Case Report

A Rare Case of Caroli Disease in a 32-year-old Man with Vitiligo

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ABSTRACT

Caroli disease is characterized by bile duct ectasia without other liver abnormalities. In contrast, Caroli syndrome is characterized by bile duct dilatation with congenital liver fibrosis. Caroli disease is rarer than Caroli syndrome. This paper introduces a 32-year-old man with vitiligo and asymptomatic Caroli disease who was accidentally diagnosed following a fall from a height.

Keywords: Caroli disease; Intrahepatic bile ducts; Vitiligo

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INTRODUCTION:

Caroli disease (CD) occurs in two forms, pure type or CD, characterized by dilatation of intrahepatic bile ducts without other histological disorders. The combined type or Caroli syndrome(CS) is characterized by intrahepatic bile duct ectasia, congenital liver fibrosis, and polycystic kidney disease. The adult congenital disease has been reported in adults, adolescents, and children, and the mode of inheritance is autosomal recessive in most cases (1), although the genetic basis of the differences in CD and CS has not been defined.

The pathogenesis of CD is the cessation of normal regeneration of the larger intrahepatic bile ducts during the fetal period, resulting in varying degrees of inflammation and segmental dilatation of the bile ducts (1). Cholangitis, liver cirrhosis, cholangiocarcinoma, liver abscesses, and gallstones are potential complications of CS (2). Due to the rarity of this disease, death in such patients is often due to sepsis and liver abscesses (3).

CASE REPORT:

A 32-year-old man, a factory worker, was brought to the clinic due to falling down. During the physical examination and paraclinical workup, dilatation of the biliary duct was detected accidentally by sonography, so he was referred to a gastroenterologist for further evaluation. The patient

had a negative history of pruritus, abdominal pain, fever and chills, weight loss, discoloration of urine, or dysuria, and had no history of smoking or drug abuse. In physical examination, asymmetry of the shoulder and hypo-pigmented areas on the chest and back skin and dorsal surface of the penis were seen (Figure 1). The patient had complaints of itching in these areas for about 5-10 years. The vital signs were normal with no jaundice, and lung and heart sounds were normal. There was no tenderness or organomegaly on the abdominal examination.

In paraclinical data, Complete blood count(CBC), Liver function tests(LFT), and kidney function were normal, viral markers were negative, alpha-fetoprotein (AFP) was 4.8 (ng/mL),and cancer antigen 19-9(CA-19-9)was 3.2 (U/mL). With an impression of CD, he underwent Magnetic resonance cholangiopancreatography (MRCP), in which multiple cystic dilatations in intrahepatic bile ducts (central dot signs) with normal extra-hepatic bile ducts were reported (Figure 2), which confirmed CD. We

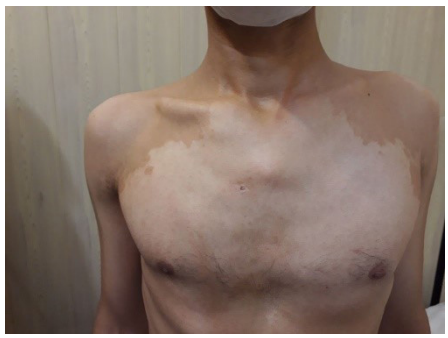

Fig. 1: Hypopigmented skin lesions in the chest

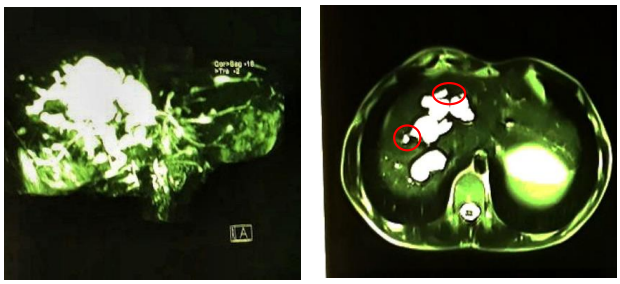

Fig. 2: Magnetic resonance cholangiography. Multiple dilated intrahepatic ducts with tiny dots of strong contrast are seen in the liver. These represent portal radicles and constitute the characteristic central dot sign for CD (red oval)(a) irregular cystic dilation of the large proximal intrahepatic bile duct (IHD) with a normal common bile duct (b).

did not do an additional workup for malignancy because the patient did not have clinical and lab data in favor of malignancy until this age. The patient was advised to perform liver tests and sonography at intervals of 3-6 months. Selenium sulfide shampoo and fluconazole capsules were also prescribed for the patient's skin lesions. After 20 days of taking the prescribed drugs, except in the dorsal area of the penis, other areas of the hypopigmented areas were disappeared. Therefore, vitiligo was diagnosed for the dorsal region of the penis.

DISCUSSION:

CD is a congenital disorder characterized by multifocal segmental dilatation of the large intrahepatic bile ducts. This disease is usually associated with cystic kidney disease of varying severity (4). CD is a less common form and is characterized by bile duct ectasia without other liver abnormalities. However, CS, in which duct dilatation with congenital liver fibrosis is observed, is more common (5). CD and CS are autosomal recessive disorders and are associated with autosomal recessive polycystic kidney disease (ARPKD). Rare cases have occurred with autosomal dominant polycystic kidney disease.

In addition, CD and CS are associated with other fibrocystic diseases, including nephronophthisis 13, Meckel-Gruber syndrome, COACH syndrome , Joubert syndrome, and related disorders, and Biedl and Bardet syndrome. An oral-facial-digital syndrome is also associated (6). The incidence of this disease is 1 in 1000 population (7). The onset of symptoms can be infancy or asymptomatic in the first 5-20 years of life. However, 80% of patients become symptomatic by the age of 30 (8,9), but our patient was not symptomatic until the age of 32 years. No kidney involvement was also seen.

The molecular pathogenesis of the CD and CS is not fully understood. Nevertheless, the polycystic kidney and hepatic disease 1(PKHD1) gene, which causes ARPKD located on chromosome 6 (6p21-p12), encodes a large protein (4074 amino acids) called fibrocystine. Impaired production of this protein is the leading cause of structural abnormalities in the liver and kidneys. This gene is primarily expressed in the kidneys and to a lesser extent in the liver, pancreas, and lungs (10).

Mutations in two different genes Polycystic Kidney Disease (PKD1 or PKD2) lead to the predominant polycystic kidney, which, as mentioned above, has rarely been associated CD. Protein products of PKD genes (polycystic-1 and polycystic-2) are expressed in the kidney, liver, and biliary system and may be involved in the growth and differentiation of these organs (11).

Proteins that are defective in many fibrocystic liver and kidney diseases, including ARPKD and ADPKD, are expressed in the primary cilia and the centrosome complex of renal tubular cells and cholangiocytes. Ear cilia are immobile organs found on the duct's surface of many distinct epithelial cells, sensing mechanical, chemical, and osmotic stimuli connected with duct fluid flow and transmitting these signals to various signaling pathways within cells such as intracellular calcium and cyclic adenosine monophosphate (AMP). The natural activity of these primary cilia is essential for the normal growth of the liver and biliary system. (12).(??please rephrase this part0

It is necessary to show the connection between the sacs and bile ducts to diagnose the disease (13). Although ultrasound and Computed Tomography(CT) findings help diagnose the disease, they may not show an association between intrahepatic dilatation sacs and bile ducts. Therefore, Endoscopic retrograde cholangiopancreatography (ERCP) and MRCP can be used for a definitive diagnosis. However, due to ERCP's invasive nature, MRCP is preferred (14).

For cases in which Magnetic resonance imaging (MRI) findings are doubtful, direct cholangiography can be used (15). Prenatal diagnosis of CD with ARPKD is performed with 3-D ultrasound and MRI (16). Examination of the liver biopsy in CS typically shows extensive fibrotic tissue bands and deformed structures of the bile ducts that characterize congenital liver fibrosis. Hypoplasia of the portal vein branches and acute and chronic inflammatory cell infiltration around dilated bile ducts may also be seen. However, liver biopsies are rarely used to diagnose the disease (17).

In both CD and CS, the gallbladder's dilatation provides the basis for bile stasis, leading to biliary sludge and intraductal lithiasis formation. Bacterial cholangitis occurs frequently and may be exacerbated by sepsis and the formation of liver abscesses. Secondary biliary cirrhosis can also occur due to biliary obstruction (18). Patients with CS can experience portal hypertension and its complications, such as esophageal varices.

However, people with CD only experience intermittent abdominal pain. Itching and hepatomegaly are common in both types of cases. Children with CS usually develop symptoms and advanced disease earlier due to the combined effects of cholangitis and hypertension (19). The liver is repeatedly enlarged on physical examination, and splenomegaly may be detected.

Laboratory studies typically show elevated serum alkaline phosphatase (ALP), direct bilirubin, and a neutrophil-dominated leukocytosis. Also, impaired blood coagulation due to vitamin K absorption may occur in cholestatic form (19).

However, no vitiligo has been reported in these patients so far. Clinical findings may be confused with extra-hepatic v-type Chaldean cysts that spread into the hepatic bile ducts, but it should be noted that these Chaldeal cysts are not associated with CD (6).

Although there is no cure for the disease, supportive measures, including antibiotics for sepsis and cholangitis, can be used. Additionally, supplementation with fat-soluble vitamins in patients with chronic cholestasis and non-selective beta-blockers in patients with esophageal varices and pharmacological treatments such as ursodeoxycholic acid, which increase bile flow and decrease bile stop, can be used for gallstones (20,21). However, in patients who experience recurrent cholangitis and have complications associated with portal hypertension, studies have shown that liver transplantation further increases survival chances (22).

The prognosis varies depending on the severity of the disease and the presence of renal dysfunction. Recurrent biliary lithiasis infections can be associated with significant complications. As mentioned above, liver transplantation may be the only option for patients with refractory disease. Due to significant biliary stagnation and the presence of high concentrations of unconjugated secondary bile salts, the risk of cholangiocarcinoma increases by up to 7%, and amyloidosis has been seen due to inflammation caused by chronic or recurrent cholangitis (23).

CONCLUSION:

CD, also known as communicating cavernous ectasia of the intrahepatic ducts, is a rare congenital disorder characterized by non-obstructive multiple cystic dilatations of the intrahepatic bile ducts. The rarity of the disease and the absence of specific clinical signs make the diagnosis difficult.

CLINICAL SIGNIFICANCE:

CD is a rare entity. The patients might go undiagnosed for a long time.

ETHICAL APPROVAL:

The Ethics Committee of Hamadan University of Medical Sciences approved the protocol of this study (IR.UMSHA.REC.1399.885).

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