中文題目：以不明熱、多囊腎及肝硬化為臨床表現的 Caroli's syndrome 個案報告

英文題目：Fever of unknown origin, polycystic kidney disease and cirrhosis in a case of Caroli's syndrome

作　　者：曾上宸[1], Geana Creslyn Hanson[2], Francesca Shamika Steven[2], Roymar Adriana Idiaquez[2], 洪士元[2,3]

服務單位：[1]義大醫院內科部, [2]義守大學醫學院學士後醫學系, [3]義大醫院內科部腎臟科

Introduction

Caroli's disease is characterized by non-obstructive cystic dilatation of the intrahepatic bile ducts, while Caroli's syndrome consists of Caroli's disease with congenital hepatic fibrosis[1]. Intrahepatic stone, recurrent cholangitis and liver abscess were the most common complications. It also attributes to higher incidence of cholangiocarcinoma, with an incidence around 7%[2,3,4].

Caroli's syndrome is often associated with autosomal recessive polycystic kidney disease (ARPKD)[5]. Genetic studies found that ARPKD and some cases of Caroli's disease shared the same mutation on polycystic kidney and hepatic disease 1 (PKHD1) gene[6]. Therefore, some authors believed that these two conditions are actually different stages of the same disease[1]. On the other hand, the association of Caroli's syndrome with autosomal dominant polycystic kidney disease (ADPKD) is very rare[7].

Herein, we introduced a case of polycystic kidney disease and end-stage renal disease underwent peritoneal dialysis, who presented with cryptogenic cirrhosis and fever of unknown origin (FUO).

Case Report

The 29-year-old man is a case of polycystic kidney disease resulting in end-stage renal disease

and has received peritoneal dialysis since 2011. There was no presentation of polycystic kidney disease among his family members. Cryptogenic liver cirrhosis was diagnosed in March 2020. He suffered from recurrent fever episodes and had been admitted to E-Da hospital twice within half year before this admission period. Despite of serial survey, fever focus could not be clearly identified. FUO was then diagnosed.

This time, the patient was admitted due to fever and chills for 1 day. He also reported epigastric dull pain and poor appetite without cloudy dialysate. Laboratory data showed elevated C-reactive protein: 134.9 mg/L and mild leukocytosis (white blood cell count: 10690 /uL). The dialysate cell counts for red blood cell and white blood cell were both 0 /uL. Under the impression of intra-abdominal infection, intravenous ceftazidime and vancomycin were prescribed empirically.

Abdominal computerized tomography (CT) scan was performed later. It revealed bilateral polycystic kidney disease, liver cirrhosis and diffuse intrahepatic bile duct cystic lesions, which is compatible with Caroli's disease; (Figure 1). An echocardiography showed no evidence of infective endocarditis. Gallium-67 inflammation scan also revealed no evidence of active inflammatory process. Acute cholangitis or intrahepatic cyst infection resulted from Caroli's syndrome were suspected clinically. He responded well to prolonged antibiotic treatment with levofloxacin for 4 weeks, and there was no more fever episode noted again for more than 9 months after being discharged.

Discussion

Caroli's syndrome has previously been described in conjunction with ARPKD since the patients with both diseases have mutation on the same gene PKHD1[6,8]. However, other researchers also found rare cases suffered the combination of ADPKD and Caroli's sydrome[7]. The mutated genes for ADPKD are different from that of Caroli's syndrome, there are polycystic kidney disease 1 or 2 genes[7,9]. Therefore, coincidence might be one of the explanations of this situation. For our case, the family history of polycystic kidney disease is not detected. Because ADPKD is predominantly autosomal-dominant inherited, the possibility of ADPKD for our reported case is relatively low. Although the gene study is not available, we suppose this is a case of Caroli's syndrome-associated ARPKD.

Patients with Caroli's disease often remain asymptomatic before the age of twenty years[10]. After entering early adulthood, intrahepatic stone, cholestatic jaundice, cholangitis, liver abscess and sepsis would emerge[11]. As a consequence, patient might suffer from fever and abdominal pain. Our patient developed the symptoms of repeated fever episodes with abdominal pain in the age of 29, just mimicked the common clinical presentations of Caroli's disease.

The diagnosis of Caroli's disease depends mainly upon image studies. CT scan or magnetic resonance cholangiography could reveal irregular aspect of the saccular or cystic dilatations, communication of these structures within the biliary trees, and even the formation of intraductal

lithiasis[6]. Our case was also first suspected to be a case of Caroli's disease by the images of CT scan. Accompanied cryptogenic liver cirrhosis noted since March 2020 and the history of ARPKD further supported the diagnosis of Caroli's syndrome.

There was one case report noted that meropenem needed to be administered intravenously during every hemodialysis session to achieve fever-free for a patient of Caroli's disease getting cholnagitis.[7] Our case had received 2 courses of intravenous ceftazidime and vancomycin during last 2 admissions, but still developed fever and sepsis in this admission, indicating inadequate course or poor tissue penetration to the infectious foci. It eventually subsided after shifting to intravenous and then oral levofloxacin treatments for 4 weeks. This finding suggested that the infection foci might not only simple cholangitis, but be more complicated cyst infection or microabscess formation.

Conclusion

Caroli's disease is a rare autosomal recessive disorder that some of the cases shares same genetic mutation with ARPKD. Composed of dilated intrahepatic bile duct, cirrhosis and ARPKD, Caroli's syndrome is mainly diagnosed by image studies.

Our case presented with FUO and epigastric pain. Although CT and inflammation scans could not found the definite infection foci, careful clinical suspicion and prolonged antibiotic course would be an ~~important~~ considerable strategy for the treatment of patients with Caroli's syndrome. .

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Figure legend

Figure 1. The abdominal computerized tomography (CT) scan on 2021/9/2 showed diffuse intrahepatic peri-biliary (arrowhead) and peri-portal (arrow) cystic lesions at both lobes, compatible with Caroli disease (a); and bilateral renal atrophy with thin cortex, calcification and cystic changes, compatible with polycystic kidney disease (b).