

Diabetes Insipidus and Sclerosing Cholangitis in a child may be a clue to the diagnosis of Langerhans' Cell Histiocytosis: A Case Report

Dr. Abdulaziz A. Al Salloom,¹ MBBS, MD, CABPath

Department of Pathology, College of Medicine, Qassim University, Qassim, Saudi Arabia.

Dr. Salman T. Almalki,² MBBS

Department of Pathology, Riyadh Armed Forces Hospital, Riyadh, Saudi Arabia.

Dr. Hadeel Al Mana,³ MD

Department of Pathology, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia.

Prof. Martin Burdelski,⁴ MD

Department of Organ Transplant, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia

burdelsk@uke.uni-hamburg.de.

Abstract:

Langerhans cell histiocytosis (LCH) is a rare disease that usually affects children and young adults. Sclerosing cholangitis (SC) can occur in 10-15% of patients with disseminated form of the disease. Central diabetes insipidus (CDI) is a rare disorder that may be caused by a variety of diseases mainly LCH and germinoma especially in children. In this case report, a 4-year-old girl who is a known case of CDI and a single bone lesion in the left humerus, presented with jaundice, abdominal distention and itching. The diagnosis of SC was made by histopathology on liver biopsy. In this case, we found a link between CDI and SC through LCH, the diagnosis of which was made by histopathology of the explanted liver. The combination of CDI, liver involvement with SC and a single bone lesion is remarkable, since the histological diagnosis of LCH was made outside the biliary tract in the liver parenchyma.

Correspondence to:

Dr. Abdulaziz AlSalloom

Department of Pathology,

College of Medicine

Qassim University,

Qassim, Saudi Arabia

Email: dr.abdulaziz.s@hotmail.com

Introduction:

LCH is a rare disease that is defined as clonal proliferation of Langerhans cells (CD1a⁺ dendritic cells).⁽¹⁾ Clinically, its manifestations range from skin lesions, isolated bone lesions to multisystem disease. LCH typically presents with hepatomegaly, SC and secondary biliary cirrhosis in the later course only. In other way, LCH is considered as a rare cause of the secondary SC. CDI may be caused by a variety of diseases, but about half of the cases, the cause of CDI is unidentified. The combination of 1) CDI, 2) SC, and 3) single bone lesion should be raised the suspicion of LCH.

Case Report

A 4-year old girl, a known case of CDI (diagnosed by excessive urination and extremely thirst associated with pituitary lesion), was in her usual state of health until 5 months prior to admission when she developed jaundice, abdominal distention and itching. Physical examination revealed abdominal distention and hepatomegaly. Her biochemical and hematology laboratory profile showed the following values: liver enzymes with total bilirubin 106 U/L (0-21), gamma-glutamyl transpeptidase (GGT) 331 U/L (7-32), alkaline phosphates 1,331 (100-240) U/L, ALT reaching 1,700 U/L (10-25), and AST 3,300 (10-45) U/L which was the maximum. Ultrasound abdomen showed heterogeneous parenchyma of the cirrhotic liver and there was no defined focal lesion. Further radiological studies showed that there was a single osteolytic lesion in the left humerus (Figure 1).



Fig. 1: There is a single osteolytic lesion in the left humerus seen in radiograph

Because of the nonspecific radiological picture, a decision to perform a wedge liver biopsy was made.

The liver wedge biopsy reported micronodular cirrhosis associated with significant ductular proliferation, bile plugs and suggestive features of paucity of intrahepatic bile ducts which are compatible with the diagnosis of SC (Figures 2&3).

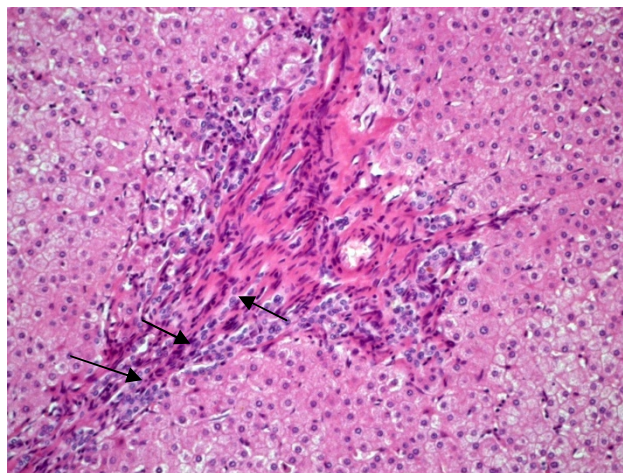


Fig. 2: Sclerosing cholangitis. Medium magnification (X100) showing a significant ductular proliferation.

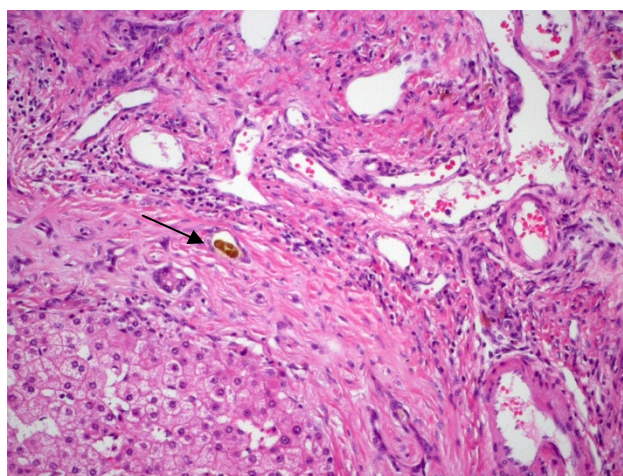


Fig. 3: Sclerosing cholangitis. Medium magnification (X100) showing bile plugs and features suggestive of paucity of intrahepatic bile ducts.

Therefore a liver transplantation was recommended. At transplantation, the explanted liver is weighing 520g and measuring 16X12X7.2 cm. The outer surface was firm nodular and glistening. Serial sections of the liver revealed pale brown nodular cut surface without an individual lesion. Histopathological examination revealed two foci with langerhans cells surrounding bile ducts and infiltrate portal tract associated with eosinophils, lymphocytes, and plasma cells (Figure 4).



Fig . 4: Langerhans cell histiocytosis. Medium magnification (X100) showing langerhans cells surround a bile duct and infiltrate a portal tract associated with eosinophils, lymphocytes, and plasma

Immunohistochemical stains showed strong positivity of the lesion cells with CD68, S100 protein and CD1a (Figure 5). A final diagnosis of secondary SC to LCH was eventually made. She was discharged home after 4 weeks.

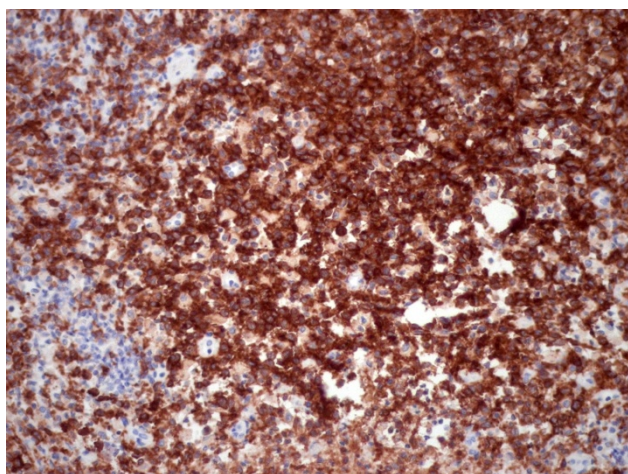


Fig . 5: CD1a antigen. Langerhans cells showing positive staining with CD1a antigen (specific marker)

Discussion:

LCH of liver is considered as a poor prognostic factor. It precipitates the occurrence of biliary cirrhosis. Usually, SC responds poorly to Langerhans histiocytosis treatment and liver transplantation must be considered. ⁽²⁻³⁾ However, LCH and SC are two rare diseases that are frequently linked in children. ⁽⁴⁾ Patients with hepatic involvement usually have a disseminated form of

the disease. ⁽⁵⁾ but may have isolated liver involvement. ⁽⁶⁻⁷⁾

Morphological changes and clinical findings in LCH of the liver may resemble primary SC or chronic non-suppurative destructive cholangitis. Therefore, LCH is an important differential diagnosis of chronic destructive cholangitis with cholestatic liver disease, especially in children and young adults. The diagnosis can be verified by S-100 and CD1a immunohistochemistry. ⁽⁸⁾

Because liver lesion in LCH is usually patchy without gross lesions, diagnosis of LCH is too tricky to be discovered. The first biopsy was reevaluated and showed no such single lesion.

Our case represents a rare example of LCH showing an unusual presentation of the liver involvement with rare complications.

A child presenting with CDI and SC should herald an intensive investigations for either a proof or an exclusion of LCH.

The literature search revealed, to the best of our knowledge, that liver involvement associated with CDI and SC in the same patient as a clue to the diagnosis of LCH was not reported before. ⁽⁵⁻¹³⁾

Conclusion:

Although LCH is considered to be one of the usual disorders in children, its initial presentation with CDI, SC as a clue to find LCH are not (to the best of our knowledge) reported before. CDI and SC are rare complications of LCH. This combination is even very rare in the same patient, but it may be a clue to the diagnosis of LCH.

References:

1. Stockschrader M, Sucker C. Adult Langerhans Cell Histiocytosis. *Eur J Haematol* 2006; 76:363–368. doi: 10.1111/j.1600-0609.2006.00648.x.
2. Sabib M, Ettair S, Erreimi N, Mouane N. Sclerosing cholangitis revealing Langerhans cell histiocytosis in a 15-month-old child. *Arch Pediatr*. 2011 Sep; 18(9):974-8.
3. Lee RJ, Leung C, Lim EJ, Angus PW, Bhathal PS, Crowley P, Gonzales M, Stella D, Seymour JF, Speer AG. Liver Transplantation in an adult with Sclerosing cholangitis due to multisystem Langerhans cell histiocytosis. *Am J Transplant*. 2011 Aug; 11(8):1755-6. doi: 10.1111/j.1600-6143.2011.03661.x.
4. Gey T, Bergoin C, Just N, Paupard T, Cazals-Hatem D, Xuan KH, Tavernier JY, Wallaert B. Langerhans cell histiocytosis and sclerosing cholangitis in adults. *Rev Mal Respir*. 2004 Nov; 21 (5 Pt 1):997-1000.
5. Pagnoux C, Hayem G, Roux F, Palazzo E, Meyer O. Sclerosing cholangitis as a

- complication of Langerhans' cell histiocytosis. *Rev Med Interne*. 2003 May; 24(5):3247.
6. Kaplan KJ, Goodman ZD, Ishak KG. Liver involvement in Langerhans' cell histiocytosis: a study of nine cases. *Mod Pathol*. 1999 Apr; 12(4):370-8.
 7. Buza N, Lagarde DC, Dash S, Haque. Langerhans cell histiocytosis: report of a single organ involvement in a child. *J Cell Mol Med*. 2004 Jul-Sep; 8(3):397-401.
 8. Haas S, Theuerkauf I, Kühnen A, Wickesberg A, Fischer HP. Langerhans' cell histiocytosis of the liver. Differential diagnosis of a rare chronic destructive sclerosing cholangitis. *Pathology*. 2003 Mar; 24(2):119-23.
 9. Prosch H, Grois N, Prayer D, Waldhauser F, Steiner M, Minkov M, Gadner H. Central diabetes insipidus as presenting symptom of Langerhans cell histiocytosis pediatric Blood Cancer. 2004 Oct; 43(5):594-9.
 10. Adam Z, Balsíková K, Krejčí M, Pour L, Stěpánková S, Svčina P, Hermanová M, Vaníček J, Krupa P, Staníček J, Koukalová R, Neubauer J, Krivanová A, Mayer J, Hájek R. Central diabetes insipidus in adult patients--the first sign of Langerhans cell histiocytosis and Erdheim-Chester disease. Three case studies and literature review. *Vnitr Lek*. 2010 Feb; 56(2):138-48.
 11. Badalian-Very G et al. Recent advances in the understanding of Langerhans cell histiocytosis. *BJH* 2011; 156: 163-172.
 12. Marchand I et al. Central Diabetes Insipidus as inaugural manifestation of Langerhans cell histiocytosis: natural history and medical evaluation of 26 children and adolescent. *J Clin Endocrinol Metab* 2011; 96: E 1352-1360.
 13. Gail E et al. Natural History of Idiopathic Diabetes Insipidus. *J Pediatr* 2011; 159: 566-570.