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Langerhans Cell Histiocytosis with Uncommon Liver Involvement: A Case Report

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient: Female, 60-year-old
Final Diagnosis: Langerhans cell histiocytosis
Symptoms: Fatigue • weight loss
Medication: —
Clinical Procedure: —
Specialty: Radiology

Objective: Rare disease

Background: Langerhans cell histiocytosis (LCH), also called histiocytosis X, belongs to a group of rare neoplasms and is a clonal pathology characterized by infiltration of Langerhans cells. The pathology can occur with the involvement of only 1 organ, more frequently the bone or with multi-visceral involvement, and patients frequently receive a delayed diagnosis and empirical treatments.

Case Report: We report a case of LCH in a 60-year-old woman who presented atypical symptoms, imaging findings of lung and liver involvement. Imaging showed increased liver volume and subverted structure by multiple nodular formations. For the differential diagnosis with other neoplastic liver diseases, the patient underwent liver biopsy, with microscopic typical findings of the disease and positive immunohistochemical markers.

Conclusions: Liver involvement in LCH is rare and the differential diagnosis with neoplastic pathology may pose a challenge for the clinician and radiologist, also due to the possible association between LCH and malignant tumors.

MeSH Keywords: Histiocytosis, Langerhans-Cell • Liver Neoplasms • Multidetector Computed Tomography

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/923505

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Background

Langerhans cell histiocytosis (LCH), also called histiocytosis X, is a rare clonal pathology characterized by infiltration of Langerhans cells [1]. The World Health Organization (WHO) considers LCH to be a neoplastic pathology of the hematopoietic compartment, presenting BRAF V600E mutations in approximately 50% of patients and MAPK/ERK mutations in approximately 90% of patients. LCH has an annual incidence of <5 cases per million population [2]. It can affect patients of all age groups, and is most common in women (F/M=2/1.5) and in children ages 1–3 years [3]. The pathology can occur with the involvement of only 1 organ. It usually has bone or multi-visceral involvement (e.g., lung, liver, gastrointestinal tract, spleen, lymph nodes, hypothalamus, pituitary gland); therefore, the spectrum is quite variable. LCH often id an incidental finding in imaging of patients with severe multi-organ failure, frequently receiving a delayed diagnosis and empirical treatment. We report a case of LCH in a 60-year-old woman who presented atypical symptoms and imaging findings of lung and liver involvement, who subsequently underwent liver biopsy, which led to a definitive diagnosis.

Case Report

A 60-year-old female patient was sent to our department to receive total-body CT with contrast medium for suspected liver cancer according to clinical indication. The patient had paternal history of hepatic cancer and she was in iatrogenic menopause from a previous hysterectomy for uterine fibromyomatosis. She had contracted acute HBV infection at age 6 years, and had a previous cholecystectomy for lithiasis. She was a smoker but denied use of alcohol. At the specialist examination,

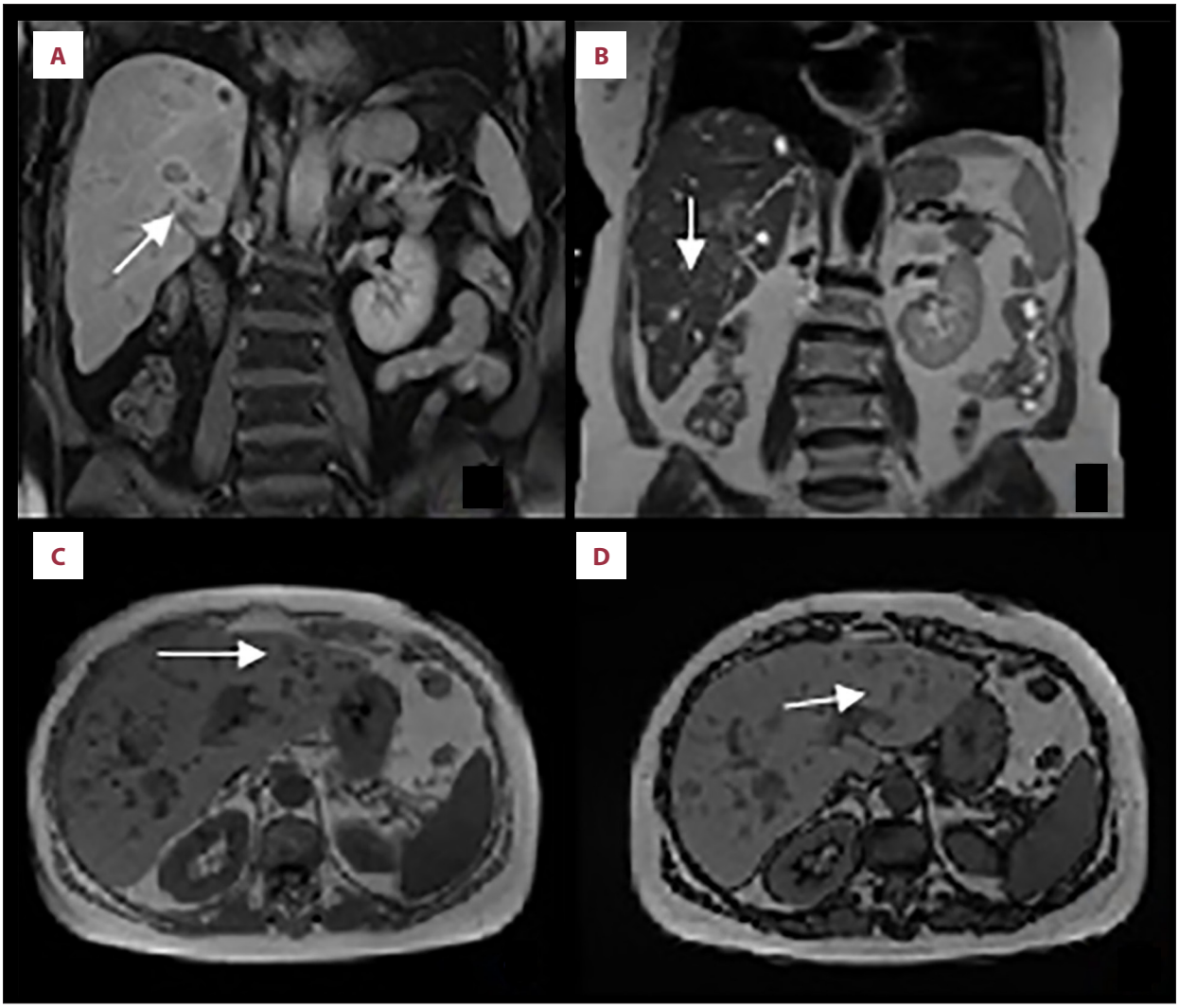

Figure 1. (**A–D**) MRI coronal and axial scans showing ectatic intra- and extrahepatic biliary tracts, as well as inhomogeneous signal intensity due to the presence of multiple centimetric nodular areas partly confluent (arrows).

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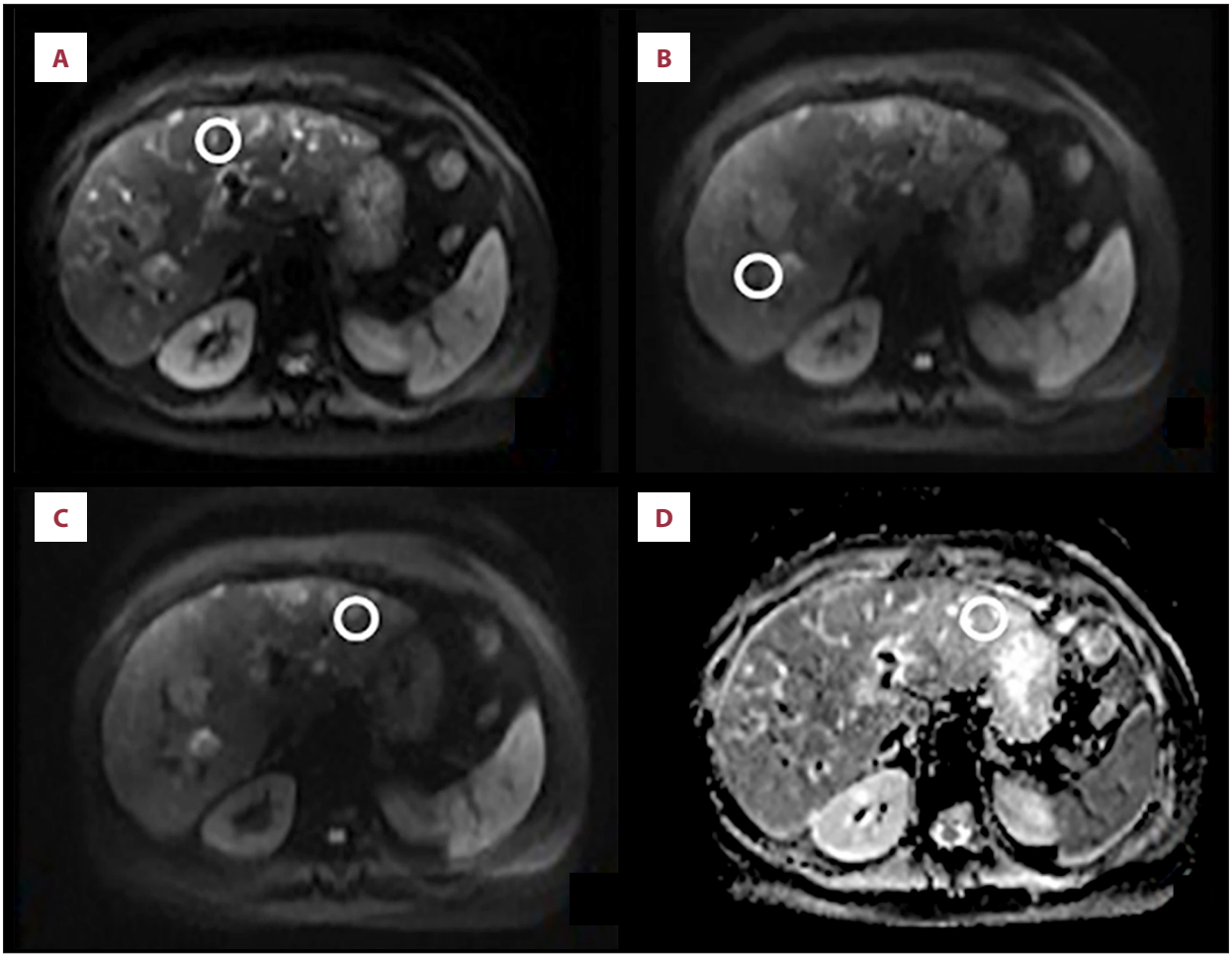

Figure 2. (**A–D**) MR axial diffusion-weighted imaging (DWI) scans. Dilated intrahepatic biliary tracts (empty circle).

she reported weight loss and fatigue. The physical examination showed hepatomegaly. Laboratory tests showed an increase in cholestasis indicators (GGT about 30 times the normal value), increased cytolysis indexes, neutrophil leukocytosis, HbsAg, and negative Ab-HCV. Due to suspicion of cholangitis, she received an ultrasound of the abdomen supplemented with contrast medium (CEUS), which showed slight ectasia of the biliary tract and numerous nodular formations with a maximum diameter of 2 cm, which appeared isovascular in the arterial phase. Washout in portal and late phase oriented the diagnostic framework toward neoplastic lesions. MRI of the abdomen was performed using a 1.5 T MR system, including axial, coronal, and sagittal images, and post-contrast scans performed with axial three-dimensional fat-suppressed T1-weighted gradient echo imaging after intravenous administration of hepatobiliary contrast media. MRI showed markedly ectatic intra- and extrahepatic biliary tracts with parietal enhancement after contrast, liver increased in volume at inhomogeneous signal intensity due to the presence of multiple centimetric nodular areas partly confluent, some with signs of contextual colliquation, with predominantly peripheral enhancement after administration of contrast medium (Figure 1). The remaining abdominal findings were normal. These findings suggested a possible inflammatory process of the biliary tract with abscess phenomena in the differential diagnosis, with metastatic hepatic lesions of unknown origin (Figure 2). Therefore, she underwent a total-body TC at our institute, which showed significant pulmonary and hepatic findings, which directed the suspected diagnosis towards LCH. The CT scan showed cystic thin-walled lung lesions, some confluent in bizarre cysts, maximum size 3 cm, with a predilection for the middle and upper areas, and regional sparing of costophrenic recesses (Figure 3). The liver appeared to be increased in volume and had structure subverted by multiple nodular formations, with predominantly peripheral enhancement and late-stage washout, as well as dilated bile ducts that also showed contrast enhancement (Figure 4). The brain CT scan showed no abnormalities. The bone segments were disease-free. For diagnostic confirmation and adequate therapy, the patient underwent liver biopsy, with microscopic typical finding of the disease and positive immunohistochemical markers: the granulomas consisted mainly of macrophages that had a strong antibody positivity

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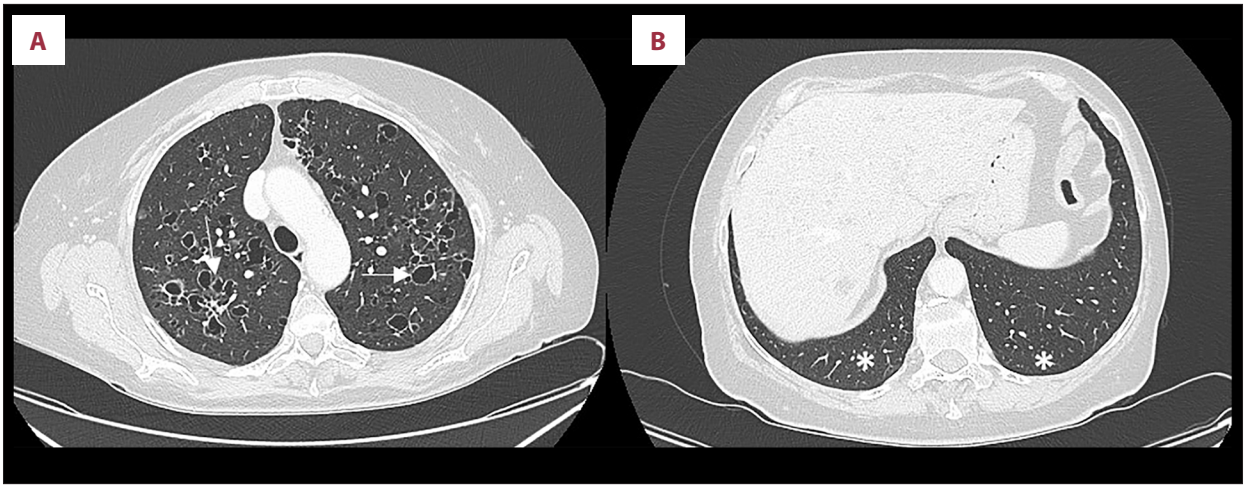

Figure 3. (**A, B**) axial thoracic CT images (lung window) shows typical confluence of cysts in bizarre shapes with predilection for the middle and upper zones (arrows) and regional sparing of the costophrenic recesses (asterisks).

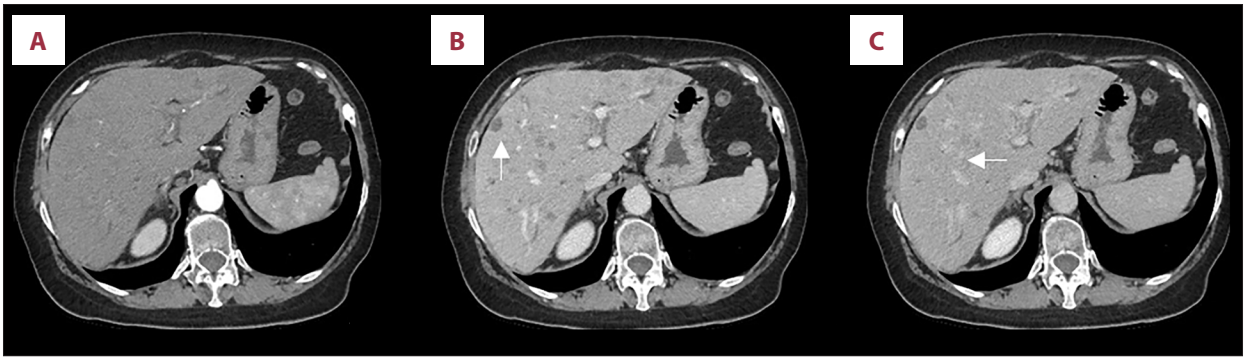

Figure 4. (**A–C**) Axial contrast-enhanced abdominal CT shows multiple diffuse hypodense nodules, some of them confluent (arrows).

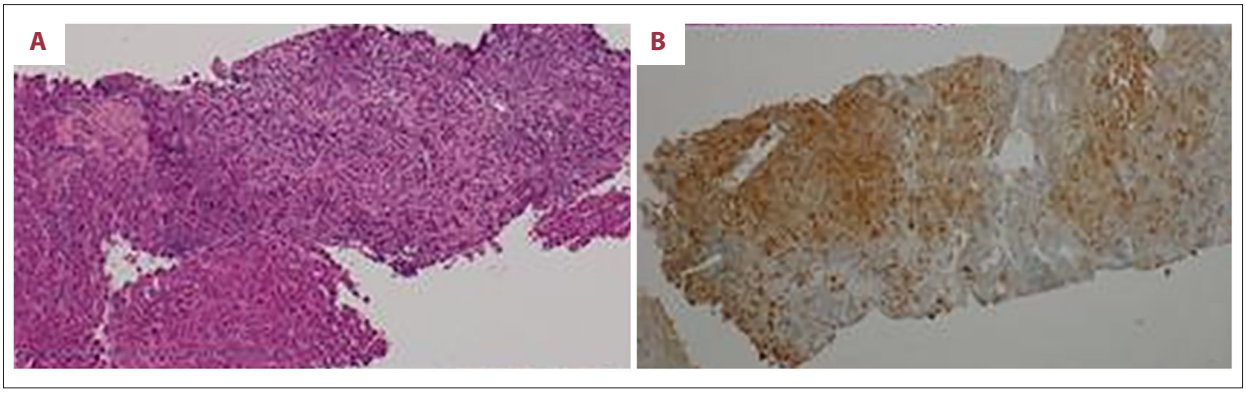

Figure 5. (**A**) Hepatic core needle biopsy: Hematoxylin/eosin-stained slides show hepatic parenchyma almost completely substituted by a middle-size cell population characterized by nuclei with membrane irregularity, with incision, dispersed chromatin, and slightly eosinophilic cytoplasm. A mixed infiltrate composed of lymphocytes, plasma cells, histiocytes, and numerous eosinophil granulocytes were also present around the lesions. There was moderate fibrosis, with disappearance of the portal spaces. (**B**) Immunohistochemistry showed positivity for CD1a.

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towards the S100 antigen, suggesting a diagnosis of histiocytosis X (Figure 5); therefore, the patient was sent to a specialized center for care.

Discussion

LCH is a rare Langerhans cell proliferative disease that mainly affects children and young adults, with higher prevalence in males. It most frequently affects the bone as a localized pathology, although it can have serious multisystem involvement [4]. Pulmonary disease presents imaging with suggestive findings that can guide the diagnosis. Most adults with pulmonary LCH are active or ex-smokers and about one-third are asymptomatic [5]. Functional lung test results may be normal or show a limitation of flow and a reduction in diffusion capacity. Chest X-ray is a first-line examination, but can show non-specific findings, frequently with a widespread bilateral symmetric reticulonodular pattern. HRCT is a level II examination, but can provide findings highly suggestive of LCH, in the early stages showing small nodules (about 2 cm), sometimes with central cavitation and centrilobular distribution, and may also be peribronchial or peribronchiolar. Advanced-stage diffuse cystic disease may involve 2 or more cysts with bizarre shapes. The typical distribution of the lesions is in middle and upper lung tissue, with sparing of the costophrenic grooves [6]. Bronchoscopic and surgical biopsy can confirm the diagnosis, supplemented by further instrumental investigations such as echocardiography and cardiac catheterization to identify patients with pulmonary hypertension. Hepatic LCH is rare, with an incidence in adults of about 16% and 27% of all LCH cases, while in children with multisystem LHC, it is more common, with incidence rates reported from 19% to 60% [3]. The involvement of the liver, often in the form of nodules, hepatomegaly, and involvement of the bile ducts by sclerosing cholangitis, causes a worse prognosis, with a mortality rate of 30%. Differential diagnosis with primary or secondary neoplastic disease of the liver can present a challenge, also due to the possible combination with other malignant neoplasms [7,8]. However, the discovery of involvement of other organs such as the lung, as in our case, helps to make the diagnosis of LCH [9]. In adults, liver involvement is often poorly recognized, with a focus on affected organs such as skeleton, skin, lung, and pituitary glands. The most frequent clinical symptoms of onset of the lung type are dyspnoea, non-productive cough, and pleuritic chest pain, and symptoms of the extrapulmonary type include bone pain, skin rash, and polyuria due to central diabetes insipidus [3]. In our case, the clinicians focussed on a primary or secondary hepatic neoplastic pathology due to their familiarity with neoplastic liver diseases, as well as due to the previous HBV-related infection, a laboratory picture of alteration of the liver function, and the ultrasound-MRI findings. Despite the subsequent finding of advanced pulmonary LCH, the patient did not have respiratory symptoms, but only had non-specific symptoms of fatigue and weight loss, without severe emaciation and skin changes. However, CT total body with contrast medium revealed an unexpected and surprising lung involvement. The findings, interpreted by an experienced radiologist, were highly suggestive of LCH, leading to the performance of a liver biopsy to quickly select more appropriate therapeutic procedures within a multidisciplinary assessment. The definitive diagnosis is, however, histological integrated with immunohistochemical tests that detect the expression of the following antigens: HLA-DR, CD1a, CD207 (langerin), S100, Ki-67, and possible BRAF V600E mutation. In the case of lung and liver involvement, treatment with ursodeoxycholic acid (for cholestatic disease), vinblastine, and prednisone may be indicated, which may lead to regression of liver nodules. The early stages of the disease are more sensitive to therapy, while liver transplantation may be indicated at an advanced stage [10]. Our objective in presenting this case report is to suggest, in the presence of recently found liver disease, among the diagnostic hypotheses, even rarer pathologies such as LCH, as the search for further radiological findings such as in our case can lead to making a diagnosis and more timely treatment with better patient outcome.

Conclusions

Isolated involvement of the liver in the LHC is infrequent, being more often present in multisystemic disease. The differential diagnosis with other primary or secondary liver cancer can be difficult. Together with the spleen and the hematopoietic system, it affects high-risk organs whose involvement is associated with a worse prognosis. Multi-organ involvement can in some cases help in diagnosis, which is, however, histological supplemented by immunohistochemical tests; the prognosis is mainly related to the disease burden and multisystem involvement. Chemotherapy is indicated in multisystemic forms and with involvement of organs at risk, while in advanced cases, hepatic transplantation may be considered.

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Conflicts of interest

None.

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