Adult Langerhans' cell histiocytosis with multisystem involvement

A case report

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Abstract

Rationale: Langerhans' cell histiocytosis (LCH), also called histiocytosis X, is an uncommon disorder manifesting in a variety of ways. Although LCH can involve various organs including bone, skin, and lymph nodes, multisystem involvement of LCH is rare in adults.

Patient concerns: A 31-year-old woman first presented to our hospital with left leg pain. She had a history of a 20-kg weight gain over three months.

Diagnoses: X-ray, magnetic resonance imaging (MRI), computed tomography (CT), and bone scan images revealed enhancing lesions in the left femur and right temporal bone, multiple cystic lesions in the lung, enhancing mass in the pituitary stalk, and fat density lesions in the liver. The patient underwent excisional biopsy for the femoral lesion and histologic examination confirmed the diagnosis of LCH.

Interventions: Excisional biopsy was performed for the bony lesion in the left femur. She received chemotherapy with vinblastine and prednisolone.

Outcomes: The patient expired after 21 months from initial admission following recurrent episodes of pneumothorax, pneumonia, and sepsis.

Lessons: Our case showed LCH involvement in bone, lung, central nervous system (CNS), and liver. Although it is occasionally difficult to discriminate LCH from other disorders, systemic evaluation might be helpful for differential diagnosis. Familiarity with the various multisystemic involvements of LCH on imaging is vital for diagnosing and managing patients in daily practice.

Abbreviations: CNS = central nervous system, CT = computed tomography, DI = diabetes insipidus, LAM = lymphangioleiomyomatosis, LCH = Langerhans' cell histiocytosis, MRI = magnetic resonance imaging, SI = signal intensity.

Keywords: bone and bones, histiocytosis, Langerhans' cell, liver, lung, pituitary gland

1. Introduction

Langerhans' cell histiocytosis (LCH), which is also known as histiocytosis X, refers to a clonal proliferative disorder characterized by infiltration of Langerhans cells.[1,2] Although LCH is a rare disorder, multisystem involvement of LCH is relatively common in children; however, it is very rare in adults.[3,4] It has been described using various terms according to the clinical and pathologic findings. Since 1987, Langerhans' cell histiocytosis has been considered the precise term to present a conglomeration of previous conditions.[3,5,6] The bone is the most common site of LCH involvement, and lung, skin, lymph node, central nervous system (CNS), and liver can also be involved.[7–9] Here, we report a case of LCH that showed the involvement of multiple organs including bone, lung, CNS, and liver in a 31-year-old woman.

2. Case description

This study was approved by the institutional review board of the First Affiliated Hospital of Soonchunhyang University (Cheonan, Republic of Korea). Verbal informed consent was obtained from the patient's family for publication of the case details and the accompanying images. A 31-year-old female presented with left leg pain. She had a history of 20-kg weight gain over 3 months and did not reveal other specific clinical history. Serum levels of eosinophils (7.5%) and C-reactive protein (6.8 mg/L) were elevated. Other laboratory studies were in the normal range: white blood cell

count, 8,500/mm^3; hemoglobin, 13.6 g/dL; hematocrit, 42.6%; platelet count, 272,000/mm^3; total protein, 7.2 g/dL; albumin, 4.4 g/dL; AST, 24 IU/mL; ALT 30 IU/mL; and γ-GTP, 85 IU/mL. The initial X-ray examination showed a well-defined osteolytic lesion in the cortex of the left femur (Fig. 1A). The lesion showed high signal intensity (SI) on T1- and T2-weighted images of magnetic resonance imaging (MRI), respectively (Fig. 1B). Differential diagnoses of the bony lesion were osteoid osteoma, metastasis, and eosinophilic granuloma. Bone scan showed increased activity in the left femur and right temporal bone (Fig. 2), and chest computed tomography (CT) showed multiple cystic lesions with nodules in both lungs (Fig. 3A). The bony lesion was thought to be eosinophilic granuloma associated with LCH due to cystic lesions in the lung. The patient underwent excisional biopsy for the femoral lesion, and a histologic examination demonstrated diffuse infiltration of histiocytes with destruction of bony structure (Fig. 4A). The Langerhans cell was a large cell with indented, grooved, or folded nuclei and eosinophilic cytoplasm. A high level of eosinophils was also noted (Fig. 4B). S-100 (Fig. 4C) and CD1a (Fig. 4D) immunohistochemical staining highlighted the presence of Langerhans cells, and LCH was diagnosed. After histopathological confirmation, systemic evaluation was conducted. Brain MRI demonstrated an enhancing soft tissue in the right temporal bone, which showed increased activity on the bone scan and another enhancing mass in the pituitary stalk (Fig. 5). These lesions were supposed to be due to involvement of LCH. A hormonal examination revealed diabetes insipidus (DI), and previous history of rapid weight gain was considered to be caused by pituitary involvement of LCH. The patient received chemotherapy with vinblastine and prednisolone. Follow-up CT after 6 months showed pneumothorax (Fig. 3B) and 2 fat density lesions were newly discovered in the liver, which were located around the portal vein (Fig. 6A and B). The fat density lesions decreased in size during the follow-up and finally disappeared (Fig. 6C and D). The patient expired after 21 months from initial admission following recurrent episodes of pneumothorax, pneumonia, and sepsis.

3. Discussion

LCH is a rare proliferative disorder, with an incidence 2.6–5.4 cases per million in children; however, the precise incidence of LCH in the general population is not known due to its low prevalence in adults.[3,4] There are 3 clinical variants of LCH according to the involved organ: eosinophilic granuloma, the most common form characterized by a solitary bony lesion; Hand-Schuller-Christian disease, the chronic recurrent form, which classically shows the triad of skull lesion, exophthalmos, and DI; and Letterer-Siwe disease, the fulminant form with
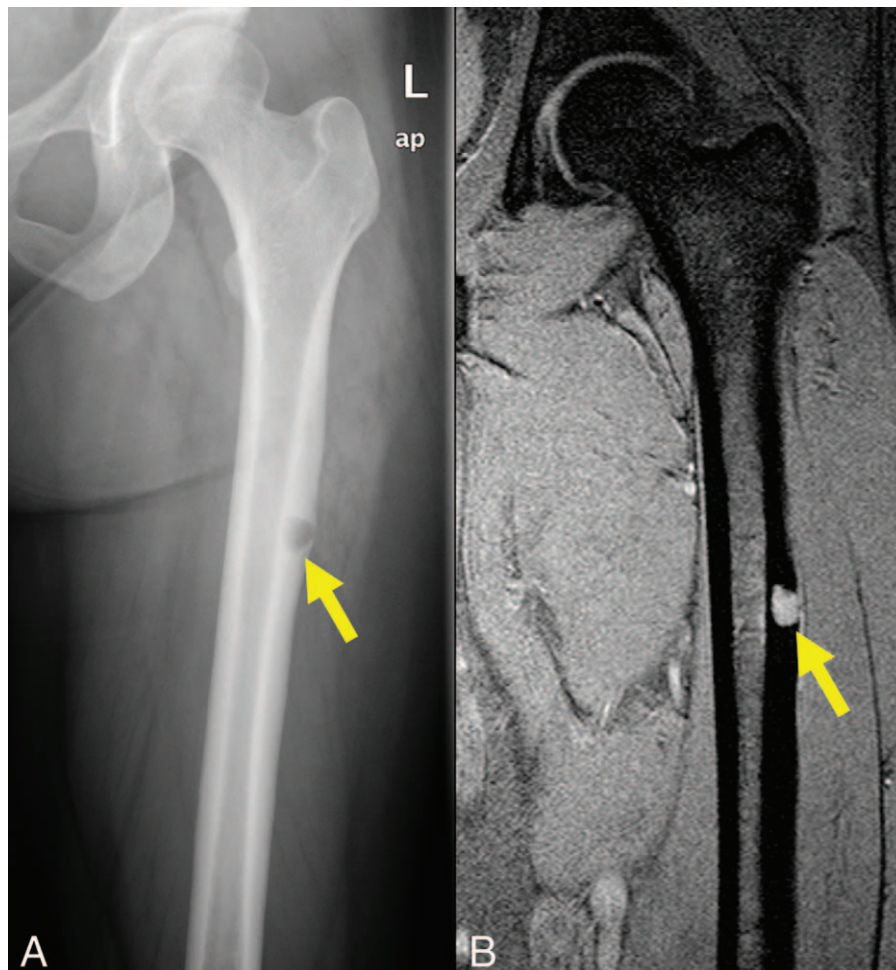

Figure 1. Initial X-ray and MR images of the left femur. (A) X-ray image shows an osteolytic lesion with a well-defined margin (arrow) in the cortex of the femur. (B) Coronal fat suppressed T2-weighted image shows a well-demarcated hyperintense lesion (arrow) in the cortex of the femur. MR = magnetic resonance.

Figure 2. Bone scan image shows increased activity (arrow and open arrow) in the left femur and right temporal bone.

multiple organ involvement.[5] LCH is also subdivided into single- and multi-system types according to the number of involved organs.[10] In our case, although only one enhancing lesion in the left femur was pathologically confirmed, typical imaging findings of LCH were observed in lung, pituitary gland, temporal bone, and liver without exophthalmos. Therefore, the LCH in the subject was considered to be the multisystem and fulminant form among clinical variants.

Bone is the most common site of involvement in LCH. Any bone can be involved, but in the majority of cases, LCH involves the skull, rib, spine, and long bone.[5] Osseous LCH usually presents as swelling or pain. Although it typically appears as a lytic bony lesion, radiologic features of LCH depend on the phase of the disease. In the early phase, LCH shows a more aggressive pattern of osteolysis, and the lesion becomes sharply demarcated in the later phase. Remodeling of the bone may cause an expanded appearance, as in our case.[5,11] Bony LCH is relatively common in children; thus, if there is an osteolytic lesion in children and young adults, LCH should be included in the differential diagnosis.

Lung involvement is not a common form of LCH and is associated with smoking.[12] Pulmonary LCH presents as multiple nodules and cysts on high-resolution CT, and these lesions affect the upper and middle lung zones with sparing of lung bases. A previous study described that predominance of the nodular pattern is an early manifestation of pulmonary LCH, whereas a predominant cystic pattern is typically noted in the later phase.[13] According to that study, pulmonary LCH progresses from a cellular nodule to a cavitary nodule and will change into a cyst. In our case, cystic lesions were predominant; therefore, our subject may have been in the later stage of pulmonary LCH. Pneumothorax occurs in about 10% of patients with pulmonary LCH.[12] The differential diagnoses of pulmonary LCH includes lymphangioleiomyomatosis (LAM), which also shows cystic destruction of the lung. However, LAM shows an even distribution of cystic lesions without pulmonary nodules, in contrast, LCH reveals sparing of lung bases.[14]
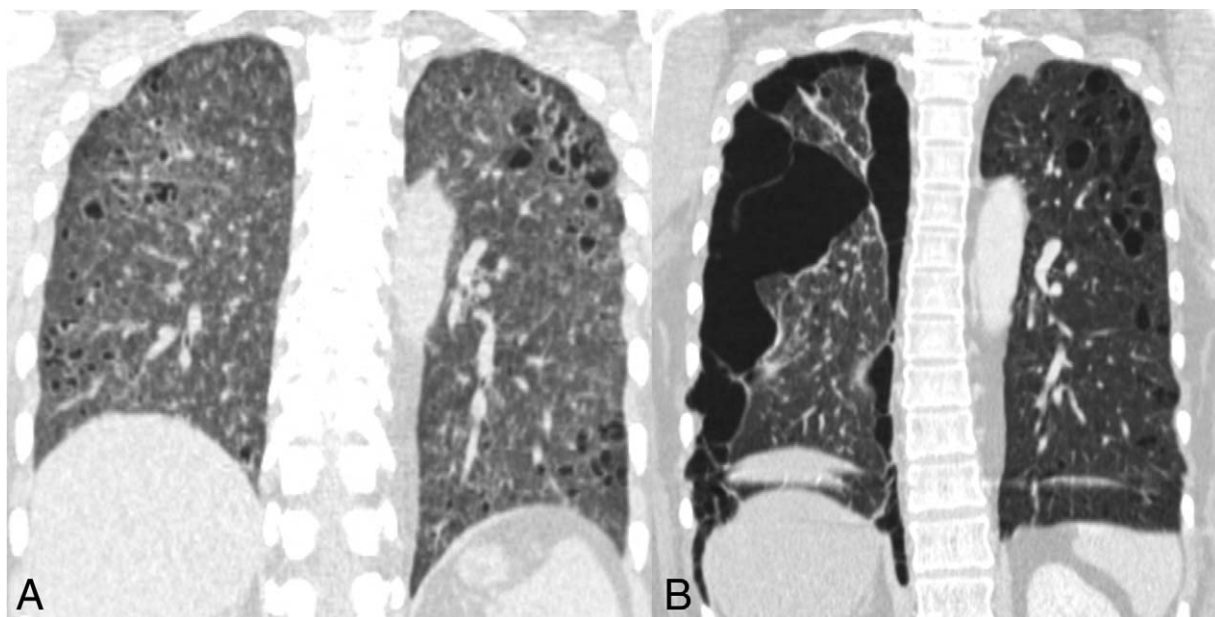

Figure 3. (A) Coronal reformatted chest CT image shows multiple small cysts and nodules in both lungs. (B) Follow-up CT image after 6 months shows pneumothorax in the right hemithorax. CT = computed tomography.
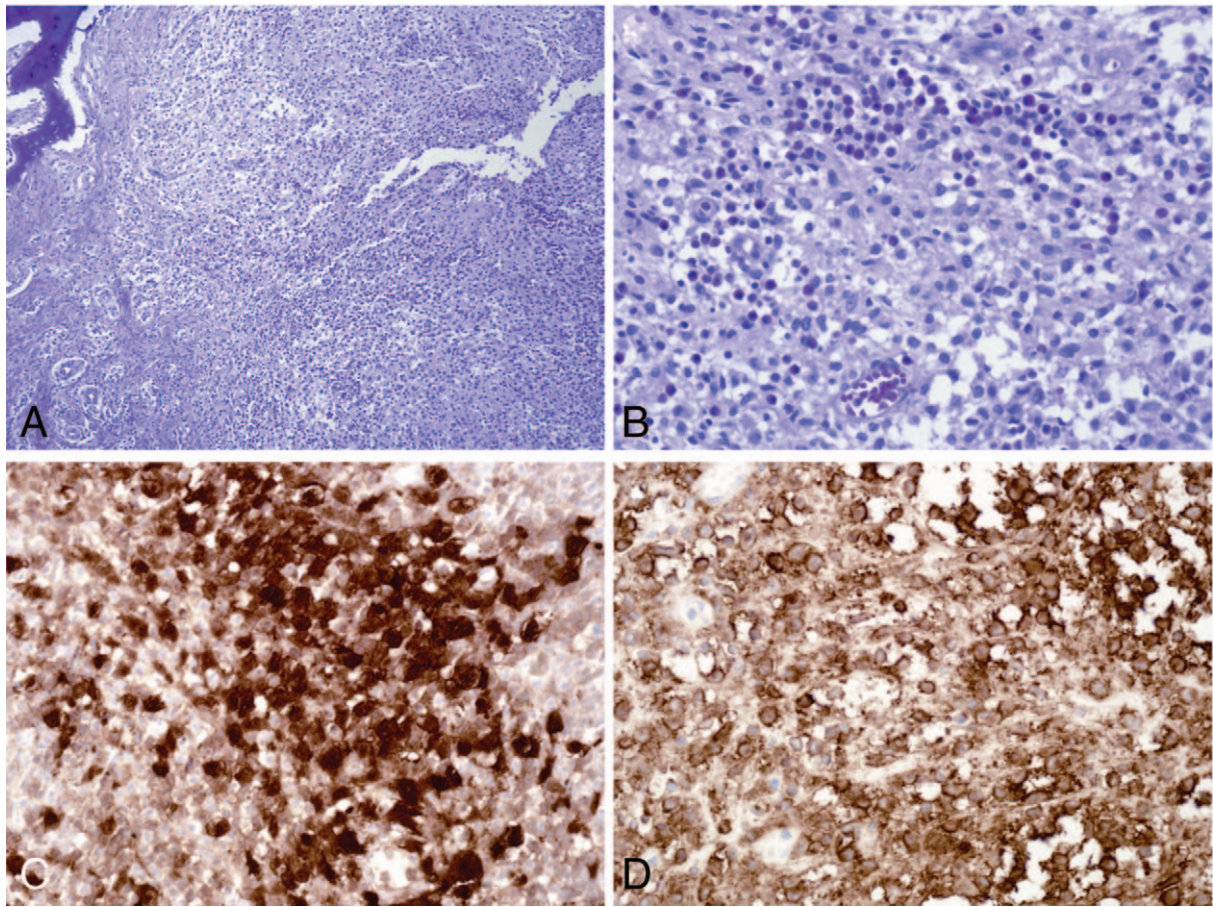
Figure 4. (A) Histologic examination demonstrates diffuse infiltration of inflammatory cells with bony destruction. (B) Langerhans cells with abundant eosinophils are observed. (C, D) Langerhans cells show immunopositivity for S-100 (C) and CD1a (D).
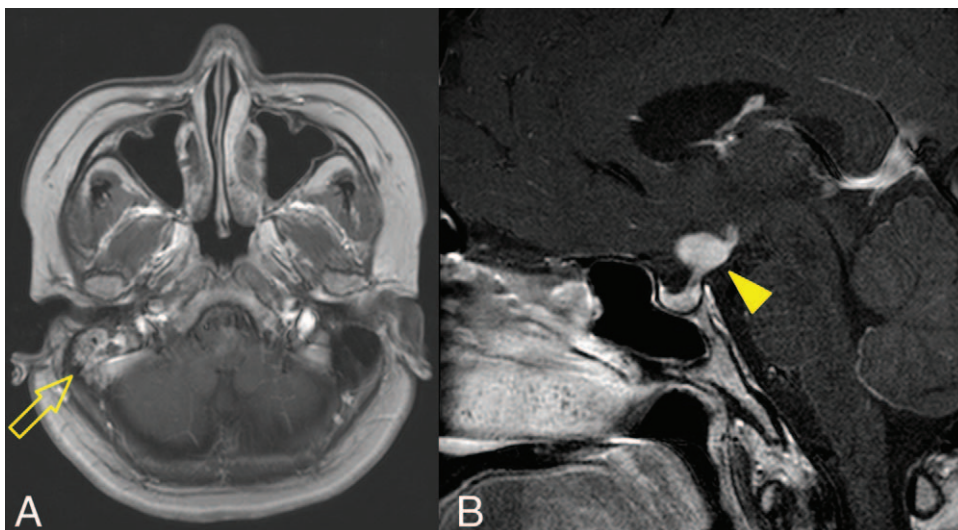

Figure 5. (A) Axial and (B) sagittal contrast-enhanced T1-weighted MR images show an enhancing soft tissue lesion (open arrow) in the right temporal bone and another enhancing mass (arrowhead) in the pituitary stalk.
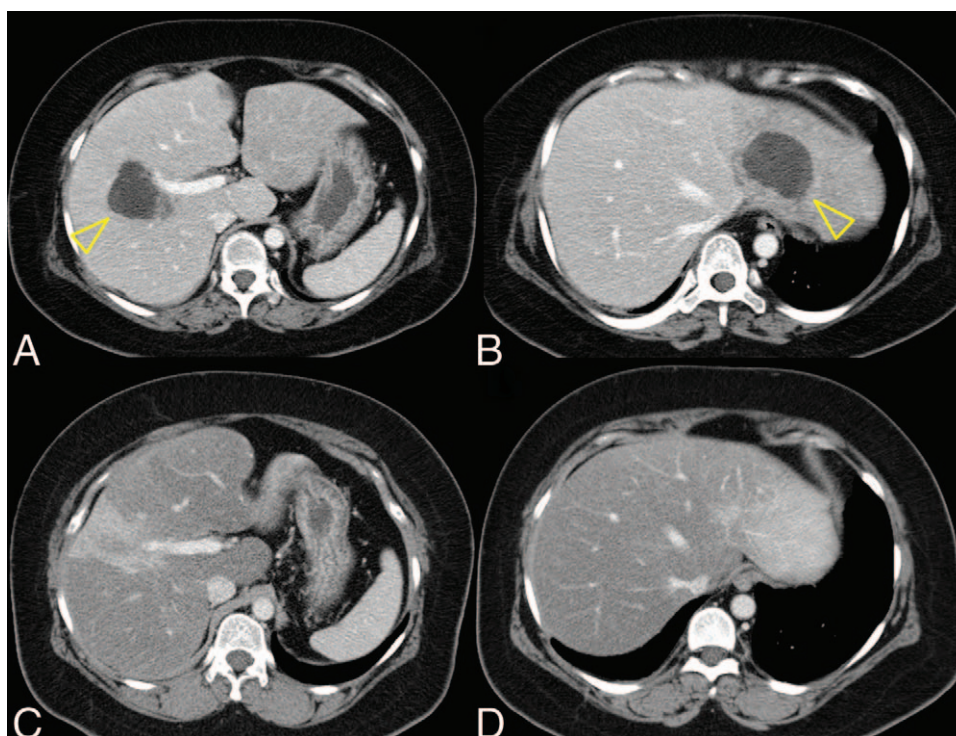
Figure 6. (A, B) Follow-up axial CT images after 6 months show two fat density lesions (open arrowheads) in the liver. (C, D) Follow-up CT images after 17 months show the disappearance of fat density lesions in the liver. Note focal fat sparing and atrophic change at sites where lesions were seen. CT = computed tomography.

Our case showed involvement of the pituitary gland, although CNS is an uncommon site of involvement with LCH.[9] The pituitary stalk is the most common site of CNS involvement and is usually associated with DI.[15,16] The imaging finding of hypothalamic involvement varies from mild thickening of the pituitary stalk to a hypothalamic mass.[16] However, sarcoidosis, leukemia, and brain tumors also show a hypothalamic lesion, and it is difficult to differentiate LCH from these disease entities.[16,17] Further evaluation such as bone scan or chest CT may be helpful for discrimination of LCH from other diseases involving the pituitary stalk because isolated CNS involvement is rare in patients with LCH.[16]

Hepatic involvement of LCH is observed in patients with extensive LCH but is rare in adults.[8] There are 4 histologic phases of hepatic LCH with different imaging features: proliferative, granulomatous, xanthomatous, and fibrous phases.[9,11,18] The proliferative and granulomatous phases show periportal infiltration of histiocytes and inflammation, and they present as a hypodense lesion on CT and show low and high SI on T1- and T2-weighted images of MRI, respectively.[19] The xanthomatous phase is characterized by periportal fatty lesion due to the lipid-rich character of histiocytes, therefore CT demonstrates fat density lesions in the xanthomatous phase.[8] In the fibrous phase, biliary cirrhosis develops owing to sclerosing cholangitis.[18] Our case was considered to be in the xanthomatous phase of hepatic LCH. Hepatic involvement is usually seen in patients with extensive LCH and is a poor prognostic factor.[20] Our subject expired 15 months after the detection of hepatic fat density lesions, although fat density lesions had disappeared during follow-up.

In summary, we describe a case of LCH involving the bone, lung, CNS, and liver. In each imaging feature in 1 organ, it is occasionally difficult to discriminate LCH from other disorders. Therefore, systemic evaluation is needed when LCH is suspected. Familiarity with the various features of LCH on imaging is paramount for diagnosing and managing patients in daily practice.

Author contributions

All authors contributed to the patient care, had access to the data, and played a role in writing this manuscript.
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