE REPORT

A case Report of Pulmonary Langerhans Cell Histiocytosis in a Child

Ziyin Huang *, Zuoxin Deng *, Fang Lan, Lifang Nong, Chunyun Fu

** Ziyin Huang and Zuoxin Deng contributed equally to this study and should be considered as co-first authors*
Department of Clinical Laboratory, Maternal and Child Health Care of Guangxi Zhuang Autonomous Region, Nanning, Guangxi Zhuang Autonomous Region, China

SUMMARY

Background: **Langerhans cell histiocytosis (LCH) is a clonal neoplastic disorder characterized by the aberrant proliferation of CD1a+/CD207+dendritic cells that infiltrate tissues and organs, resulting in organ dysfunction.**
Methods: **This case report describes a 2-year-old boy who presented with abdominal pain and fever. The etiology was ultimately confirmed through clinical symptoms, imaging studies, pulmonary histopathological examination, and genetic testing.**
Results: **The final diagnosis was pediatric pulmonary Langerhans cell histiocytosis (PLCH).**
Conclusions: **Although pulmonary involvement is not classified as a high-risk in consensus guidelines, PLCH requires diagnostic consideration in children presenting with persistent respiratory symptoms and recurrent fever.**
(Clin. Lab. 2026;72:xx-xx. DOI: 10.7754/Clin.Lab.2025.250761)

Correspondence:
Chunyun Fu
Department of Clinical Laboratory
Maternal and Child Health Care of
Guangxi Zhuang Autonomous Region
Guangxi Zhuang Autonomous Region
530000, Nanning
People's Republic of China
Phone/Fax: +86 0771-5807372
Email: fuchunyun2008@sina.com

Case Report accepted August 3, 2025

KEYWORDS

langerhans cell histiocytosis, children, lungs

CASE PRESENTATION

A 2-year-and-11-month-old boy presented to the emergency department with a 2-week history of recurrent paroxysmal periumbilical abdominal pain and a 4-day history of fever. The parents reported no obvious precipitating cause for the abdominal pain. One week prior to presentation, during hospitalization at a local hospital, abdominal color Doppler ultrasound revealed hepatomegaly with diffuse hepatic lesions and abnormal echo nodules of undetermined nature. Ultrasound examination of the inguinal, cervical, and axillary lymph nodes was unremarkable. Chest CT demonstrated multiple thin-walled cystic and solid nodules in both lungs and diffuse patchy low-density shadows in the liver, suggestive of LCH. The patient was subsequently transferred to the emergency department of Guangxi Maternal and Child Health Hospital for diagnostic confirmation and further management. Based on the provided outside hospital records, the admitting physician's provisional diagnosis was 1) Suspected LCH, 2) Infectious fever, 3) Hepatic impairment, and the child was admitt-

ed.

Physical examination revealed a child with normal physical development, moderate nutritional status, and a clear level of consciousness with an appropriate mental state. Multiple small (approximately 0.5 cm x 0.5 cm), soft, non-tender, mobile cervical lymph nodes were palpated. Lung auscultation revealed bilateral coarse breath sounds without crackles or wheezes. The abdomen was soft, non-distended, non-tender, with no palpable masses or guarding. The liver edge was palpable approximately 3 cm below the costal margin; the spleen was not palpable. The neurological examination was unremarkable. No other significant findings were noted.

Laboratory tests on admission revealed a complete blood count showing white blood cells (WBC) 10.6 x 10^9/L, hemoglobin (Hb) 114 g/L, platelets (PLT) 491 x 10^9/L (↑), lymphocytes 21.1% (↓), neutrophils 71.4% (↑), and C-reactive protein (CRP) 27.84 mg/L (↑). Serological and biochemical analyses revealed the following elevated parameters: procalcitonin (PCT) 0.63 ng/mL↑, alanine aminotransferase (ALT) 32 U/L↑, aspartate aminotransferase (AST) 71 U/L↑, γ-glutamyltransferase (GGT) 962 U/L↑, lactate dehydrogenase (LDH) 407 U/L↑, α-hydroxybutyrate dehydrogenase (HBDH) 292 U/L↑, alpha-fetoprotein (AFP) 1.43 ng/mL (normal), carbohydrate antigen 125 (CA125) 16.80 U/mL (normal), carbohydrate antigen 153 (CA153) 26.94 U/mL↑, carbohydrate antigen 199 (CA199) 35.7 U/mL↑, and carcinoembryonic antigen (CEA) 1.73 ng/mL (normal). The bone marrow cytomorphological analysis revealed markedly active bone marrow hyperplasia, with significant proliferation of both granulocytic and erythroid lineages. Megakaryocytes were adequate in number and morphologically normal. No Langerhans cells were identified.

Upon admission, the pediatric patient exhibited persistent recurrent fever, reaching a maximum temperature of 39.5℃, accompanied by productive cough with audible rattling breath sounds and nasal discharge. To assess the pulmonary status, clinicians ordered a follow-up CT scan (Figure 1).

Considering the clinical manifestations and diagnostic findings, LCH was strongly suspected. To confirm the diagnosis, the patient underwent both liver biopsy and lung biopsy procedures. The pathological examination of the lung tissue biopsy revealed the following microscopic findings: Lesion cells were distributed in sheets and nests adjacent to small airways, characterized by abundant lightly eosinophilic cytoplasm, reniform (kidney-shaped) nuclei, and nuclear grooves, against a background of eosinophil-lymphocyte infiltration - findings consistent with LCH (Figure 2).

Supplementary molecular profiling was performed synchronously. The results of BRAFV600E gene detection in pathological tissues were as follows in Table 1.

Based on integrated lung biopsy histopathology and molecular genetic testing, the patient was definitively diagnosed with LCH. In accordance with the LCH GROUP1 protocol, treatment was initiated with a regimen of prednisone, vinblastine, and cytarabine. To date, the patient has completed the second course of chemotherapy. Clinical status remains favorable with stable hematologic parameters and significant improvement in liver function.

DISCUSSION

LCH is a rare disorder characterized by clonal proliferation of myeloid-derived dendritic cell precursors. It occurs across all ages, with an annual incidence of 2 - 5 per million children under 15 years (peak: 1 - 3 years). Commonly involved sites include bone, skin, pituitary, liver/spleen, hematopoietic system, lungs, lymph nodes, and central nervous system (including pituitary; 2 - 4% additional CNS manifestations) [1].

While the pathogenesis of LCH remains incompletely elucidated, adult pulmonary LCH (PLCH) is strongly associated with tobacco smoke exposure. However, this pediatric case represents multisystem LCH (not isolated PLCH). Current evidence indicates that somatic BRAF mutations (identified in this patient) drive aberrant MAPK pathway activation in myeloid precursors. Although tobacco smoke can induce GM-CSF-mediated LC recruitment in adult airways [2], pediatric LCH pathogenesis is primarily mutation-dependent and unrelated to environmental toxins.

The BRAF proto-oncogene critically regulates the MAPK signaling cascade, driving cellular proliferation and survival. Its mutations constitutively activate this pathway, directly promoting tumor growth, invasion, and metastasis [3]. LCH is formally classified as a myeloid neoplasm based on 1) clonality of pathological cells, 2) high-frequency BRAF mutations, and 3) irreversible MAPK pathway activation [4].

The clinical manifestations of LCH demonstrate significant heterogeneity: 1) Cutaneous involvement in infants often mimics seborrheic dermatitis or eczema, with diagnostic confusion in 60% of cases. 2) Osseous lesions show dense Langerhans cell infiltrates initially; fibrosis develops later (reversing original error). 3) Nodal involvement features paracortical and sinusoidal expansion by CD1a+ cells. 4) Pulmonary LCH progresses from nodular Langerhans cell proliferation to end-stage cysts/fibrosis. 5) External auditory canal disease presents as granulomatous tissue with CD207+ cells, not hyperplasia. 6) Serous cavity involvement is exceedingly rare (< 0.5%), with only 8 validated CSF cases reported. Additionally, GI tract (15 - 30%), neonatal eyelids, and oral mucosa involvement remain underrecognized sites requiring immunohistochemical confirmation [5-8]. Early diagnosis using CD1a/Langerin staining is critical to prevent organ damage.

LCH is classified by the Histiocyte Society into single-system LCH (SS-LCH), multisystem LCH (MS-LCH), and MS-LCH with risk-organ involvement (RO+ MS-LCH), where the lungs are not designated as risk organs. Pulmonary involvement in LCH is termed PLCH

Table 1. Genetic testing identified a BRAF exon 12 mutation, specifically c.1399_1413del (p.N486_P490del), characterized as an in-frame deletion resulting in the loss of amino acids 486 - 490.

Detect content	Mutant gene	Mutation site	Source of mutation	Clinical significance
Genetic mutations	BRAF NM_004333.6	Exon12 c.1457_1471del p.N486_P490del	System variation	The mutation was clearly related to LCH

This mutation occurs within the protein kinase domain and is a clinically validated variant in LCH.

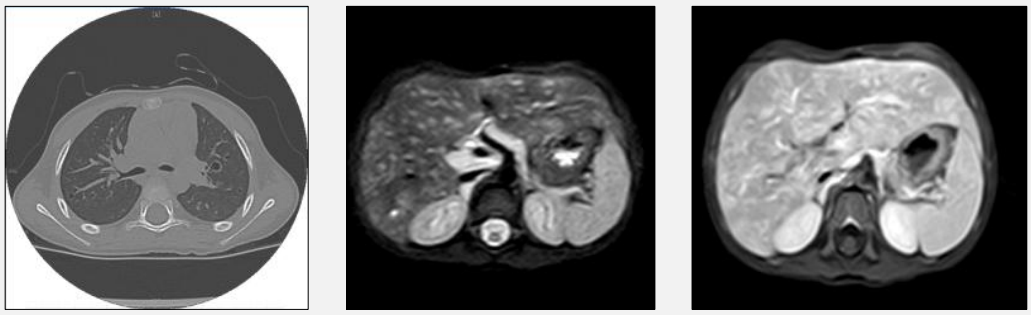

Figure 1. The CT imaging demonstrated: 1) Bilateral bronchial wall thickening with multiple parenchymal cysts; 2) Hepatomegaly with multiple hypodense lesions.

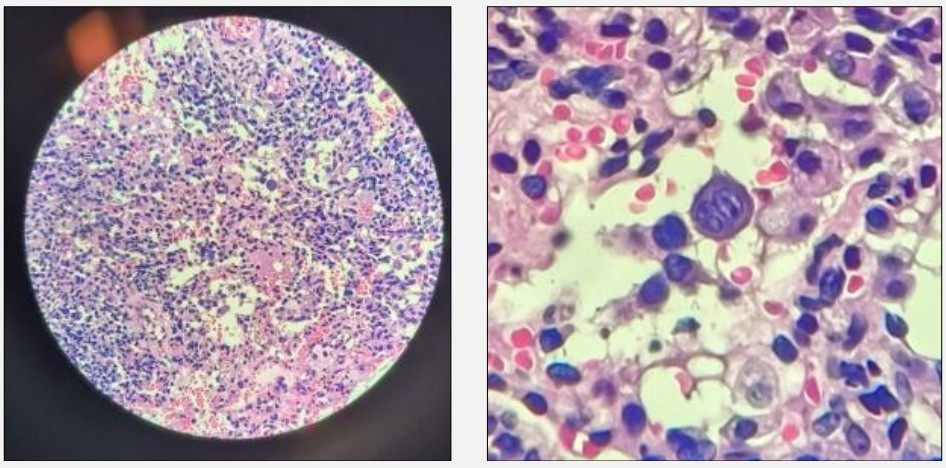

Figure 2. The lesion cells were distributed in sheets and nests.

The cytoplasm was abundant and pale, and the nucleus was kidney-shaped, coffee-bean like, with nuclear furrow.

(typically referring to isolated pulmonary disease). In this pediatric case, pathological involvement of both liver (a risk organ) and lungs classifies the condition as MS-LCH with risk-organ involvement.

Pulmonary involvement in LCH can occur in patients of any age, and its clinical manifestations lack absolute specificity, though early chest imaging is beneficial for detecting pulmonary lesions. Common imaging findings include: 1) thickened alveolar walls; 2) micronodules (less common); 3) ground-glass opacities; and 4) interstitial thickening. The pulmonary lesions primarily manifested in two forms, cystic lesions and reticular lesions. Cystic lesions are relatively characteristic of PLCH, presenting with various clinical symptoms upon onset, among which bilateral small cysts exhibit a relatively high incidence and larger lesion diameters. The cyst walls are generally thin, though thicker or nodular walls may occasionally be observed. Reticular pulmonary lesions are uncommon and represent end-stage manifestations. Patients with pulmonary involvement often develop complications due to factors such as multiple cystic lesions, as was also observed in this pediatric case.

LCH lacks specific laboratory markers. Imaging examinations such as CT and MRI can only suggest the extent of lesions and cannot directly confirm the diagnosis, posing significant challenges for physicians in achieving accurate LCH diagnosis. Pathological examination serves as the "gold standard" for diagnosing LCH [9].

Given the aggressive progression of pediatric PLCH, persistent recurrent fever combined with respiratory symptoms in children should raise clinical suspicion for possible PLCH. Although current expert consensus no longer classifies the lungs as high-risk organs for LCH involvement, this case is noteworthy as the diagnosis of PLCH was confirmed through lung tissue histopathological examination - a relatively uncommon occurrence. This case report aims to demonstrate how comprehensive evaluation - integrating clinical imaging features, histopathological biopsy, immunohistochemical staining, and genetic testing - ultimately established the diagnosis of Langerhans cell histiocytosis. It seeks to provide new diagnostic insights and improve early detection rates for LCH.

Declaration of Interest:

The authors declare that they have no conflict of interest.

References:

1. Morimoto A, Oh Y, Shioda Y, Kudo K, Imamura T. Recent advances in Langerhans cellhistiocytosis. Pediatr Int 2014;56(4): 451-61. (PMID: 24840547)

2. Radzikowska, E. Update on Pulmonary Langerhans Cell Histiocytosis. Front Med (Lausanne) 2020;7:582581. (PMID: 33763431)

3. Sconocchia T, Foßelteder J, Sconocchia G, Renish A. Langerhans cell histiocytosis: current advances in molecular pathogenesis. Front Immunol 2023;14:1275085. (PMID: 37965340)

4. Héritier S, Emile JF, Hélias-Rodzewicz Z, Donadieu J. Progress towards molecular-based management of childhood Langerhans cell histiocytosis. Arch Pediatr 2019;26(5):301-7. (PMID: 31281037)

5. Tommasino F, Cardamone C, Tortora V, Sabbatino F, Di Sarno C, Caputo A. Diagnosis of Langerhans cell histiocytosis on cytological examination of cerebrospinal fluid: Report of the first case. Diagn Cytopathol 2022;50(12):E377-E381. (PMID: 35950687)

6. Thapaliya I, Basnet B, Banjade DS, Kantha A, Mijar S. Gastrointestinal LCH: a rare manifestation of Langerhans cell histiocytosis. Ann Med Surg (Lond) 2024;86(11):6824-7. (PMID: 39525794)

7. Elhusseiny AM, Azhari JO, Kornhauser T, et al. Isolated eyelid neonatal Langerhans cell histiocytosis. Orbit 2025;44(1):82-6. (PMID: 38288964)

8. Cherian LM, Sasikumar D, Sathyan P, Varghese BE. Langerhans cell histiocytosis: A diagnostic enigma in the oral cavity. J Oral Maxillofac Pathol 2021;25(Suppl 1):S27-s31. (PMID: 34083966)

9. Tillotson CV, Reynolds SB, Patel BC. Langerhans Cell Histiocytosis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing 2025 Jan.2024 Apr 18. (PMID: 28613635)