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LIVER HISTIOCYTOSIS MASQUERADING AS HEPATIC DYSFUNCTION: RARE CASE STORY

Emilija Nikolovska Trpchevska[1, 2], Meri Trajkovska[1, 2], Dafina Nikolova[1, 2], Beti Todorovska[1, 2], Elena Curakova Ristovska[1, 2], Gjorgji Deriban[1, 2], Gregor Krstevski[1, 2], Dragica Nikolova[3], Anita Ristoska Nanusheska[4]

[1] University Clinic for Gastroenterohepatology, "Ss. Cyril and Methodius" University in Skopje, North Macedonia
[2] Medical Faculty, "Ss. Cyril and Methodius" University in Skopje, North Macedonia
[3] General Hospital Strumica, North Macedonia
[4] General Hospital Struga, North Macedonia

Corresponding author: Emilija Nikolovska Trpchevska, University Clinic for Gastroenterohepatology, 1000 Skopje, North Macedonia, e-mail: emilijanikolovskageh@gmail.com

ABSTRACT

Introduction: Langerhans cell histiocytosis (LCH) is a rare histiocytic neoplasm occurring less frequently in adults than in children. Although various organs can be affected, resulting in a heterogenous clinical presentation, liver involvement is uncommon, particularly in adults. Herein, we present a case of LCH with liver involvement in an adult patient.

Case Report: A 40-year-old man presented with painless jaundice and abnormal liver function tests. Diagnostic work-up revealed hepatosplenomegaly, and excluded common causes of liver dysfunction. Liver biopsy revealed microscopic findings typical of the disease and positive immunohistochemical markers. Hepatoprotective therapy resulted in improvement in liver function and withdrawal of symptoms.

Conclusions: Isolated LCH-related liver injury is rare. The differential diagnosis with other liver pathology may pose a challenge for clinicians and radiologists.

Keywords: Langerhans cell histiocytosis (LCH), hepatocellular injury, liver biopsy

INTRODUCTION

Langerhans cell histiocytosis (LCH) is a rare clonal pathology characterized by infiltration of LCs and migration of dendritic antigen-presenting histiocytes. Its clinical presentation is diverse, ranging from a single indolent lesion to an explosive multisystem disease [1]. Although various organs can be affected, alone or in combination, LCH infiltrates most frequently occur in the skin, bones, and pituitary gland. Involvement of the spleen, liver, and bone marrow is uncommon, reported in 15-20% of cases; however, damage to these organs may be life-threatening [1]. While involvement of the liver is well recognized in children, in adults, it is poorly understood and a cause of severe morbidity and mortality [2, 3]. Hepatic LCH might present as solitary tumor-like or cystic lesions, or as part of a systemic disease. Even when LCs are not demonstrable, sclerosing cholangitis can be

seen [4]. Herein, we present a case of liver injury caused by LCH in an adult patient.

CASE REPORT

A 40-year-old man presented at the Department of Gastroenterohepatology with a chief complaint of painless jaundice and headaches. Apart from that, the rest of the physical examination by systems showed no abnormalities. He had no underlying diseases and no history of alcohol or drug abuse. The abdominal ultrasound showed slightly enlarged liver with rounded edges and a coarser parenchymal structure, portal vein diameter of 13 mm, and diffusely enlarged spleen with a longitudinal diameter of 15 mm. The laboratory analyzes indicated preserved synthetic function of the liver, with elevated levels of gamma-glutamyl transpeptidase (500 U/L), alkaline phosphatase (211 U/L), alanine transaminase (236 U/L), aspartate transaminase (84 U/L), and total bilirubin (320 μmol/L) with a predominance of the direct bilirubin (246 μmol/L). The tumor marker tests, including carcinoembryonic antigen, alpha fetoprotein, carbohydrate antigen 19-9, and carbohydrate antigen 72-4, returned negative results. The immunological tests showed quiescent IgG and IgM, nonreactive HBsAg, anti-HCV, EBV, and CMV tests, and reactive anti-HBc test, although no HBV DNA was detected serologically. The conventional autoantibodies were also negative. Given the above findings, the patient was admitted for further evaluation and treatment. The ultrasound elastography revealed second- and third-degree liver fibrosis, and the magnetic resonance cholangiopancreatography showed only liver enlargement without biliary pathology. Subsequently, we performed ultrasound-guided liver biopsy. Although the Kayser–Fleischer ring was not observed at the inspection, the ophthalmological consultation was requested and Wilson's disease was ruled out. The ceruloplasmin levels and iron metabolism and thyroid function parameters were within the normal ranges. The urinary culture test returned positive for Klebsiella pneumoniae and Escherichia coli, and the antibiotic treatment was initiated according to the antibiogram. Due to the persistent headaches, the patient was evaluated by a neurologist and underwent brain computed tomography, which showed normal findings. Chest radiographs also showed no pathological changes. Due to the portal hypertension, screening gastroscopy was performed with no finding of varicosities. Pending the histopathological results, after laboratory parameters were normalized within the reference values, the patient was discharged with the following therapy prescribed: non-selective beta-blocker, potassium-sparing diuretic, ursodeoxycholic acid, vitamin E, and a hepatoprotective agent. An IgG-4 test was recommended, which was completed at the Institute of Immunology with a negative finding. The liver biopsy findings showed histological diversity, including lobular LC infiltrate with mixed inflammatory background, primary biliary cholangitis-like pattern, sclerosing cholangitis-like pattern, and even cirrhosis at later stages. The patient was diagnosed with LCH-induced liver injury. He has regular outpatient follow-ups, regularly takes his therapy, and is in good clinical condition, with liver function test results within the normal limits.

DISCUSSION

LCH is considered an inflammatory myeloid tumor presenting with abnormal LC proliferation and accumulation in various organs. Its pathogenesis remains unclear, and the clinical manifestations are largely dependent on the organs involved [5]. LCH incidence in adults is approximately 1-2 cases per million. Hepatic LCH is rare in adults, accounting for approximately 16-27% of all cases, while it is more common in children with multisystem disease, with a reported incidence ranging from 19% to 60% [6]. The laboratory tests show abnormal liver function tests, with mild to moderate increase in transaminase levels, as well as cholestatic biochemical profiles, with increased levels of total bilirubin, gamma-glutamyl transferase, and anaplastic lymphoma kinase. Our patient was a 40-year-old man with liver dysfunction as the first symptom. Based on the patient's history and laboratory examination findings, we ruled out the common causes of liver dysfunction.

Liver imaging studies may show solitary or multiple low-density nodular lesions [7,8], diffuse hepatomegaly, periportal signal abnormalities, and biliary duct dilation and wall thickening [9]. In our case, the abdominal ultrasound showed liver and spleen enlargement.

Hepatomegaly and splenomegaly occur either due to direct LCH infiltration or due to the

Kupffer cell hypertrophy and hyperplasia secondary to a generalized immune reaction [10]. Liver biopsy is the cornerstone of LCH diagnosis and staging. A definitive diagnosis can be established based on positive immunohistochemical staining with CD1a and S100 antigens, typical for LCs. However, these cells predominate in early-stage lesions, while in later stages, their presence decreases and that of foamy macrophages and fibrosis increases. Hence, when liver biopsy is performed at an advanced stage of the disease, it may show only fibrosis with little or no LCs. Furthermore, it is difficult to differentiate hepatic LC clusters from primary biliary cirrhosis-associated granulomas in small biopsy samples. In such cases, the lack of usual histological features of primary biliary cirrhosis, such as dense portal lymphocytic infiltrate and mild degree of interface activity, and antimitochondrial antibody negativity might be a clue. In addition, recognizing nuclear grooves of LCs might be helpful for the diagnosis along with immunohistochemistry [11]. LCH-related involvement of the small and large intestines is very rare, occurring in approximately 2% of systemic LCH cases [12]. In such scenarios, even if a clinical history of LCH is provided, it would be very difficult to differentiate LCH- associated secondary sclerosing cholangitis from primary sclerosing cholangitis. To make this distinction, the entire biopsy sample should be carefully examined for evidence of LCH, and a "beaded" appearance of the extrahepatic biliary tree on imaging may be helpful for the diagnosis of primary sclerosing cholangitis. The histopathological finding of liver biopsy in our patient is as follows. Dilated portal space, infiltrated with a moderate lymphoplasma-monocyte inflammatory infiltrate with swelling of the border membrane and focal piecemeal necrosis. Single neutrophils are seen in places, and epithelial transformed histiocytes are also seen. LCH is more sensitive to therapy in the early stages of the disease, while liver transplantation may be indicated at an advanced stage [13]. In adult patients, various treatment strategies have been employed, depending on the clinical course and degree of organ involvement. In cases of liver involvement, treatment with ursodeoxycholic acid (for cholestatic disease), vinblastine, and prednisone may lead to regression of liver nodules [14,15]. If symptoms disappear quickly after diagnostic biopsy, remission can occur even without further therapy [16]. In our case, the patient received hepatoprotective therapy only, and further treatment was not received. After discharge, the patient was regularly controlled with liver function test results within normal limits.

CONCLUSION

Isolated liver involvement in LCH is infrequent, being more often present in multisystemic disease. The differential diagnosis with other primary or secondary liver tumors can be difficult. Liver biopsy plays an important role in the diagnosis and management of hepatic LCH.

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Резиме

ХИСТИОЦИТОЗА НА ЦРНИОТ ДРОБ ПРЕЗЕНТИРАНА КАКО ХЕПАТАЛНА ИНСУФИЦИЕНЦИЈА: РЕДОК ПРИКАЗ НА СЛУЧАЈ

Емилија Николовска Трпчевска[1, 2], Мери Трајковска[1, 2], Дафина Николова[1, 2], Бети Тодоровска[1, 2], Елена Чуракова Ристовска[1, 2], Ѓорѓи Дерибан[1, 2], Грегор Крстевски[1, 2], Драгица Николова[3], Анита Ристоска Нанушеска[4]

[1] Универзитетска клиника за гастроентерохепатологија, Универзитет „Св. Кирил и Методиј" Скопје, Северна Македонија

[2] Медицински факултет, Универзитет „Св. Кирил и Методиј" Скопје, Северна Македонија

[3] Општа болница Струмица, Северна Македонија

[4] Општа болница Струга, Северна Македонија

Вовед: Хистиоцитозата на Лангергансовите клетки (ЛХК) е исклучително ретка хистиоцитна неоплазма што се јавува поретко кај возрасните отколку кај децата. Иако може да бидат зафатени различни органи, што доведува до хетерогена клиничка слика, зафатеноста на црниот дроб е невообичаена, особено кај возрасните. Во овој труд прикажуваме случај на ЛХК презентирана со црнодробно оштетување кај возрасен пациент.

Приказ на случај: Станува збор за 40-годишен маж со безболна жолтица и абнормални параметри на црнодробната функција. Дијагностичката обработка покажа хепатоспленомегалија и ги исклучи вообичаените причини за црнодробна дисфункција. Биопсијата на црниот дроб покажа микроскопски наоди типични за ЛХК, како и позитивни имунохистохемиски маркери. Примената на хепатопротективна терапија доведе до подобрување на функцијата на црниот дроб и повлекување на симптомите.

Заклучоци: Изолираното оштетување на црниот дроб како резултат на ЛХК е ретко. Диференцијалната дијагноза со други црнодробни заболувања може да претставува предизвик за клиничарите и за радиолозите.

Клучни зборови: хистиоцитоза на Лангергансови клетки (ЛХК), оштетување на хепатоцити, биопсија на црн дроб