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Mini Review

Primary Sclerosing Cholangitis

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Abstract

We present a case of a 47-year-old woman with non-specific symptoms and signs of anaemia. Her liver function tests were abnormal and Anti-Nuclear Antibodies (ANA) was significantly elevated. Magnetic Resonance Cholangio-Pancreaticography (MRCP) revealed multiple strictures of intrahepatic ducts and colonoscopy revealed mucosal inflammation and polyps. Imaging-guided liver biopsy was also performed and the findings were compatible with Primary Sclerosing Cholangitis (PSC) with ulcerative colitis. Patient was treated for anaemia and appropriate drugs were prescribed for the auto-immune condition. Prevalence of PSC is very rare in Singapore. It is characterized primarily by inflammation and fibrosis of the biliary tree. It is associated with inflammatory bowel disease and a host of other conditions, eventually leading to cirrhosis and death. Diagnosis is achieved by imaging, laboratory markers and histology. ERCP is the current gold standard investigation, although MRCP is the non-invasive investigation of choice. Early diagnosis and medical intervention slow the disease progression and decrease mortality and morbidity.

Keywords: Sclerosing cholangitis; MRCP; Inflammatory bowel disease

Introduction

A 47-year-old woman presented with exhaustion and shortness of breath on exertion. She also had history of occasional giddiness. She had regular menses and no abdominal pain or malena. On general examination, pallor was present. Abdominal examination revealed mild tenderness in the right upper quadrant. There was no guarding or rigidity. Rest of the physical examination was unremarkable. She had history of stones in the gall bladder and bile duct for which she had undergone Endoscopic Retrograde Cholangio-Pancreaticography (ERCP) and removal of a calculus few years ago. She was diagnosed to have iron deficiency anaemia at that time, but she did not undergo any further evaluation. Presently, her haemoglobin was low (6.4 g/dl) and liver function tests were abnormal (Alkaline phosphatase – 423U/L (normal range 22-104 U/L), Gamma glutaryltransferase 664U/L (normal range 7-32 U/L). Aspartate Transamine (AST) was 97 (normal range 10-30U/L)) and the albumin: globulin ratio was reversed. The bilirubin and alkaline transaminase were within normal limits. Antinuclear Antibodies (ANA) were significantly elevated measuring 210%. Other autoantibodies were negative Colonoscopy was done as a part of investigation for anaemia and features of pancolitis were observed with pseudopolyps in the descending and sigmoid colon (Figure 1). Inflammation was also noted in the terminal ileum (active colitis was proven by biopsy as well). Ultrasonography of the abdomen was unremarkable. Magnetic Resonance Cholangio-Pancreaticography (MRCP) was done in view of abnormal liver function tests (Figure 2). What is the diagnosis?

Diagnosis

Primary sclerosing cholangitis.

Image interpretation

MRCP demonstrated diffuse intrahepatic strictures and mild dilatation of the common hepatic duct and left and right main ducts.

Treatment and clinical course

Patient underwent liver biopsy under imaging guidance, which demonstrated mild portal hepatitis with septal fibrosis and destructive cholangitis which were compatible with the diagnosis of sclerosing cholangitis. Anaemia was treated with blood transfusion. Patient was discharged after improvement in symptoms. She was advised various drugs including Azathioprine, Prednisolone, Mesalazine and iron supplements and is on regular follow-up.

Discussion

Primary Sclerosing Cholangitis (PSC) is a chronic cholestatic liver disease of intra and/or extrahepatic bile ducts, probably of auto-immune origin [1]. This condition is commonly associated with inflammatory bowel disease [1], especially ulcerative colitis as in our patient. Other conditions which may be associated or be present along with PSC include celiac disease, diabetes mellitus, rheumatoid arthritis, Sjogren's disease, chronic pancreatitis, cystic fibrosis and systemic lupus erythematosus [1]. The diagnosis is very important because the risk of colorectal malignancies and cholangiocarcinoma is very high in these patients [2]. Although autoimmune aetiology is likely, portal bacteraemia, viral infection, toxic bile acid and ischemic injury are some of the hypothesized causes. Certain studies have shown PSC to be more prevalent in non-smokers as compared to controls [3,4]. Males are twice more commonly affected and the peak age is around third to fifth decade [5]. Africans and Afro-Caribbean's are at an increased risk of developing PSC due to genetic factors [5,6] and increased prevalence is also reported among Caucasians [6,7]. Exact incidence and prevalence in Singapore is not known [7]. According to Ang et al, prevalence of inflammatory bowel disease and positive pANCA is very less in patients with PSC in Singapore [7].

The clinical features are highly variable and patients may present with fatigue, abdominal discomfort, pruritus and weight loss. Liver function tests are often abnormal and patients may have background

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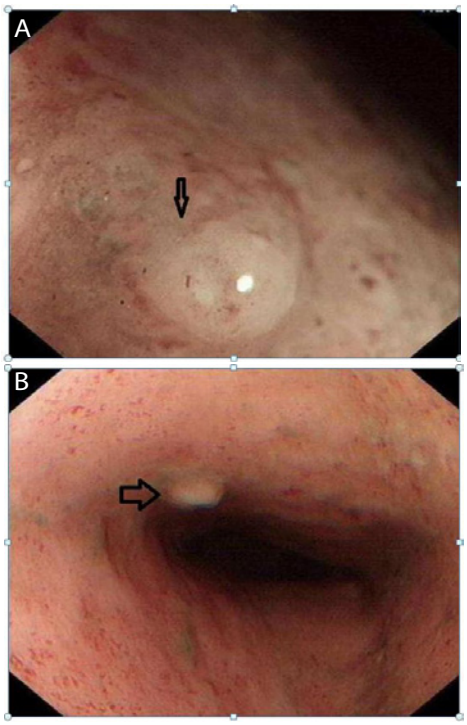

Figure 1: Colonoscopy images of descending colon (A) and sigmoid (B) showing the inflamed mucosa and pseudopolyps (arrow).

of inflammatory bowel disease. Eventually there may be signs of liver failure or they may develop cholangiocarcinoma [8].

Immunochemistry is gaining popularity with increased Immunoglobulin M (IgM) in 50% of cases and hypergammaglobuminemia in a third of the patients. Low titre autoantibodies such as Anti-Nuclear Antibody (ANA), Smooth Muscle Antibodies (SMA) and perinuclear Anti-Neutrophil Cytoplasmic Antibodies (pANCA) can be present.

Early changes can be focal and missed on liver biopsy. The most common finding is of periductal concentric 'onion-skin' obliterative fibrosis surrounding the bile ducts. In advanced disease, an entity called 'vanishing bile duct syndrome' is noted with loss of bile ducts as the central feature [9].

The diagnosis can be made on imaging by identifying the typical cholangiographic findings coupled with clinical presentation. Exclusion of conditions mimicking PSC such as cholangiocarcinoma, secondary cholangitis or stone disease is an important step in making the diagnosis [10]. The role of ultrasound is very limited and can detect changes of cirrhosis only in advanced stage. Visualization of intrahepatic biliary radicals is often difficult on ultrasound. Contrast enhanced computed tomography showing mural contrast enhancement of the extrahepatic ducts is a consistent finding, along with dilatation, stenosis, wall thickening and nodularity. ERCP is the gold standard examination and can be used for diagnosis as well as treatment of strictures and/or removal of debris within the ducts. Common findings include cobble stoning, stricture formation and duct dilatation. The presence of diverticula or pseudodiverticula is pathognomonic. Magnetic Resonance Cholangio-Pancreaticography (MRCP) is becoming investigation of choice due to inherent

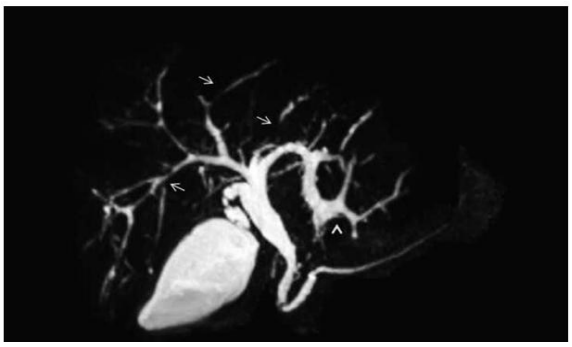

Figure 2: Thick slab MRCP image showing multiple strictures in the intrahepatic biliary ducts (arrows). And dilated left hepatic duct (arrowhead).

advantages over ERCP. The advantages of MRCP apart from being non-invasive modality, include lack of radiation, faster imaging and visualization of dilated peripheral intrahepatic ducts. Other findings in MR imaging include periportal lymphadenopathy, periportal increased T2 signal and signal changes in the liver parenchyma [11]. There are advantages of ERCP over MRCP, such as increased sensitivity in the visualization of peripheral ducts, mechanical dilatation of ducts, ability to obtain specimen for histopathological analysis and placement of stent. However the risks and complications such as haemorrhage, infection, perforation of the duct or intestine can occur. Hence MRCP is preferred diagnostic modality and ERCP is generally used for therapeutic guidance, rather than for diagnosis [12].

The median reported survival in patients with PSC is 10-12 years [13]. Early diagnosis and management is essential to delay the progress of the disease. Ursodeoxycholic Acid (UDCA), a naturally occurring bile acid, is proven to improve the liver enzyme function in PSC, but its role in improving liver histology is controversial. Surgical management of precirrhotic patients involves resection of the entire extrahepatic biliary tree, including the hepatic duct bifurcation. Ductal dilatation with/without stenting of intrahepatic ducts leads to a longer symptom free period. The interventions can delay but not prevent development of cirrhosis. Once cirrhosis has developed, liver transplantation is the treatment of choice [14].

Conclusion

Primary sclerosing cholangitis is a chronic liver disease of unknown etiology, characterised primarily by inflammation and fibrosis of the biliary tree. It is closely associated with inflammatory bowel disease and a host of other conditions, eventually leading to cirrhosis and death. Diagnosis is achieved by imaging, laboratory markers and histology. ERCP is the current gold standard investigation, although MRCP is the non-invasive investigation of choice. Early diagnosis and medical intervention slow the disease progression and decrease mortality and morbidity.

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