

# Isolated Langerhans cell histiocytosis of the spleen

## A case report

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### Abstract

**Rationale:** Langerhans cell histiocytosis (LCH) is a relatively rare disorder characterized by the proliferation of abnormal Langerhans cells. Splenic involvement usually presents in children with multisystem LCH, and isolated LCH of the spleen is a very rare disease. Herein, we report a case of isolated splenic LCH in an adult man.

**Patient concerns:** We report a case of isolated splenic LCH that first manifested with recurrent left upper abdominal pain.

**Diagnosis:** Unenhanced CT revealed multiple nodular lesions located at the spleen. Magnetic resonance imaging speculated that these lesions were lymphomas. On the basis of histopathological and immunohistochemical findings, the diagnosis of isolated splenic LCH was confirmed.

**Intervention and outcomes:** The patient underwent splenectomy. Histopathologic examination revealed the proliferation of Langerhans cell. Immunohistochemical staining revealed that cells of the tumor were positive for S-100, CD1a, CD45RO, and Vimentin. The patient is alive without recurrence 9 years after operation.

**Lessons:** Isolated LCH of the spleen may have a favorable prognosis and splenectomy is an effective therapeutic method.

**Abbreviations:** CD = cluster of differentiation, CT = computed tomography, EMA = epithelial membrane antigen, FSH = follicle-stimulating hormone, LCH = Langerhans cell histiocytosis, LH = luteinizing hormone, MRI = magnetic resonance imaging, WBC = white blood cell.

**Keywords:** diagnosis, isolated Langerhans cell histiocytosis, prognosis, spleen, therapy

## 1. Introduction

Langerhans cell histiocytosis (LCH), which was formerly named histiocytosis X, is a relatively rare and unique disease characterized by an abnormal proliferation of clonal CD1a-positive immature dendritic cells (LCH cells) in the skin, bone, lymph nodes, and other organs.<sup>[1,2]</sup> The estimated incidence of LCH in children less than 15 years old is 4 to 5 cases per million per year, while it is estimated 1 case per 560,000 per year in adults.<sup>[3]</sup> Any organ or system of the human body can be affected by LCH, but those more frequently involved are the skeleton (80% of cases), the skin (33%), and the pituitary (25%).<sup>[4]</sup> However, isolated LCH of the spleen is extremely rare, and only 1 case of LCH forming a solitary nodule in the spleen has been documented as

an incidental finding on necropsy.<sup>[5]</sup> Here, we present a case of LCH with isolated splenic involvement in an adult man.

## 2. Case presentation

A 34-year-old male presented to our hospital with recurrent left upper quadrant pain for 1 month. Findings of physical examination were unremarkable. The hematology laboratory tests were also unremarkable, including the hemoglobin level was 154 g/L, the white blood cell (WBC) count was  $7.4 \times 10^9/L$ , and the platelet count was  $219 \times 10^9/L$ . The liver function and coagulation tests were normal. Abdominal ultrasound showed splenomegaly and multiple hypoechoic masses about  $1.0 \times 1.2$  cm scattering in the spleen. Unenhanced computed tomography (CT) revealed multiple nodular lesions located at the spleen, and these lesions demonstrated marginally marked enhancement on contrast-enhanced CT. On magnetic resonance imaging (MRI), these lesions revealed low signal intensity on T1-weighted images and high signal intensity on T2-weighted images, and lymphoma of the spleen was presumed. No malignant infiltration was found in the bone marrow examination.

The patient underwent splenectomy. Multiple nodules measuring 1.0 to 1.5 cm in diameter were presented as the surgical specimen. Histopathologic examination revealed the proliferation of Langerhans cells with ovoid nuclei, which have a longitudinal nuclear groove, imparting a “coffee-bean” appearance and infiltration of eosinophils (Fig. 1 A, B). Immunohistochemical staining revealed that cells of the tumor were positive for S-100, CD1a, CD45RO, and Vimentin (Fig. 2 A~D) and negative for CD20, CD79a, CD3, CD23, CD35, and EMA. Taking the morphological and immunohistochemical features into account, the diagnosis of LCH was confirmed. In order to

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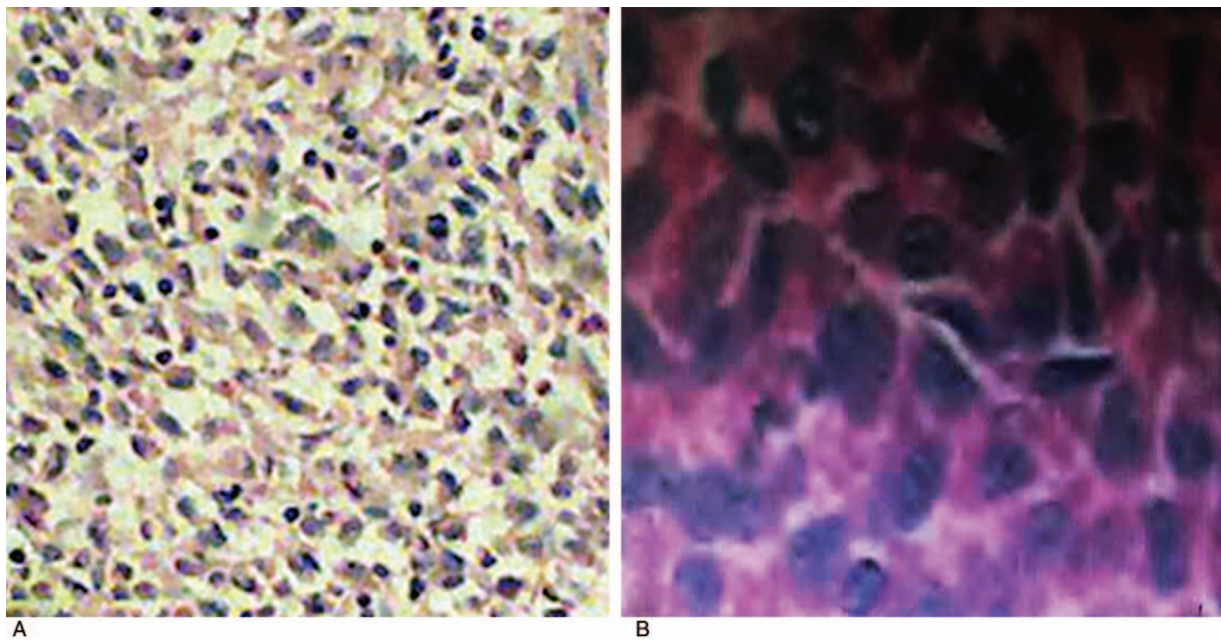
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**Figure 1.** Histological examination shows that tumor cells with ovoid nuclei that have a longitudinal nuclear groove, imparting a “coffee-bean” appearance and infiltration of eosinophils [(A) low magnification 100 × ; (B) high magnification 200 ×].

determine LCH was isolated or not, the patient completed further examination as follows. Thyroid hormone levels as well as luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin, and cortisol were all within normal limits. Urine osmolarity was normal, and chest CT and head MRI scan were unremarkable. Whole-body bone scintigraphy did not show any specific lesion. Being no evidence of diseases beyond the spleen, a definitive diagnosis of isolated LCH of the spleen was made. The patient received no follow-up adjuvant treatment and had remained tumor free for 9 years after surgery.

The Ethics Review Board of the First Affiliated Hospital of Nanchang University approved this study. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

### 3. Discussion

LCH is a relatively uncommon histiocytic disorder. It is characterized by the cells with similar features of bone marrow derived Langerhans-type cells (LCs), which are accompanied by a backdrop of hematopoietic cells, including macrophages, T-cells, and eosinophils.<sup>[6]</sup> LCH often affects the skin, bone, and lymph nodes and occasionally invades important organs, such as lung, spleen, liver, and pituitary gland.<sup>[3,7]</sup> Splenic involvement by LCH usually presents as a part of a multifocal systemic disease, whereas isolated splenic LCH is very rare.

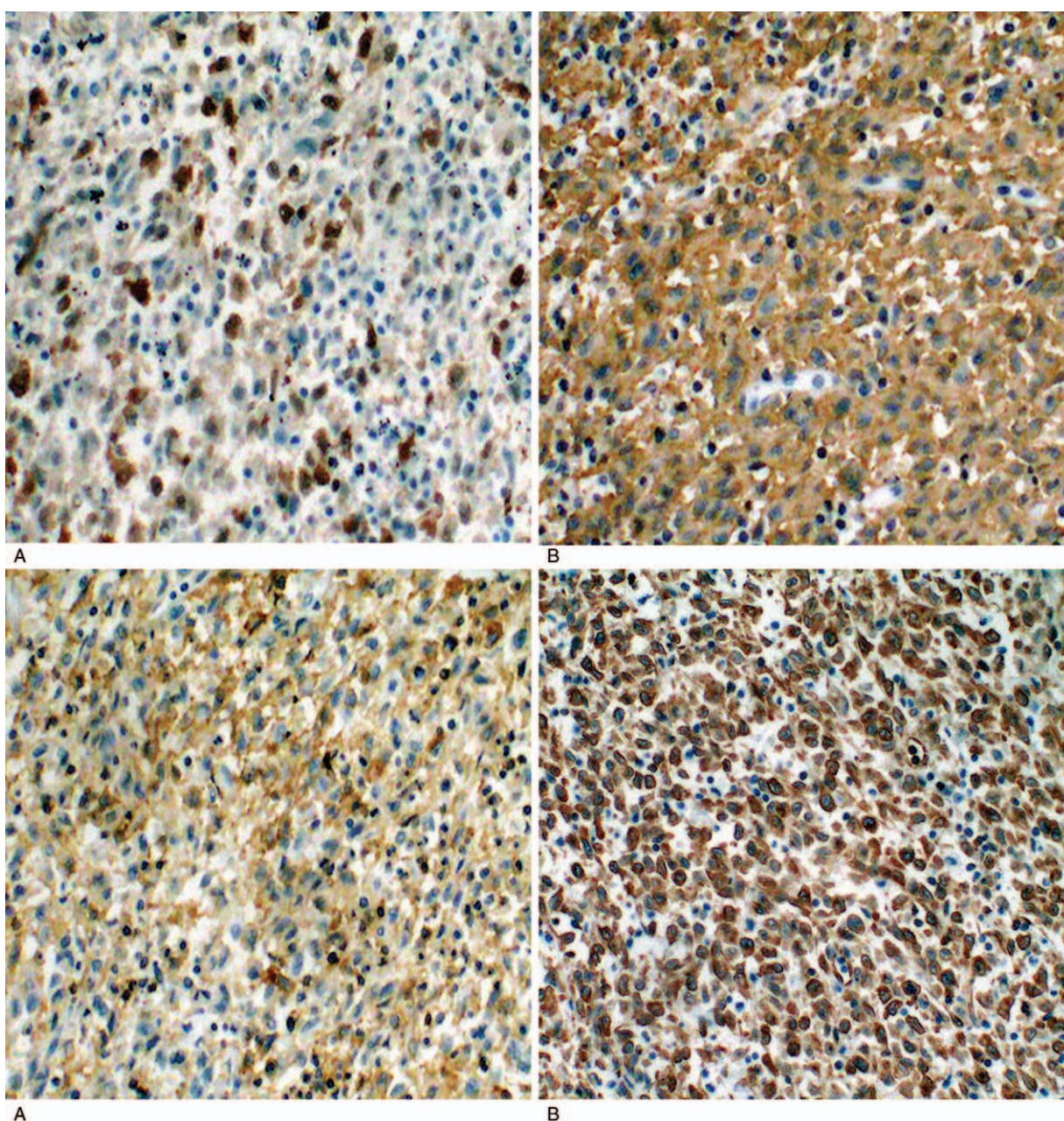
Clinical manifestations of LCH vary depending on the organ or system affected, from self-healing disease to chronic recurrences. The present case presented with nonspecific symptom of recurrent left upper quadrant pain, and the imaging examinations showed splenomegaly and multiple hypoechoic masses in the spleen. The diagnosis of LCH was confirmed by histopathological and immunohistochemical examination after splenectomy; meanwhile, diseases beyond the spleen were excluded. Histologically, the tumors of LCH are composed of LCs with ovoid nuclei

that often have a longitudinal nuclear groove. These are admixed with infiltration of inflammatory cells, including lymphocytes, eosinophils, and conventional histiocytes.<sup>[3,8]</sup> Immunohistochemically, Langerhans cells express CD1a and S-100 protein, as well as CD68, Vimentin, Langerin, p53, and Bcl-2.<sup>[9]</sup> As in the present case, the immunohistochemical staining was positive for S-100, CD1a, CD45RO, and Vimentin, while negative for CD20, CD79a, CD3, CD23, CD35, and EMA.

On the basis of the extent of involvement at diagnosis, LCH can be subdivided into single-system disease (SS-LCH) and multisystem disease (MS-LCH).<sup>[3,10,11]</sup> In SS-LCH, only 1 organ or system is involved such as lymph node (not the draining lymph node of another LCH lesion), bone (unifocal or multifocal bone involvement), skin, lung, or others such as thymus or thyroid.<sup>[3,11]</sup> In MS-LCH, 2 or more organs, or systems are involved either with or without involvement of risk organs. Patients with MS-LCH are further divided into low-risk and high-risk categories on the basis of involvement of the risk organs. According to the modified Lahey criteria,<sup>[12]</sup> risk organs and their involvement are defined as follows: hematopoietic system (thrombocytopenia and/or anemia and/or leukopenia), liver (dysfunction, enlargement more than 3 cm below the costal margin or both), lung (typical changes were revealed through histopathological diagnosis, high-resolution CT, or both), and spleen (enlargement more than 2 cm below the costal margin). The present patient is classified as SS-LCH without risk organs involvement, because there have been no evidence of diseases beyond the spleen after systemic examination.

Although LCH has been described for many years, its precise pathogenesis is still unclear. Proinflammatory cytokines and chemokines are known to play a role in LCH, which suggests that LCH is an immune disorder. However, the oncogenic *BRAF* V600E mutation is also detected in more than half of LCH patients, which suggests that LCH is a neoplastic disorder.<sup>[13]</sup> Therefore, current knowledge defined LCH as an inflammatory





**Figure 2.** Immunohistochemistry of the tumor specimen. (A) Positive staining for S-100 (100 $\times$ ). (B) Positive staining for CD1a (100 $\times$ ). (C) Positive staining for CD45RO (100 $\times$ ). (D) Positive staining for Vimentin (100 $\times$ ).

myeloid neoplasia driven by activating mutations in the mitogen-activated protein kinase (MAPK) pathway.<sup>[14]</sup> Due to the diversity of clinical course, the standard treatment for LCH has not been established. Generally speaking, there have 4 basic types of treatments for LCH, including operation, chemotherapy, radiation therapy, and immunotherapy.<sup>[4]</sup> Treatment options vary depending on the extent of the disease and the severity at onset. In SS-LCH, the main aims of treatment are to lessen symptoms and reduce the chance of permanent sequelae, such as phototherapy and topical steroids for skin involvement, curettage, and radiation therapy for single bone involvement. In MS-LCH, the main aims of treatment are to increase survival and to reduce the incidence of late sequelae. The most commonly used

regimen is systemic chemotherapy with vinblastine and corticosteroid for 6 to 12 months.<sup>[2]</sup>

As for the prognosis, the 5-year overall survival of LCH had a great relationship with the classification of the disease. Kim et al<sup>[15]</sup> identified 603 patients with LCH between 1986 and 2010 from 28 institutions in Korea. The 5-year overall survival rates of SS-LCH, MS-LCH without risk organ involvement and MS-LCH with risk organ involvement were 99.8%, 98.4%, and 77.0%, respectively. Maria Postini et al<sup>[16]</sup> analyzed the data of 121 pediatric patients with LCH between 1968 and 2009; the overall survival at 10 years from diagnosis for “risk” patients (involvement of bone marrow, spleen, liver, lungs) and “low-risk” patients was 50% and 94%, respectively. Therefore, it is

significant to differentiate the present case from MS-LCH with risk organ involvement, because they have a different prognosis. Meanwhile, every patient should be requested to a close follow-up for LCH has malignant and recurrent potential.<sup>[11,17]</sup> In the present case, the patient was treated with splenectomy, and without other adjuvant therapy. Moreover, no recurrence and metastasis were found 9 years after surgery. This result suggests that isolated LCH of the spleen may have a favorable prognosis after splenectomy.

In conclusion, isolated LCH of the spleen is a rare disease. Its diagnosis depends on histopathological and immunohistochemical examination, and requires excluding MS-LCH involvement of the spleen. Splenectomy is an effective treatment for isolated LCH of the spleen. Furthermore, this case could provide a helpful reference to aid in the decision-making process for the diagnosis and treatment of isolated splenic LCH.

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### Author contributions

**Weidong Xiao:** Design of the study, drafting, revision, approval of the final manuscript.

**Le Hong:** analyzed the data and drafted the manuscript.

**Gen Sun and Long Peng:** collected the data and presented the clinical features.

**Yi Tu:** made the pathologic diagnosis.

**Yong Li, Weidong Xiao and Long Peng:** performed the operation.

**Conceptualization:** Weidong Xiao.

**Data curation:** Le Hong, Gen Sun, Long Peng, Yong Li.

**Formal analysis:** Yi Tu.

**Investigation:** Gen Sun, Long Peng.

**Supervision:** Weidong Xiao.

**Validation:** Weidong Xiao.

**Writing – original draft:** Le Hong.

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