Case report

Primary Sclerosing Cholangitis and Biliary Cirrhosis associated with Ulcerative Colitis

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Primary sclerosing cholangitis and ulcerative colitis are caused by progressive inflammation of the bile duct and large intestine respectively. The existence of any plausible association between primary sclerosing cholangitis and ulcerative colitis remains highly elusive. Little is known about the incidence and prevalence of primary sclerosing cholangitis with concomitant ulcerative colitis in the Indian subcontinent. We report a case of primary sclerosing cholangitis with long standing ulcerative colitis which later also developed primary biliary cirrhosis.

Key words: Primary sclerosing cholangitis, Ulcerative colitis, Primary biliary cirrhosis

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Primary sclerosing cholangitis (PSC) is a chronic liver disease characterized by obliterative inflammation and fibrosis which usually involves the whole biliary tree¹. PSC causes damage to the bile ducts both inside and outside the liver, resulting in scarring of the bile ducts and blockage of bile flow, causing cholestasis. Chronic biliary obstruction causes portal tract fibrosis and ultimately biliary cirrhosis and liver failure. It is reported that almost 70% of patients suffering from PSC present with concomitant idiopathic Ulcerative colitis (UC)². UC, one of the two most common manifestations of inflammatory bowel disease (IBD) is usually characterized by mucosal inflammation limited to the colon, always involving the rectum and a variable extent of the more proximal colon in a diffuse or continuous manner. The extent of disease varies from isolated proctitis to extensive disease i.e. pancolitis³.

The incidence of UC is approximately 10–20 per 100,000 per year with a reported prevalence of 100–200 per 100,000⁴. The incidence remains stable, but the prevalence is likely to be an underestimate because this implies average disease duration (prevalence/incidence) of 10 years for a condition that is known to last for life⁵. There are marked differences between ethnic groups with some (such as Ashkenazi Jews) having a particularly high incidence⁶. It is reported that annual frequency of PSC is 0.9-1.31/100,000 with point prevalence of 8.5-13.6/100,000 and this appears to be growing⁶. PSC is twice more frequent in men than in women (men constitute 2/3 of all cases). PSC occurs in 5% of patients with UC and UC occurs in 60–75% of patients affected with PSC⁶.

We present a rarely-reported case, of an Indian ethnic male with typical presentation of primary sclerosing cholangitis with long standing ulcerative colitis.

Case Report

In January 2005, a 44 year old male patient presented with jaundice, profuse bleeding per rectum, and frequency of stools [8-10/day]. The patient also...
suffered with fever, chills, rigors and severe abdominal pain over the preceding 10 days. Jaundice was found to be progressive and accompanied by pruritus.

His past record revealed that he had presented with complaint of blood in stools for about a year, occurring about 4-5 times per day, in 1993. The patient had been advised regular surveillance and follow-up for 6 months, but he had not returned for any medical visit subsequently. He had no history or evidence of other extra-intestinal manifestations, such as in joints or skin. The patient had no history of smoking or use of alcohol.

At this visit, tests for coronary artery disease (CAD), diabetes mellitus (DM), hypertension (HTN), and chronic obstructive airways disease (COAD), were found to be negative. Colonoscopic examination, followed by histopathology, revealed pancolitis with discrete multiple ulcers, MELD Mayo score of 10.

The patient was started on Salazopyrine (3000 mg / daily) and oral corticosteroids (Prednisolone, 30mg) with 5mg tapering per week.

The patients liver function tests (LFT) performed in January 2005 showed: Bilirubin - 9.5/7.0mg/dL, serum glutamic oxaloacetic transaminase (SGOT) – 605U/L, serum glutamic pyruvate transaminase (SGPT) – 235U/L, serum alkaline phosphatase (SAP) – 1400U/L, thymidine phosphorylase (TP) – 6.4U/mL, albumin (Alb) - 3.0 g/dl, haemoglobin (Hb)-12gm%, total leucocyte count (TLC) - 20,400 cu.mm. All viral markers were found to be negative.

The endoscopic retrograde cholangiopancreatography (ERCP) report indicated mildly dilated common bile duct CBD with multiple filling defects. The patient also underwent sphincterotomy, followed by balloon trawl, at this time, and multiple pigment stones were extracted. Cholangiogram revealed primary sclerosing cholangitis.

The patient was started on: Tab. Ursodeoxycholic acid (300 mg, twice daily), Tab. Mesalamine (800 mg, thrice daily), Proton pump inhibitor (PPI), Vitamin E and Vitamin B12 support.

He was discharged 3 days later with the diagnosis of UC with hepato-biliary complications and common bile duct (CBD) calculi causing obstructive jaundice.

In March 2005, the patient was reviewed. At this time the lab results were as follows: Bilirubin - 2.1mg/dl, SGOT - 38U/L, SGPT - 52U/L, SAP - 421U/L, Alb – 3.6g/dl, TP - 7.2 U/mL. The ultrasound abdomen showed subtle intrahepatic biliary dilatation (IHB) in both the lobes of liver, a CBD of 4 mm, and sludge in the gall bladder.

In September 2005, the patient came back with recurrent jaundice, fever, abdominal pain, but with UC in remission. The LFT results showed - Bilirubin 6.8mg/dl, SGOT - 362U/L, SGPT - 334U/L, SAP - 745U/L, Alb – 3.5g/dl, TP - 7.8U/mL. The ultrasound abdomen tested positive for IHBD and showed a mild dilation in CBD with multiple calculi. Again ERCP was performed, and after the balloon trawl test and extending the sphicterotomy, some pigmented calculi were extracted.

After 15 days the LFT showed normal results: Bilirubin - 0.9mg/dl, SAP - 451U/L). Colonoscopy showed pancolitis and in the biopsy (Bx) - Lamina propria showed diffuse infiltrates of plasma cells, lymphocytes and neutrophils; some of the glands showed degenerative changes. Granulomata and dysplasia were consistent with chronic UC in remission.

In May 2007, the patient presented with progressive abdominal distension and bilateral pedal edema since 3 months, and UC in remission. He had no fever, gastrointestinal (GI) tract bleeding, jaundice with pruritus, abdominal pain or alteration in sensorium. But the patient had generalized weakness, anorexia with fatigue & lethargy, and had ascites. Lab reports were as follows: Hb - 7.5gm%, TLC - 8,100 cu.mm; Platelets were adequate, bilirubin-1.4/0.3mg/dl, SGOT - 38U/L, SGPT -24U/L, SAP - 841U/L, Alb - 2.6g/dl and TP - 5.9U/mL. Ultrasound abdomen showed cirrhosis of liver with portal hypertension; upper gastrointestinal endoscopy indicated Grade II- Grade III esophageal varices.

The magnetic resonance cholangiopancreatography (MRCP) showed (Fig. 1 A & B) intrahepatic sectoral and segmental ducts which showed multifocal stenosis with minimum proximal dilation. A short segment with high grade stenosis of proximal left main hepatic duct was seen with moderate dilation of left hepatic ductal system. CBD involved two short segment high grade structures with smooth margins. Choledocholithiasis was positive. No hepatic encephalopathy or hepato-renal syndrome was found. All the findings were consistent with sclerosing cholangitis, and our final diagnosis was established as primary sclerosing cholangitis with biliary cirrhosis and long standing ulcerative colitis.

Discussion

Primary sclerosing cholangitis is a chronic cholestasis with progressive bile duct obliteration but the root cause remains largely unknown and it is more frequent in men. Primary sclerosing cholangitis has been considered to be a rare disease associated with inflammatory bowel disease, mainly ulcerative colitis and seems to be a risk factor for colon cancer.
Fig 1 (A & B). Magnetic resonance cholangiopancreatography (MRCP) shows intrahepatic sectoral and segmental ducts with multifocal stenosis, minimum proximal dilation and short segment with high grade stenosis of proximal left main hepatic duct (arrow mark) and moderate dilation of left hepatic ductal system.

Although the symptoms of UC usually develop before those of PSC, in some subset of patients, PSC may precede colitis by 4-5 years. It has been found that clinical outcome of hepatobiliary disease is completely independent of the activity, severity or clinical course of colitis, and vice versa.

The first study to assess the prevalence of PSC in a large series of patients with UC was performed in South America. Studies from Scandinavian countries, England and North America have shown that 2 to 3.7% of patients with UC have, or will have, PSC. The main risk factors include disease extent, dura-
tion, coexistent PSC, and a family history of colorectal cancer. Although several therapeutic trials have been conducted, effective medical therapy has not been shown to alter the progressive course of PSC. A steady increase in the serum alkaline phosphatase has been reported to be a better marker to identify patients with PSC. There are at least two possible mechanisms underlying the improvement of PSC associated in this patient. One possibility is that PSC may have improved via a mechanism similar to that underlying the improvement of UC. Recently, several studies have reviewed the role of PSC in the development of colorectal cancer in patients with UC. The risk of colorectal cancer as well as the probability of developing this complication was significantly higher in patients with UC and PSC. Liver transplant for PSC patients increases the probability for developing colorectal cancer. It has been demonstrated that in UC patients, liver transplants may worsen the colitis activity. More than a few mechanisms exist, to deal with patients with UC, PSC and liver transplants. Ursodeoxycholic acid has been definitively shown to reduce the risk of developing colorectal dysplasia and cancer in patients with UC and PSC. Recently, primary biliary cirrhosis (PBC) has also been reported in patients with UC and it should be differentiated from the more common finding of PSC. In addition to the characteristic feature of PSC in our patient, there was also PBC which developed at a later stage.

Conclusion
In this case study, we report a patient with typical primary sclerosing cholangitis associated with prolonged ulcerative colitis, which later developed choledocholithiasis and biliary cirrhosis.

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Conflict of interest: None

References