Journal of Cardiothoracic Surgery

CASE REPORT Open Access

A case of diagnosis and treatment of mediastinal Langerhans cytosis

Yumeng Niu[1], Lei Xian[1*], Yi Wang[1], Yourong Chen[1], Yifei Lu[1] and Daying Liang[1]

Abstract

Background Langerhans cell histiocytosis (LCH) is a rare disease. It mainly involves abnormal proliferation and aggregation of Langerhans cells, a type of cell of the immune system.Langerhans cytosis is more common in the bone, but it has rarely been reported in the mediastinum.

Case presentation We present a case of mediastinal thymus tumor presented with Langerhans cell histiocytosis. A 40-year-old female patient presented with left chest and back pain in April 2024. Imaging revealed abnormal signal lesions on the patient's left rib and anterior superior mediastinum. The clinical diagnosis was bone destruction and mediastinal space occupation, and the postoperative pathological diagnosis was Langerhans cell histiocytosis.

Conclusions Langerhans cytosis is characterized by mediastinal and thymus occupation and is relatively rare in clinical practice. For patients who tolerate surgery for a single or local lesion, surgical removal of the primary lesion should be considered. However, for patients with multiple lesions or distant metastases, clinicians should evaluate whether surgery will benefit the patient. After surgical treatment, targeted therapy or immunotherapy should be performed.

Keywords Langerhans cell histiocytosis (LCH), Mediastinum, Thymus

Background

Langerhans cytosis is a rare disease in clinical practice, and moreover the exact pathogenesis of LCH is not fully understood at present, and some studies have shown that it may be related to genetics, immune regulation abnormalities, environmental factors and so on. In the diseased tissue of patients with LCH, Langerhans cells proliferate abnormally and aggregate, forming granulomatous lesions leading to organ dysfunction.

*Correspondence:
Lei Xian
15369308097@163.com
[1]Department of Cardiothoracic Surgery, The Second Affiliated Hospital of Guangxi Medical University, No.166 Da Xuedong Road Nanning Guangxi, Nanning Guangxi 530007, China

Case presentation

A 40-year-old female patient complained of increased chest and left back pain at the end of April 2024. Occasionally accompanied by chest tightness and fatigue, touch the pain site will aggravate the pain, the pain site has no obvious skin rupture, redness and swelling. Symptoms worsen at night, and the pain also causes the left upper limb to be unable to lift. The physical examination revealed no other abnormalities.After admission, there were 3 abnormalities in blood routine(Table 1). Bone marrow biopsy results showed no obvious tumor signs (Fig. 1). Other test results are within normal range. Lung function and cardiovascular tests were normal. Plain CT scan of the chest showed destruction of the left 6th rib, soft tissue shadow of the anterior mediastinum, and a high possibility of thymoma. (Fig. 2) Thoracic MRI showed destruction of the left 6th rib,

Table 1 Blood routine results were examined for the first time after admission

Project name	result	unit
WBC	10.34	10～9/L
RBC	4.70	10～12/L
HGB	141.00	g/L
PLT	429.00	10～9/L
NEU%	0.709	
LYM%	0.210	
MONO%	0.057	
EO%	0.019	
BISO%	0.005	
NEU	7.33	10～9/L
LYM	2.17	10～9/L
MONO	0.59	10～9/L
EOS	0.20	10～9/L
BISO	0.05	10～9/L
HCT	0.446	
MCV	94.90	fl.
MCH	30.00	pg
MSHC	316.00	g/L
PCT	0.392	
MPV	9.10	fl.
PDM	0.16	

possibly Langerhans histiocytosis, and abnormal signal focus in the anterior superior mediastinum, possibly thymoma or thymic hyperplasia. Pituitary MRI showed no abnormality.

According to the imaging data of the patient, in order to clarify the benign and malignant tumor and relieve the existing symptoms of the patient. The patient was treated surgically in early May with video-assisted thoracic surgery (VATS) to remove the mediastinal mass and the left 6th rib. The chest tube was placed at the surgical site and connected to an underwater seal, and the chest drainage tube was removed on the third postoperative day.

The patient recovered well after operation and was discharged successfully. The routine pathological results showed that both the thymus tumor and the rib mass were Langerhans cell histiocytosis, and there was no tumor involvement in the adipose tissue of the pericardium. Immunohistochemical results: tumor cells CK(Pan)(-), CD68(+), Langerin (+), CD1a (+), S-100(+), Ki-67(+, hot spot 5%)(Fig. 3) The result of BRAF gene V600E mutation was positive. Immunotyping by flow cytometry (ARMS-PCR) was negative(Fig. 4). After the surgery, the medical oncology and radiotherapy department consulted with the patient to recommend further

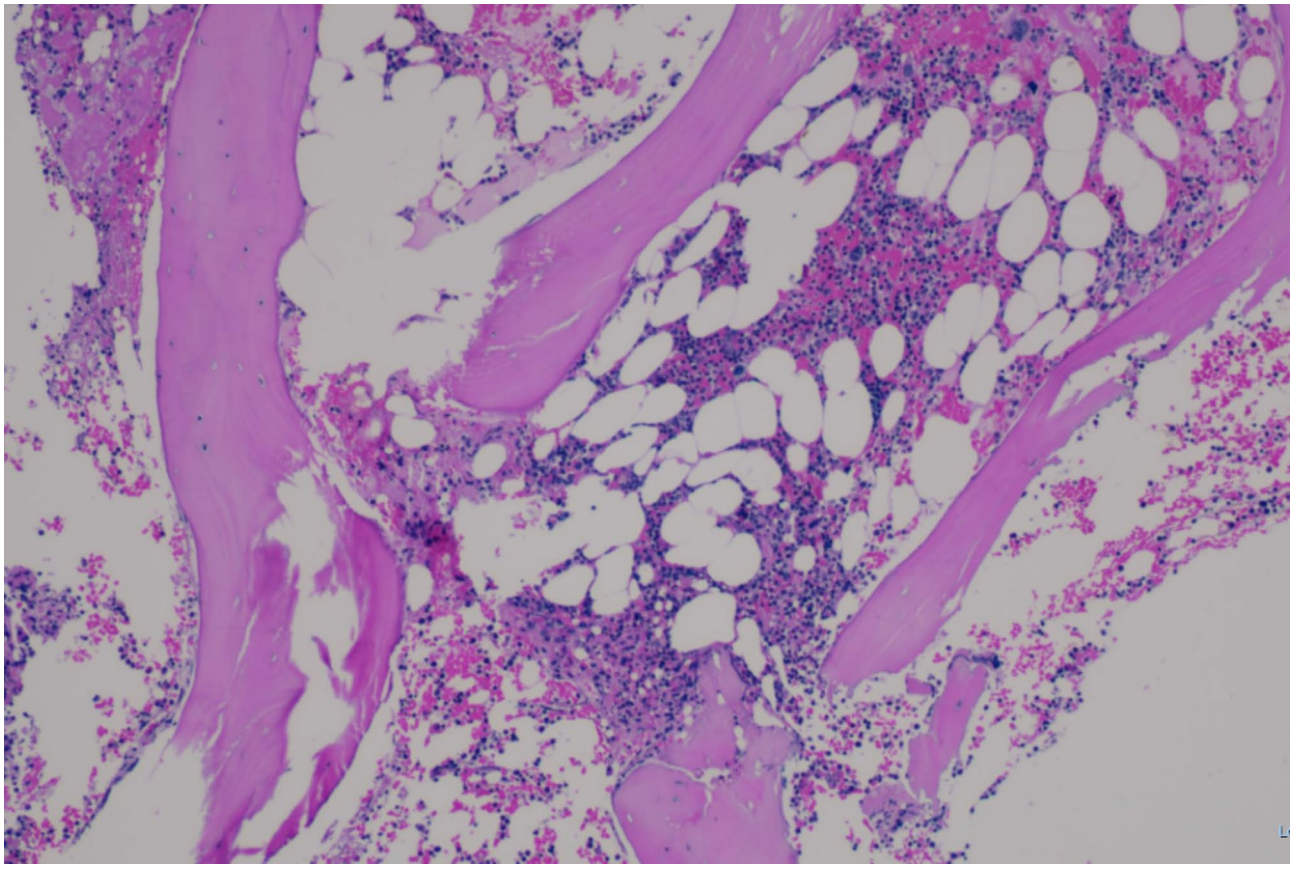

Fig. 1 The bone marrow biopsy results were negative and there were no obvious Langerhans cell signs

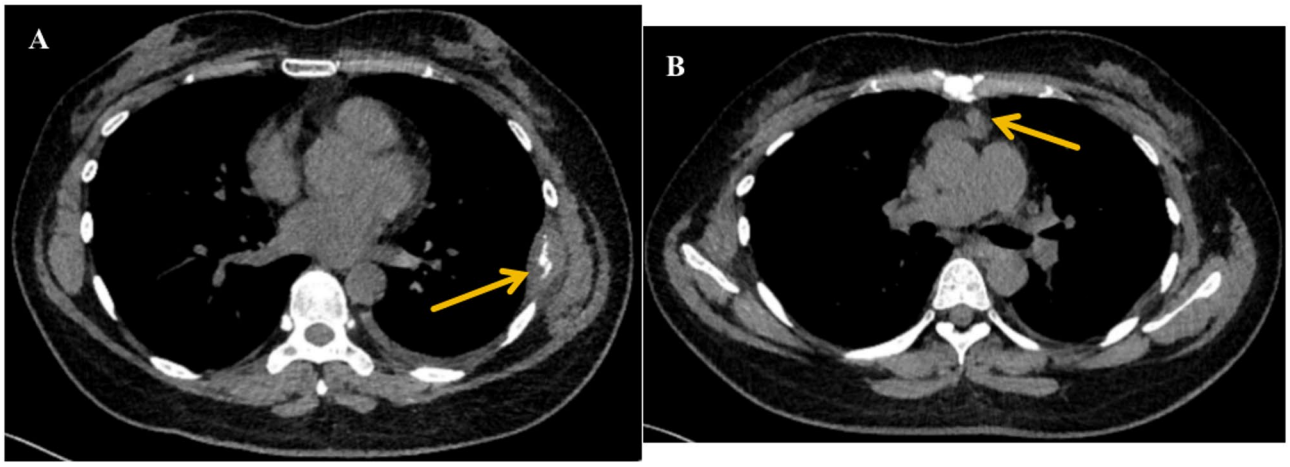

Fig. 2 **A**: Bone destruction in the left 6th rib, **B**: abnormal signal lesion in the anterior superior mediastinum。

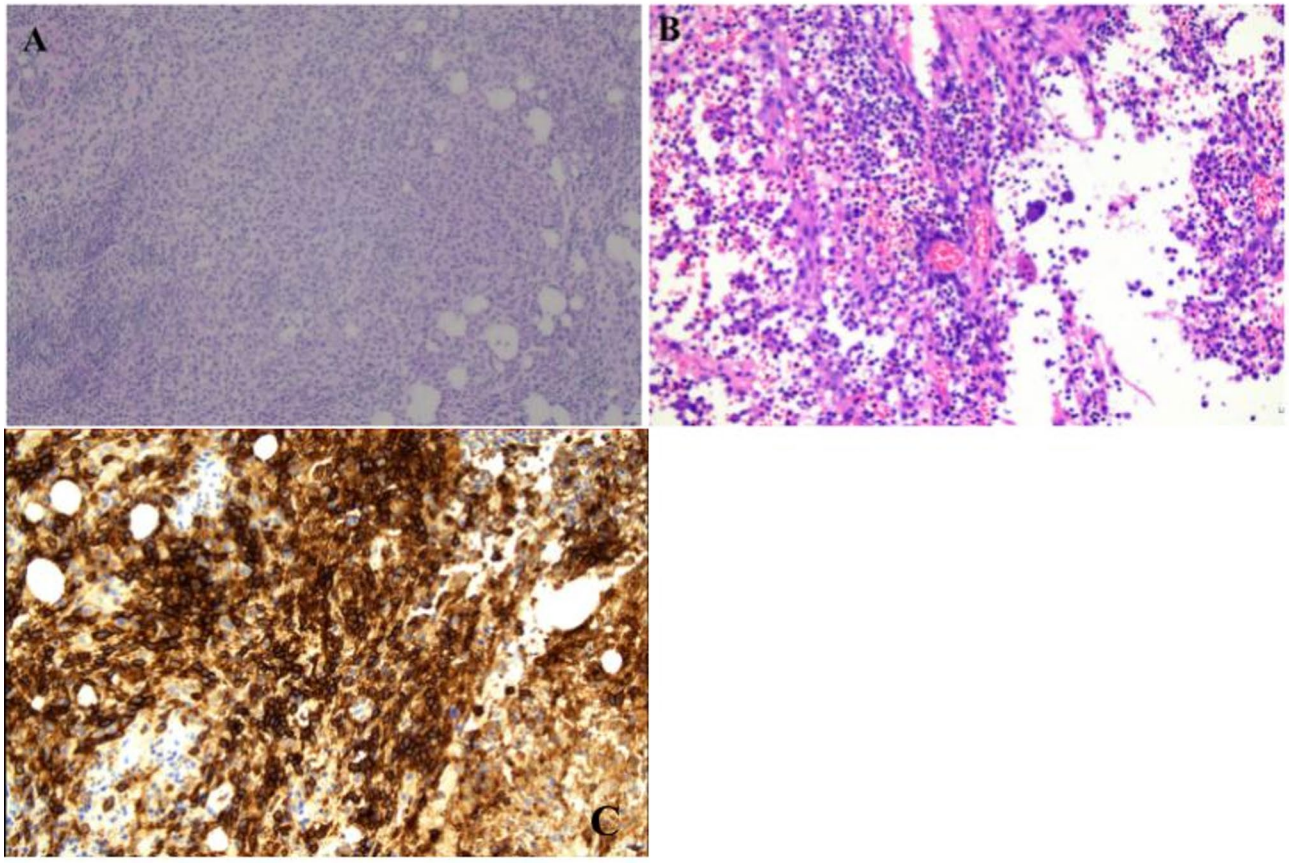

Fig. 3 **A**: thymus; **B**rib. The reaction of multinucleated giant cells in Langerhans cytosis can be seen.(H&E, 100); **C**: High resolution pathological section of thymus Langerhans cell hyperplasia

gene targeted therapy or immunotherapy based on the patient's accumulated multiple systems of Langerhans cell hyperplasia. The patient is currently receiving cytarabine therapy based on the BRAF gene V600E mutation [1].

Discussion and conclusion

Langerhans cytosis is uncommon clinically, especially in bone tissue. However, the exact pathogenesis of LCH is not fully understood, and some studies suggest that it may be related to genetic, immunomodulatory abnormalities, and environmental factors. In the diseased tissue of

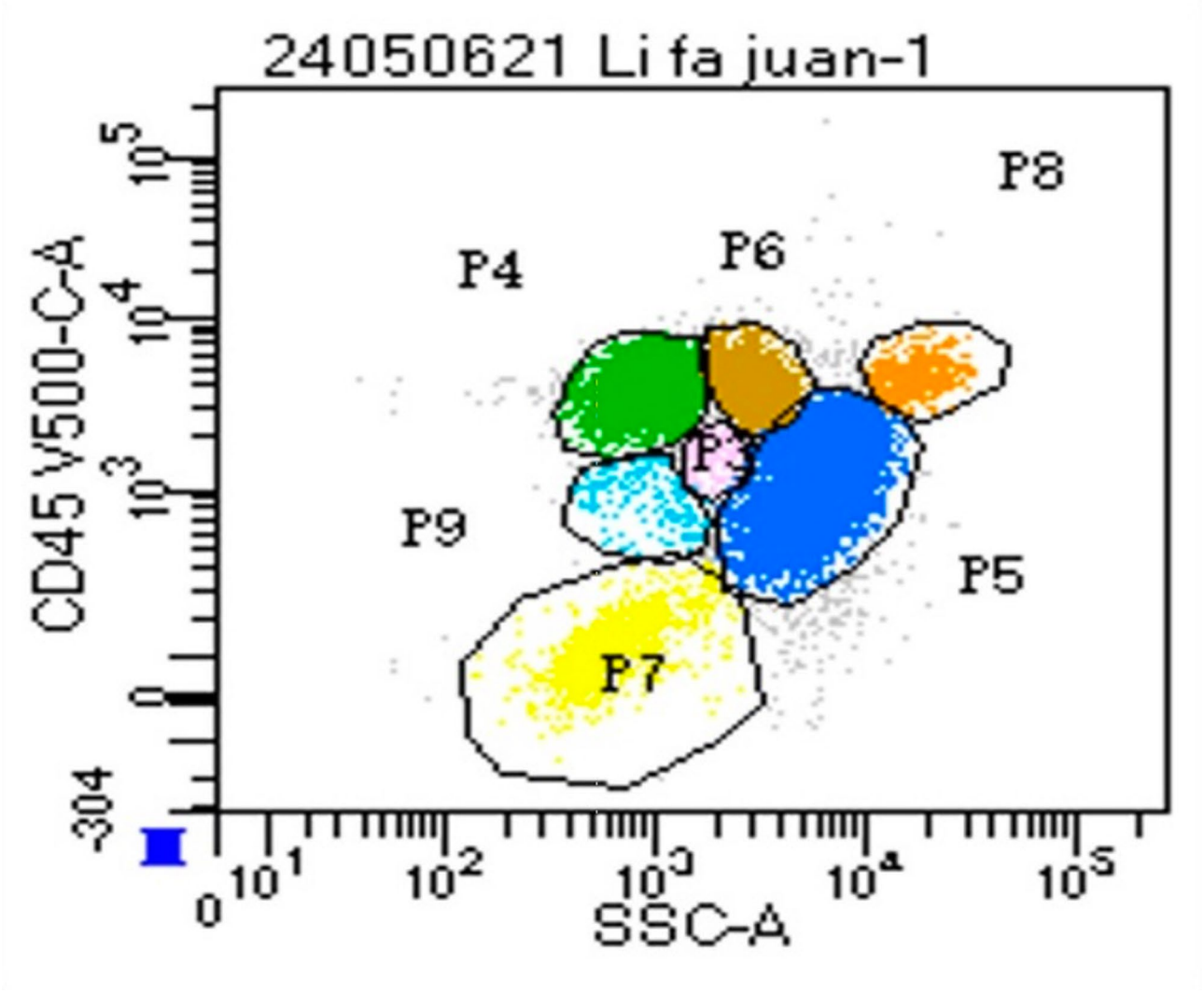

Fig. 4 Immunotyping results by flow cytometry (ARMS-PCR)

patients with LCH, Langerhans cells proliferate and accumulate abnormally, forming granulomatous lesions that lead to organ dysfunction.

In the past, LCH was divided into letter-siwe disease, HandSchuller-Christian disease and eosinophilic granuloma, but at present, it is mainly divided into single-system LCH (SS-LCH) and multi-system LCH (MS-LCH) according to the organs and systems affected. MS-LCH is particularly important。 Patients with organ involvement have a poor prognosis. The patient's examination showed that the rib was involved in addition to the thymus.The lesion involves multiple systems. However, throughout the diagnostic process, pathology and immunohistochemistry are key to diagnosing the disease.

LCH is more common in children, and the incidence in adults is lower, about 0.1–0.2 per 100,000 [2, 3]. May differ from the clinical presentation and treatment response of pediatric patients. It can invade a single tissue and organ, but also can involve multiple parts of the body, of which bone, skin and lung are the most commonly affected parts of adult LCH. LCH is divided into two typesaccording to the degree of involvement [4]:

(1) involving a single system LCH (SS-LCH);
(2) Multi-system LCH involving two or more organs (MS-LCH).

MS-LCH was divided into low risk group and high risk group according to whether it involved dangerous organs. The low-risk group accounted for about 20%, and the affected organs included skin, bone, lymph nodes, lungs, thymus, digestive tract, endocrine glands, mouth, eyes, ears, central nervous system, etc., and the prognosis of patients was good [5]. The high-risk group accounted for about 80%, and the affected organs included liver, spleen and bone marrow, and the mortality rate was higher [6].

Langerhans cytosis in this case is characterized by mediastinal and thymus occupying and is relatively rare in clinical practice. Only one report of mediastinal Langerhans cytosis was published in 1986 [7]. Patients who can undergo surgery for a single or local lesion should consider surgical removal of the primary lesion. However, for patients with multiple lesions or distant metastases, clinicians should evaluate whether surgery will benefit the patient. Surgical treatment should be followed by targeted therapy or immunotherapy.

Several authors have reported adult lung Langerhans cell hyperplasia, the pathogenesis of PLCH is not fully understood, and there are no relevant clinical diagnosis and treatment guidelines. Treatment should be classified according to the clinical type of patients. Local treatment (surgery, radiotherapy) is preferred for patients with single system and single lesion, while systemic treatment, including systemic corticosteroids, chemotherapy, targeted therapy, hematopoietic stem cell transplantation and immunotherapy, is preferred for patients with multi-system involved [8]. Due to the heterogeneity of the disease, adult PLCH attaches great importance to individualized treatment. With the development of gene sequencing technology, about 60% of cases in PLCH patients carry the BRAF V600E mutation, which is an important component of the mitogen-activated egg albumin (MAPK) pathway and is involved in regulating cell growth, differentiation, aging, and apoptosis. BRAF V600E mutation is associated with risk organ involvement, poor chemotherapy response, and increased risk of recurrence.

In childhood LCH, the presence of BRAFV600E mutations has been shown to be associated with high-risk characteristics and poor response to chemotherapy [9]. BRAF inhibitor is a therapeutic target for patients with BRAF V600E mutation MS-LCH [10]. The treatment of MS-LCH is mainly chemotherapy [11], such as vincarine combined with prednisone, which is a treatment regimen considering that the patient has both tumor and inflammation. About 64% of patients with LCH have the BRAF-V600E mutation [1]and therefore have a response.BRAF blocker dalafenib therapy [12]has been reported that molecular targeted therapy has better targeting and low adverse reactions, and has a good application prospect. In this case, we found Langerhans cell hyperplasia in the thymus and ribs. Although Langerhans cell hyperplasia is not a traditional malignant tumor, the patient still needs the next targeted therapy based on the BRAF V600E mutation after surgical resection.This patient has started targeted therapy and systemic chemotherapy for BRAF V600E mutation, and the prognosis still needs to be further tracked.

Acknowledgements
We would like to thank all the researchers and study participant for their contributions.

Author contributions
Y.M.N. and L.X. responsible for drafting the manuscript and collecting data. Y.W. and Y.R.C. analyzed and explained the clinical data of patients. Y.F.L.and D.Y. L. evaluated and revised the paper.

Funding
This study was supported by the Effects of transcription factor TCF21 on PI3K-AKT pathway on biological characteristics of non-small cell lung cancer cells(Grant No. 82060509).

Data availability
No datasets were generated or analysed during the current study.

Declarations

Consent for publication
Informed consent for the article publication was obtained from the patient in this study.

Competing interests
The authors declare no competing interests.

Received: 12 December 2024 / Accepted: 18 May 2025
Published online: 28 May 2025

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