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Case Report

Findings of cholangitis in a kidney transplant patient with Caroli disease on FDG PET/CT and MRI ☆,☆☆

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ABSTRACT

Caroli disease is a rare congenital disorder of segmental cystic dilatations of the intrahepatic biliary ducts that maintain communication with the rest of the biliary tree. Its typical clinical presentation is recurrent episodes of cholangitis. The diagnosis is usually made using abdominal imaging modalities. We present a patient with Caroli disease showing atypical presentation of acute cholangitis with ambiguous labs and initial negative imaging findings, which was later diagnosed by [18F]-fluorodeoxyglucose positron emission tomography/computed tomography and confirmed by magnetic resonance imaging and tissue pathology. The use of such imaging modalities in moments of doubt or clinical suspicion provide the patient with accurate diagnosis, proper management, and better clinical outcome, thus obviating the need for further invasive investigations.

Introduction

Caroli disease is a rare congenital disorder of segmental cystic dilatations of the intrahepatic biliary ducts that maintain communication with the rest of the biliary tree, and it falls within the spectrum of fibro polycystic liver disease [1]. It is referred to as Caroli syndrome when congenital liver fibrosis and signs of portal hypertension are evident 2,3. Males and females are equally affected, and the age of onset is variable with the majority of patients being diagnosed before the age of 30 years 3,4. According to a systematic review by Fahrner et al. [5], the risk of developing cholangiocarcinoma in patients with Caroli Disease/ Syndrome is variable with an overall incidence of 6.6%.

The diagnosis of Caroli disease/syndrome can be made using abdominal imaging modalities such as ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI) with magnetic resonance cholangiopancreatography

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(MRCP). Imaging findings include cystic dilatation of the intrahepatic bile ducts, usually saccular of variable sizes, in segmental, lobar, or diffuse distribution. The most characteristic finding is the communication of those cysts with the main ductal branches of the biliary tree. Other imaging findings include choledocholithiasis, biliary sludge, biliary stenosis and strictures, hepatic cysts, and the central dot sign on CT or MRI, which represents the central vascular bundle surrounded by the dilated biliary duct 2,6,7.

The typical clinical presentation of Caroli disease/syndrome is recurrent cholangitis due to bile stasis in the cysts, which leads to stone formation and infection [8]. Cholangitis is typically diagnosed clinically based on Charcot's triad of fever, right upper quadrant pain, and jaundice. In cases where the clinical picture is weakly suggestive, laboratory findings and imaging studies can assist in confirmation of the diagnosis. The initial diagnostic imaging technique of choice includes abdominal US or CT scan. MRI is reserved for cases with high index of suspicion and negative findings on the usual imaging modalities [9].

We present a patient with Caroli disease showing atypical presentation of acute cholangitis with ambiguous labs and initial negative imaging findings, which was later diagnosed by [18F]-fluorodeoxyglucose (FDG) positron emission tomography/CT (PET/CT) and confirmed via MRI and tissue pathology.

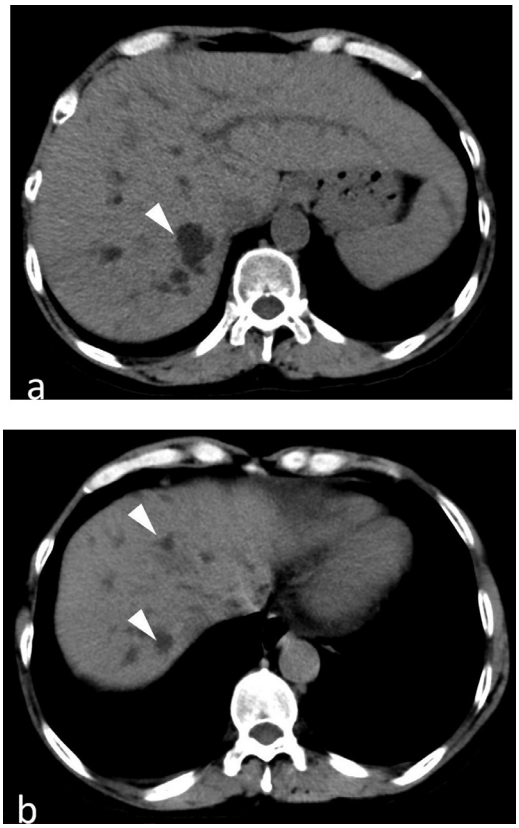

Fig. 1 – Nonenhanced axial CT scan images of the upper abdomen. Cuts (A) & (B) show focal cystic biliary dilatations in segments VII & VIII (arrowheads) of the liver. CT, computerized tomography.

Case

A middle-aged patient who had undergone kidney transplant 15 years ago for glomerulonephritis presented to the emergency department with fever, chills, nausea, vomiting, and diffuse abdominal pain. The patient's previous medical history was pertinent for recurrent biliary colic and Caroli's disease diagnosed 8 years ago on MRCP with stable imaging findings on regular follow up (Fig. 1). Laboratory tests showed elevated gamma-glutamyl transferase (GGT) at 2.5 times the normal (123 IU/L; normal range: 10-50 IU/L) and alkaline phosphatase (ALP) at the upper limit of normal (144 IU/L; normal range: 35-120 IU/L) with mild increase in lipase (120 U/L; normal range: 13-60 U/L). Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were within normal range (normal range: 0-50 IU/L for both). Blood and urine cultures were taken and came out to be negative. Abdominal CT scan and US were performed and did not show evidence of biliary stones or increased dilatation in the biliary system when compared to a recent MRCP. The diagnosis of acute cholangitis was suggested and the patient's condition improved following a course of piperacillin-tazobactam (TAZOCIN, Wyeth Lederle SRL, Italy) for 7 days after which the patient was discharged home.

Four days after discharge, the patient presented again to the emergency department with recurrence of prior symptoms. Laboratory results showed elevated white blood cell (WBC) count (15,400/ cu.mm; normal range: 4000-11,000 /cu.mm) with left shift (Neutrophils reaching 89%; normal range: 40%-65 %). AST, ALT, and ALP levels were within normal limits. C-reactive protein (CRP) level reached 125.4 mg/L (normal range: 0.0-2.5 mg/L), GGT level was elevated at twice the normal limit (105 IU/L), and lipase level was elevated to 153 U/L. Thoraco-abdominal CT scans were performed to investigate any underlying source of infection. Tigecycline (TYGACIL, Wyeth Lederle SRL, Italy) was initiated and pan-cultures (blood and urine) were taken. Although CT scans and cultures came out negative, the patient's clinical condition worsened, as she remained febrile with tachycardia and tachypnea, along with rising C-reactive protein levels (203.2 mg/L) and WBC count (17,500/mm^3). FDG PET/CT was considered in the work up for fever of unknown origin for assessment of any infectious focus, deep abscess, or malignancy, taking into account the patient's immunosuppressed state. The PET/CT showed a large, intensely radiotracer-avid, mass-like lesion in hepatic segment VII with few smaller radiotracer-avid areas in hepatic segments I and VIII (Fig. 2); however, an underlying infectious/ inflammatory process was also considered. CA 19-9 antigen level was elevated reaching 2508 U/mL (normal range: 0.0-37.0 U/mL), which raised the suspicion of a possible underlying cholangiocarcinoma. MRI was performed afterwards for further characterization and showed abnormal arterial hyper-enhancement in the same segments of radiotracer avidity with no enhancement on the remaining dynamic sequences or underlying detectable mass on the rest of the sequences (Fig. 3). These findings

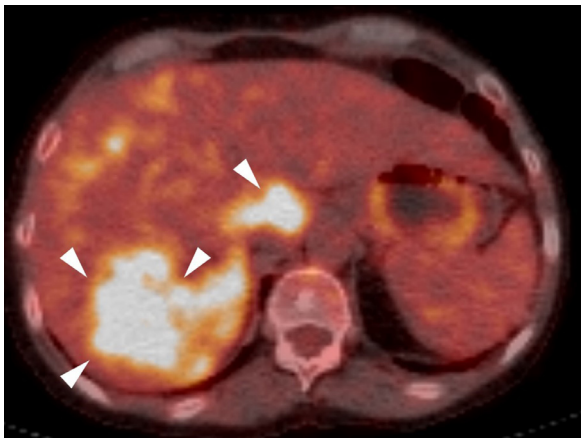

Fig. 2 – Axial fused FDG PET/CT scan image of the upper abdomen. Image shows mass-like lesions with intense FDG uptake in the caudate lobe and segments VII and VIII (arrowheads).

indicated severe hyperemia and inflammation suggestive of severe cholangitis involving mainly segments VII and to a lesser extent segments IVa, VIII, and the caudate lobe, which are the sites of biliary duct dilation and cyst formation. The patient was initiated on meropenem (MERONEM, ACS Dobfar S.P.A., Italy). Due to the high index of suspicion and based on a consensus of the team of involved physicians, a CT-guided liver biopsy was performed, and pathology results showed acute and chronic inflammatory cell infiltrates around the abnormally shaped bile ducts. The bile ducts did not show any atypia or dysplastic changes indicative of malignancy. These changes were consistent with Caroli's disease with hepatic fibrosis and superimposed acute cholangitis (Fig. 4).

The patient continued the prescribed antibiotics course of meropenem for 5 days with clinical and laboratory improvement and was then discharged home with a prescription of prophylactic antibiotics to prevent future bouts of cholangitis.

Discussion

Recurrent episodes of acute cholangitis can lead to the diagnosis of an underlying Caroli disease. Acute cholangitis is usually diagnosed clinically using Charcot's triad, which has high specificity reaching an overall value of 93.2% as mentioned in a systematic review by Rumsey et al. [10]. However, this triad is not sensitive, as not all patients with acute cholangitis present with all its components. According to Tokyo guidelines [9], in order to achieve a definite diagnosis of acute cholangitis with high sensitivity, 3 requirements must be met including 1 element of each the following: systemic inflammation, cholestasis, and imaging. The imaging component requires evidence of biliary dilatation or depiction of the etiologic factor. US is highly specific, as it outlines bile duct dilatation and stones when present. Despite that, it is operator-dependent and may be misleading when the etiology is not an obstructing stone. CT scan can also outline ductal dilation and reveal stones, and it can better specify the cause of dilatation and portray the presence of complications. MRI/MRCP is superior to the previous 2 imaging modalities due to its capability of delineating bile duct borders, depicting inflammation, differentiating between benign and malignant etiologies, and detecting complications. It is usually utilized when other imaging modalities fail to reveal any abnormality [9].

Our patient presented with fever and abdominal pain with no jaundice. Laboratory studies showed only elevated WBC and GGT with normal-limits values of ALK, AST, ALT,

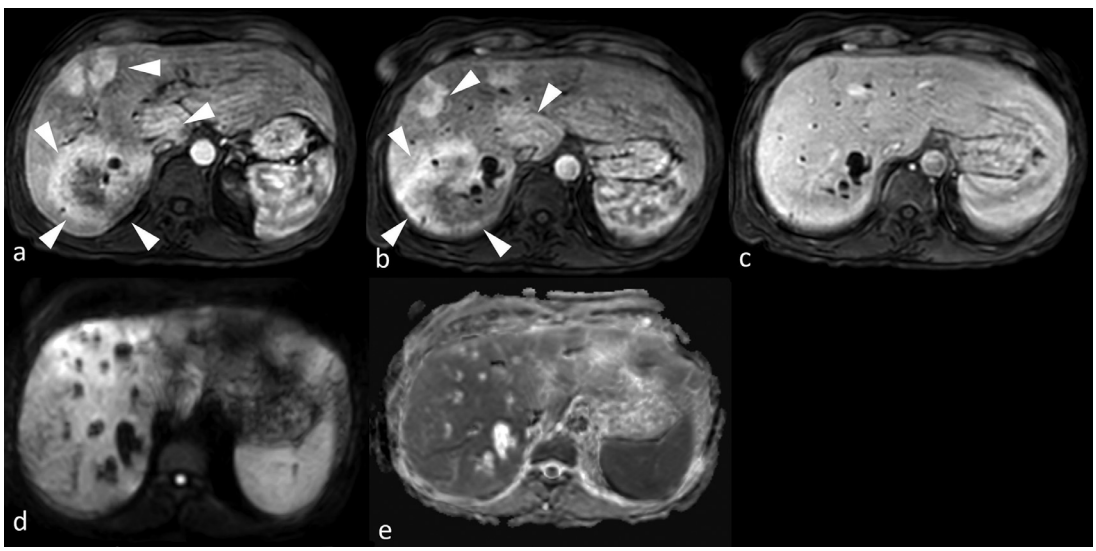

Fig. 3 – Upper abdominal axial images of different MRI sequences. (A) & (B) Arterial phase images showing large areas of intense arterial hyper-enhancement in the caudate lobe and segments VII and VIII (arrowheads). (C) Portal-venous phase image showing iso-enhancement of these segments to remaining liver parenchyma. (D) Diffusion weighted images with (E) ADC map showing no definite diffusion-restricting lesion.

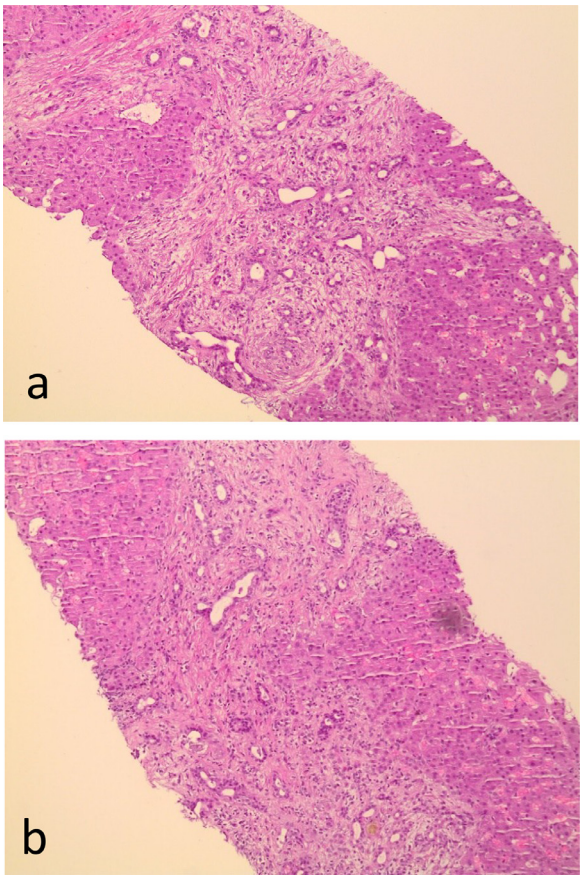

Fig. 4 – Photomicrographs of liver biopsy using Hematoxylin and Eosin (H&E) stain at 20× magnification. Images (A) & (B) show bile duct dilation and proliferation with bridging fibrosis. Acute and chronic inflammatory cell infiltrates are seen around the abnormally shaped bile ducts. There is no parenchyma and regenerative activity differentiating it from cirrhotic regenerative nodules. The bile ducts show no atypia and no dysplastic changes indicative of malignancy. These changes are consistent with Caroli's disease with hepatic fibrosis and superimposed acute cholangitis. Reticulin and Masson trichrome stains support the above description.

and bilirubin, especially on the second admission. Contrast-enhanced CT was deferred due to the patient's history of kidney transplantation. US and non–contrast-enhanced CT scan of the abdomen showed stable findings of mild Caroli Disease with no definitive findings of cholangitis (absence of obstructive stones or diffuse biliary ductal dilatation) and absence of any focus of infection or inflammation. These studies were considered limited and lacked definitive diagnosis of the underlying etiology to the patient's presentation and the persistent fever. A PET/CT scan was considered to investigate a possible inflammatory focus or malignancy. The PET/CT scan showed a large, intensely radiotracer-avid, lobulated, mass-like lesion in hepatic segment VII with few smaller radiotracer-avid areas in other hepatic segments. An MRI was performed to better characterize the PET/CT findings, and it revealed severe cholangitis in the FDG-avid segments with absence of any underlying intraductal solid mass. Histopathological biopsy confirmed the diagnosis of acute cholangitis and excluded malignancy.

The use of FDG PET/CT scan has shown increased sensitivity and specificity in detecting benign lesions in oncologic patients, with the majority being inflammatory in origin [11]. Additionally, 1 prospective study by Keidar et al. [12] showed that FDG PET/CT imaging provided necessary information to guide further assessment and depicted etiologic foci in patients with fever of unknown origin. FDG PET/CT scan has been the diagnostic modality capable of diagnosing acute cholangitis and other infectious processes in patients with negative findings on other imaging modalities or non-related clinical presentation [13–15].

Our case is the first to use PET/CT in the diagnosis of acute cholangitis in a patient with Caroli disease. In such patients, high index of suspicion must be maintained, as it might be difficult to diagnose acute cholangitis due to the baseline architectural distortions of the liver and the segmental dilatation of the biliary tree. In our patient, the pathogenesis of cholangitis can be attributed to the segmental saccular dilatations of the intrahepatic biliary duct housing biliary secretions and leading to their stasis. With lack of drainage, biliary stasis culminated in biliary sludge formation, which provided a nidus for bacterial colonization and infection. This can explain why ALP and bilirubin were not elevated throughout the patient's admission, as there was no obstruction of the biliary ducts reflected by the absence of diffuse biliary dilatation on US and non–contrast-enhanced CT of the abdomen. Similarly, a study done by Hong et al. [16] showed that acute cholangitis could occur without biliary dilation on imaging. CA 19-9 antigen levels can be elevated in benign hepatobiliary conditions including cholangitis, which may mislead the diagnosis [17]. Hence, an MRI was done to confirm and better clarify the findings on PET/CT and localize the foci of inflammation or malignancy. The usual expected findings of cholangitis, which include increased signal around the bile duct on T2-weighted images and heterogeneous enhancement of the bile duct wall [9], were not evident in this patient. Instead, the patient's MRI showed parenchymal arterial hyper-enhancement suggesting hyperemia and inflammation, which represented the foci of cholangitis, with no duct-occupying lesions or irregular thickness to indicate a cholangiocarcinoma. These findings of cholangitis were confirmed by biopsy.

Conclusion

The definite diagnosis of acute cholangitis requires clinical, laboratory, and imaging components. In patients with Caroli disease, the diagnosis of acute cholangitis may be set back as regular imaging findings can be misleading due to the underlying architectural distortion of the liver. Therefore, additional imaging modalities should be considered for outlining underlying etiologies. PET/CT and MRI have shown high sensitivity for detection of infectious etiologies and exclusion or confirmation of malignancies. The use of such imaging modalities in moments of doubt or clinical suspicion provide the patient with accurate diagnosis, proper management, and

better clinical outcome, thus obviating the need for further invasive investigations.

Patient consent

The patient provided a written informed consent to publish medical details and radiological and pathologic images.

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