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Case Report and Review of the Literature

Langerhans Cell Histiocytosis: A Complicated Case Report and Literature Review

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Abstract

Background: Langerhans cell histiocytosis (LCH) is a rare disease of unknown etiology, characterized by monoclonal proliferation and organ infiltration of Langerhans cells. The clinical manifestations are various, and may involve single or multiple organs. A complicated case of LCH is introduced and the diagnosis and treatment are discussed.

Case Presentation: A 23-year-old woman presented with a huge mass in the left lower abdomen. Computed tomography (CT) of the lung revealed multiple diffuse nodules of different sizes in the right lung. The left thorax was collapsed, the left pleura was thickened and adhered, and a small, encapsulated effusion was observed in the thoracic cavity. Enhanced CT of the whole abdomen showed a huge cystic low-density focus on the left lower abdomen, multiple nodules in the spleen, and multiple osteolytic bone destruction in the spine, thorax, and pelvis. The possibility of LCH was considered based on the presence of diffuse reticulum nodules in the lungs observed in CT imaging. The patient was performed ultrasound-guided abdominal puncture, drainage, and chemotherapy with "vinorelbine and cisplatin". Follow-up is ongoing.

Conclusion: LCH involving the serosal membrane is rare. The final diagnosis requires histopathological examination of the involved tissue. But in most cases, it's enough to diagnose through the typical imaging changes in the lung, as observed by high-resolution computed tomography (HRCT), combined with certain clinical observations. Currently, there are no clearly established treatment guidelines for LCH. At present, systemic chemotherapy is the main treatment method that has been shown to improve patient's prognosis.

K E Y W O R D S:

Langerhans cell histiocytosis, multi-system, diagnosis, treatment

1. Introduction

Langerhans cell histiocytosis (LCH) is a disease characterized by monoclonal proliferation and organ. The clinical manifestations are different, which can involve single or multiple organs [1]. Langerhans cell histiocytosis (LCH) can occur at any age, but it is most common in children, with the highest incidence before 1 year of age and decreased thereafter, with a median age of diagnosis of approximately 3.5 years old, an annual incidence of 4-5 per million [2]. The exact incidence of LCH in adults is not known [3]. The proportion of males and females varied between the studies [2, 4]. LCH can involve a single organ or several organ systems simultaneously such as the lungs, bones, skin, pituitary, liver, lymph nodes, and thyroid. LCH is clinically classified into single-system LCH (SS-LCH) and multisystem LCH (MS-LCH) based on the extent and number of organ involvement [1].

The pathogenesis and etiology of LCH are still unclear [5], and the mechanisms of involvement in various organs are not yet the same. The disease is currently considered to be associated with immune dysregulation, viral infection, and genetic factors, but there is still controversy as to whether LCH is inflammatory or neoplastic in nature. BRAF V600E mutation is discovered in patients with LCH in 2010, and there is substantial evidence that LCH is driven by pathological MAPK activation in myeloid precursors, suggesting that LCH has the characterizes of myeloid neoplastic disease. Such findings have a high positive rate in patients with risky-organ involvement or refractory MS-LCH, but fail to explain the characteristics of other types of LCH. Therefore, we can't be successful in identifying the biologic characteristics of LCH over the years [6, 7]. In this article, we present a case of a 23-year-old young female with 15 years of bone eosinophilic granuloma, 4 years of pulmonary Langerhans cell histiocytosis (PLCH) and 7 days of left lower abdominal cavity mass and her clinical feature, pathology and treatment.

2. Case Presentation

The patient was first admitted to the orthopedic surgery department, Third Xiangya Hospital of Central South University (the following text referred to as our hospital) in September 2005 for "pathologic fracture of the right radius". A whole-body X-ray showed multiple patchy, irregular, low-density foci in the middle and lower thoracic vertebrae and pedicle, operculum, multiple ribs, bilateral iliac bones, sciatic bones, pubic bone, femoral shaft and lower and middle tibia shaft, bilateral humerus and the right radius, involving the medulla; thus, an abnormal bone fiber hyperplasia (multiple) may be considered. Routine blood tests presented eosinophil percentage 15.8% (elevated), absolute eosinophil value 1.05×109 /L (elevated) and the rest of the values were normal. Bilateral humerus, femur focus debridement and bone grafting were performed and the postoperative pathological report was "Eosinophilic granuloma of bone". No follow-up treatment was performed after one dose of local radiotherapy.

In November 2016, the patient's lung lesion was found through upon physical examination she was admitted to our thoracic surgery department for the second time. Color doppler ultrasonography of the thoracic and abdominal cavities indicated pleural and abdominal effusion; high-resolution CT of the lungs showed collapse of the left thorax and diffuse reticulonodular changes in both lungs, which was considered to be due to LCH (Figure 1); enlarged lymph nodes in the bilateral supraclavicular fossa, mediastinum and bilateral axillae were revealed. CT of the whole abdomen showed multiple osteolytic bone destruction in the spine, thorax and pelvis. The preliminary diagnosis was "LCH involving multiple organs (lung, bone, spleen, lymph nodes, pleura, peritoneum)". Bronchial lavage fluid was obtained by broncho-fiberscopy and sent for examination. The pathological examination revealed a large number of columnar epithelial cells, a few lymphocytes and no tumor cells in the smear. The antacid stain was negative. Serum

immunological examination did not show any significant abnormality. Patient refused other treatments after intraperitoneal drainage.

On June 10, 2020, the patient was admitted to the general surgery department of our hospital for the third time due to "the discovery of a left lower abdominal mass for 7 days". The patient found a fist-sized mass in the left lower abdomen a week ago, while the mass grow rapidly to 30 cm×10 cm without any abdominal pain, nausea, vomiting, diarrhea, morning expectoration or blood-stained sputum. There wasn't any family history of genetic predisposition.

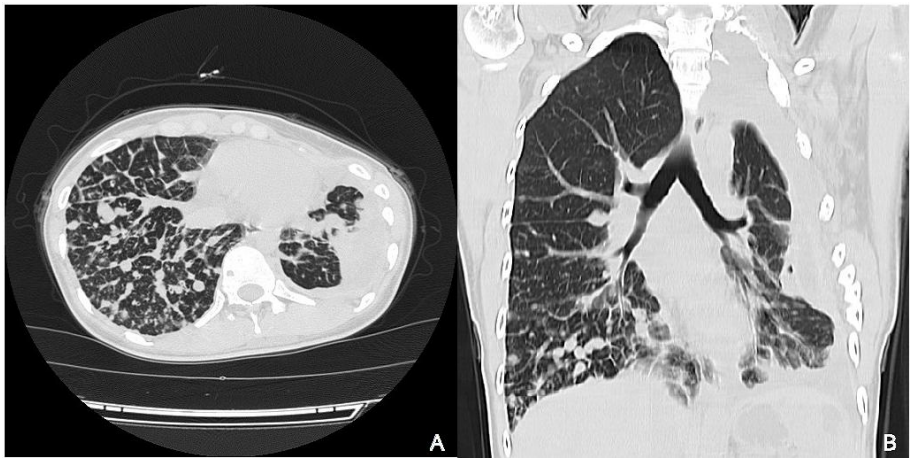

FIGURE 1: A 23-year-old female patient, pulmonary HRCT in 2016 showed diffuse nodules of different sizes in the right lung, reticular thickening of the interlobular septum, collapse of the left chest and reduction in the volume of the left lung. **A)** Horizontal plane. **B)** Coronal plane.

Physical examination showed the vital signs were stable. The skin was scattered with grayish-yellow and pale pink nodular papules, protruding from the surface with slight tenderness, and crusts were visible on the surface without secretions (Figure 2). The left thorax was slightly collapsed. The left voice tremor was enhanced, dullness to percussion and the left lung breath sounds were low. No dry or wet rales were heard. The right thorax was normal and the right voice tremor was normal. The percussion was clear. Scattered wet rales could be heard in the right lower lung, no pleural friction sounds. A 30 cm × 10 cm sized mass was seen in the left lower abdomen, with a tough texture, clear borders, movable, and no obvious pressure pain. There was no abnormality in the nervous system.

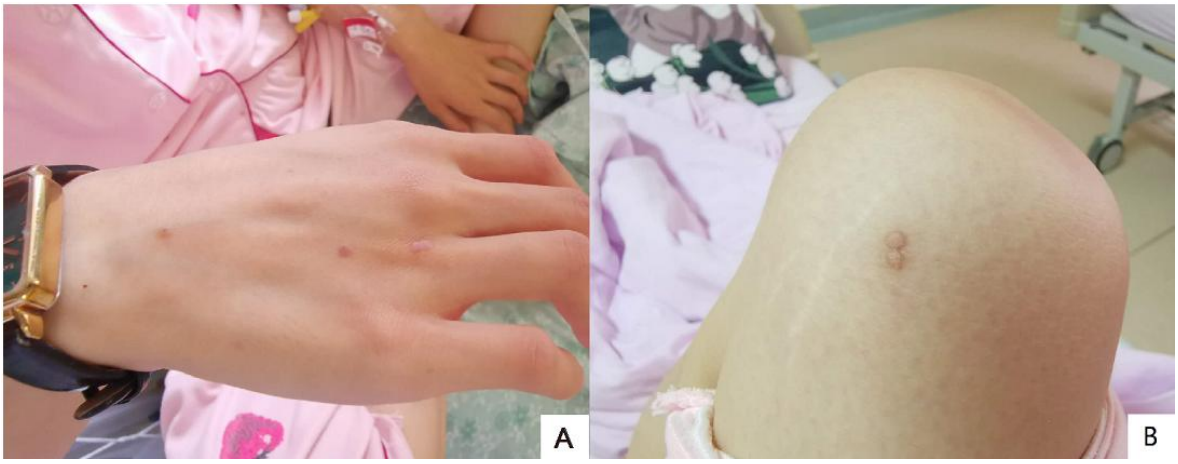

FIGURE 2: A & B) A 23-year-old female patient, the skin is scattered with grayish yellow, pale pink nodular papules protruding from the surface.

Laboratory examination presented normal routine blood, liver and kidney functions, and tumor markers. Cardiac enzymatic tests revealed lactate dehydrogenase 284 U/L (elevated), alpha hydroxybutyrate dehydrogenase 217 U/L (elevated). Abdominal color Doppler ultrasonography showed a cystic mixed echogenic mass of about 26.4 cm × 6.4 cm in the left lower abdomen. Ultrasound of uterine and bilateral showed no significant abnormalities. CT of the lungs compared to the old film of August 2019 showed that diffuse multiple nodular shadows of variable size were still seen in the right lung, with more nodular foci and some were enlarged compared to the previous ones. The left thorax was collapsed. The left pleura was significantly thickened and adherent, and a little encapsulated fluid effusion could be seen in the pleural cavity. Enhanced CT of the whole abdomen showed large cystic hypodense foci in the left lower abdomen, multiple nodules in the spleen, and multiple osteolytic bone destruction in the spine, thorax and pelvis (Figure 3). Combined with diffuse reticulonodular nodules in the lungs, the possible impact of LCH was considered. Pulmonary function suggested severe mixed pulmonary ventilation dysfunction. Whole-body bone imaging showed no significant abnormalities.

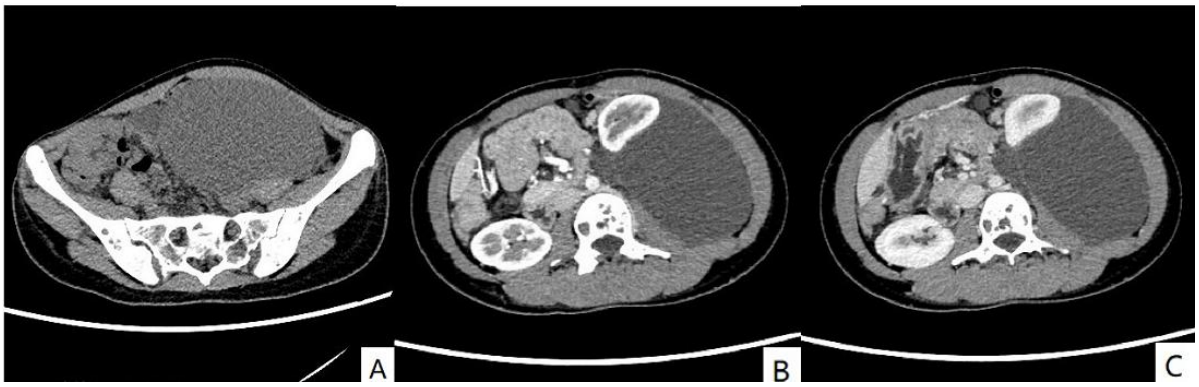

FIGURE 3: A 23-year-old female patient, the whole abdomen CT in 2020 showed a huge cystic low-density focus in the left lower abdomen, and there was no enhancement in the arteriovenous phase. Multiple osteolytic bone destruction in spine and pelvis. **A)** Plain scan. **B)** Arterial phase. **C)** Venous phase.

2.1. Preliminary Diagnosis

LCH involving lung, bone, lymph nodes, skin and serosa. After admission, the patient was given a multidisciplinary consultation. Considering the patient's poor lung function and the high risk of surgery for abdominal mass, the patient was given a color doppler ultrasonography-guided abdominal cavity puncture catheterization, and dark red fluid was drained. A portion of the puncture fluid was taken and sent for examination. The pathological examination revealed a moderate amount of mesothelial cells and lymphocytes in the smear, with degenerative, without tumor cells. After communication with the patient, she was transferred to our oncology department for treatment and given chemotherapy with the regimen of “cisplatin-vinorelbine”. After chemotherapy, a repeat abdominal color Doppler ultrasonography showed that an anechoic area of about 8.1×5.1 cm could be detected in the lower abdomen, and a free liquid dark area could be detected in the abdomen cavity, suggesting that the cystic mass in the lower abdomen was significantly smaller than before and still remained peritoneal effusion in the cavity. The patient finished this treatment and is still being followed up.

3. Results and Discussion

As early as 1950, researchers gained a consensus on that Hand-Schüller-Christian disease (triad of osteolytic lesions, ocular protrusion due to orbital involvement, and uveitis), Letterer-Siwe disease (seborrheic rash, ear discharge, and signs of severe systemic involvement), and eosinophilic granuloma were manifestations of the same disease process, and subsumed the three diseases into Langerhans cell histiocytosis [8]. Among them,

eosinophilic granuloma is widely common, accounting for about 60% to 80% of diagnoses cases, and Letterer-Siwe disease is the most severe manifestation of LCH [9]. In most cases, HRCT of the lung is the most effective imaging test for the evaluation of suspected pulmonary Langerhans cell histiocytosis (PLCH). In combination with certain clinical conditions, typical imaging changes on the lung HRCT support the diagnosis of PLCH without further examination. The early stage was commonly showed nodular changes, whereas cystic changes and fibrosis was in the late stages. The diagnosis of PLCH is strongly supported by increased levels of CD1α Langerhans cell staining in bronchoscopic alveolar lavage fluid >5% (normal value <1%). In patients with multiple organs involvement such as skin or bone, the diagnosis is usually established when combined with classical imaging features on lung HRCT. Although open or thoracoscopic lung biopsy is the gold standard for the diagnosis of PLCH, it is not the first choice for confirming the diagnosis due to the invasive nature of this test [10].

Our patient is a young female with juvenile onset. She was admitted to our hospital with "pathological fracture of the right radius" and underwent "bilateral humeral and femoral lesion removal with bone grafting". Postoperative pathological results confirmed eosinophilic granuloma of bone. During the course of the disease, the left side of the thorax was found to be collapsed, and HRCT of the lungs showed diffuse reticulonodular changes in both lungs, highly suspicious of PLCH, which is an "organs at risk" involvement [1]. The whole abdominal CT and lung CT all showed multiple osteolytic bone destruction in the spine, thorax and pelvis during this admission and the last 4 years. Then this patient can be considered to have progressive bone LCH with PLCH, which is consistent with MS-LCH, and the patient also has enlarged lymph nodes suggesting lymph node involvement and a typical LCH skin rash with translucent rose yellow papules 1~2mm in diameter [11]. Since Langerhans cell histiocytosis can occur in any organ or system throughout the body [6], even if the same organ or system is involved, there are different clinical manifestations, this patient's cystic abdominal mass could be caused by LCH.

Combining with the result of the bone lesions biopsy, the patient's previous multiple serosal cavities effusion fluids could also be suspected as a clinical manifestation of LCH involvement of serosa. Lai-San Wong [12] reported a case of neonatal LCH with diffuse hemorrhagic nodules and a huge mass of in right abdominal skin, with elevated lactate dehydrogenase (LDH), which had never been published in LCH before. Ricardo Mejia, *et al.* [13] reported a patient with endocrine problems due to a suprasellar mass. A biopsy of the suprasellar mass was taken, and after immuno-peroxidase staining showed negative S100 protein, excluding the possibility of LCH. Thereafter, the patient presented with secondary skin involvement in the form of hemorrhagic nodules. A biopsy of the nodule was performed and the results confirmed LCH, correcting the diagnosis. The authors noted that although immuno-peroxidase staining for S100 protein is expected to be positive in the diagnosis of LCH, it may be less intense in different cases or in different tissues of the same case, which may lead to a missed diagnosis.

We didn't find any report that LCH may involve the serosa and lead to recurrent serosal cavity effusion. Because of the terrible pulmonary function of the patient, cystic wall of the abdominal cystic mass was difficult to be acquired for pathological examination combined with the multiple reports of scattered, rare and varied clinical manifestations of LCH, there is even more reason to suspect that the cystic abdominal mass and recurrent serosa cavity effusion in this patient is one of the clinical manifestations of LCH. In addition, the patient's whole abdominal enhancement CT showed a large spleen with multiple nodules worth noting. The criteria for spleen involvement is that the spleen is >2 cm below the rib margin in the midclavicular line, which is also a "risk organ" involvement [1]. Fortunately, the patient has no significant abnormalities in blood routine and no signs of spleen damage, and has been treated with

chemotherapy, with attention to follow-up regular. The patient has been treated with chemotherapy, and regular follow-up treatment, review and follow-up.

At present, there is no clear uniform treatment plan for LCH, but there are chemotherapy, radiotherapy, surgery, targeted therapy and other methods were suggested. For the treatment of MS-LCH, the guideline [1] only describes chemotherapy, and recommends the first-line chemotherapeutic regimen of vincristine (VBL) plus prednisone, which can be used for 6 weeks of induction therapy, regardless of dangerous organs are involved or not. The dose to be used for maintenance therapy is determined by the state of follow-up. In conjunction with the large international prospective therapeutic studies (LCH-Ⅰ, LCH-Ⅱ, LCH-Ⅲ), the guidelines conclude that the VBL plus prednisone induction regimen has been shown to be effective in MS-LCH with minimal side effects and should be used as initial therapy for all patients with MS-LCH. A 6-week treatment with an induction regimen, regardless of dangerous organs are involved, suggests a good long-term survival rate, but a poor prognosis is possible if it is not effective [5]. *BRAF-V600E i*nhibitors and MAPK pathway inhibitors are the new direction of refractory LCH treatment. Yet the more frequent and serious side effects like *BRAF-V600E* inhibitors have been shown to have oncogenic potential, which limited the application of such targeted drugs [6]. For single lesions surgical scraping of localized lesions or intra-lesion injection of glucocorticoids can be used [14].

The prognosis of LCH is related to the age of onset, the number of organs or systems involved and the severity of the involvement [4]. The clinical presentation and subsequent course of the disease may vary widely, ranging from SS-LCH in spontaneous remission to refractory MS-LCH with a 20% mortality rate [2]. In general, the prognosis of adult LCH is better than that of children, and the prognosis of SS-LCH is better than that of MS-LCH. Some studies have shown that the long-term survival rate of children with SS-LCH is more than 90%, but the morbidity and mortality rate of children with MS-LCH with dangerous organs involvement is greatly increased with the overall mortality rate of 15% and the incidence of long-term sequelae is 30% to 40% according to foreign statistics [11]. For the complex clinical manifestations of LCH clinicians should detect, diagnosis and treat early is the key to achieve a good prognosis for patients.

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Author Contributions

Xiaoxiao Zhong: Writing - review & editing, writing - original draft, validation, data curation, conceptualization. Xiangyu Shen: Writing - review & editing, writing - original draft, validation, data curation, investigation. Jiaxuan Han: Writing - review & editing, validation, data curation, investigation. Fengjiao Ding: Writing - review & editing, data curation, investigation. Liyuan Qian: Writing - review & editing, validation, resources, supervision. Wei Wu: Writing - review & editing, validation, resources, supervision. Boni Ding: Writing - review & editing, validation, funding acquisition, resources, supervision.

Conflicts of Interest

None.

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REFERENCES

[1] Anil Kallesh, Vikram S Kumar "Congenital Langerhans-Cell Histiocytosis." *N Engl J Med*, vol. 385, no. 24, pp. e86, 2021. View at: Publisher Site | PubMed

[2] Jolie Krooks, Milen Minkov, Angela G Weatherall "Langerhans cell histiocytosis in children: History, classification, pathobiology, clinical manifestations, and prognosis." *J Am Acad Dermatol*, vol. 78, no. 6, pp. 1035-1044, 2018. View at: Publisher Site | PubMed

[3] Gaurav Goyal, Mithun V Shah, Christopher C Hook, et al. "Adult disseminated Langerhans cell histiocytosis: incidence, racial disparities and long-term outcomes." *Br J Haematol*, vol. 182, no. 4, pp. 579-581, 2018. View at: Publisher Site | PubMed

[4] Tao Wang, Beibei Su, Dawei Han, et al. "Clinical Analysis of 122 Cases of Langerhans Cell Histiocytosis." *Zhongguo Yi Xue Ke Xue Yuan Xue Bao*, vol. 39, no. 2, pp. 206-210, 2017. View at: Publisher Site | PubMed

[5] Oussama Abla, R Maarten Egeler, Sheila Weitzman "Langerhans cell histiocytosis: Current concepts and treatments." *Cancer Treat Rev*, vol. 36, no. 4, pp. 354-359, 2010. View at: Publisher Site | PubMed

[6] Carl E Allen, Miriam Merad, Kenneth L McClain "Langerhans-Cell Histiocytosis." *N Engl J Med*, vol. 379, no. 9, pp. 856-868, 2018. View at: Publisher Site | PubMed

[7] Martina C Herwig, Ted Wojno, Qing Zhang, et al. "Langerhans cell histiocytosis of the orbit: five clinicopathologic cases and review of the literature." *Surv Ophthalmol*, vol. 58, no. 4, pp. 330-340, 2013. View at: Publisher Site | PubMed

[8] Gayane Badalian-Very, Jo-Anne Vergilio, Mark Fleming, et al. "Pathogenesis of Langerhans cell histiocytosis." *Annu Rev Pathol*, vol. 8, pp. 1-20, 2013. View at: Publisher Site | PubMed

[9] Chalinee Monsereenusorn, Carlos Rodriguez-Galindo "Clinical Characteristics and Treatment of Langerhans Cell Histiocytosis." *Hematol Oncol Clin North Am*, vol. 29, no. 5, pp. 853-873, 2015. View at: Publisher Site | PubMed

[10] R Vassallo, J H Ryu, T V Colby, et al. "Pulmonary Langerhans'-cell histiocytosis." *N Engl J Med*, vol. 342, no. 26, pp. 1969-1978, 2000. View at: Publisher Site | PubMed

[11] Stefano Chiaravalli, Andrea Ferrari, Luca Bergamaschi, et al. "Langerhans cell histiocytosis in adults: a retrospective, single-center case series." *Ann Hematol*, vol. 101, no. 2, pp. 265-272, 2022. View at: Publisher Site | PubMed

[12] Lai-San Wong "An Unusual Case of Neonatal Langerhans Cell Histiocytosis Presenting with Diffuse Hemorrhagic Nodules and a Cutaneous Abdominal Mass." *Indian J Dermatol*, vol. 60, no. 4, pp. 424, 2015. View at: Publisher Site | PubMed

[13] R Mejia, J A Dano, R Roberts, et al. "Langerhans' cell histiocytosis in adults." *J Am Acad Dermatol*, vol. 37, no. 2 Pt 2, pp. 314-317, 1997. View at: PubMed

[14] Masayuki Kobayashi, Arinobu Tojo "Langerhans cell histiocytosis in adults: Advances in pathophysiology and treatment." *Cancer Sci*, vol. 109, no. 12, pp. 3707-3713, 2018. View at: Publisher Site | PubMed