

Ulcerative colitis with concomitant primary sclerosing cholangitis

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SUMMARY

Primary sclerosing cholangitis (PSC) is the most common liver disease and known hepatobiliary complication of ulcerative colitis (UC). Concomitant PSC in UC is associated with increased risk of rapid progression of primary sclerosing cholangitis, and malignancy including colon carcinoma as well as hepatobiliary carcinoma. We report a case of a 26-year-old woman who was diagnosed as ulcerative colitis during her second pregnancy. Her liver function test showed a significant elevation of alkaline phosphatase (ALP) and gamma glutamyl transferase (GGT) with other parameters being within normal range. A clinical suspicion of primary sclerosing cholangitis was then made. Magnetic resonance cholangiopancreatography (MRCP) revealed beaded appearance of the right and left intrahepatic ducts with focal narrowing seen at the ducts, suggestive of primary sclerosing cholangitis. She was subsequently started on oral Ursodeoxycholic acid (UDCA) with improvement in her liver function test within 3 weeks of initiation of treatment.

INTRODUCTION

Ulcerative colitis (UC) is a chronic immune-mediated inflammatory condition which involves exclusively the rectum and colon. The incidence of UC is lower in Asia, with 6.3 per 100,000 person-years, as compared to 24.3 per 100,000 person-years in Europe.¹ In Malaysia, reported crude annual incidence of UC is 0.59 per 100,000 persons.² Common presenting symptoms for UC include bloody diarrhoea, rectal bleeding, tenesmus and abdominal pain.

Primary sclerosing cholangitis (PSC) is a rare disorder characterized by inflammation and fibrosis of intra and extra-hepatic bile ducts, associated with progressive liver disease. A population-based study performed in Norway over 10 years' period reported an annual incidence and point prevalence of 1.3 and 8.5/100 000 inhabitants, respectively.³ Data for prevalence or incidence of PSC in the Asian context is limited.

It is estimated that, in approximately 4-5%, inflammatory bowel disease (IBD) is accompanied by PSC. Conversely, 70-80% of IBD patients have coexisting UC. Ang et al reported 20% of PSC cases are associated with IBD in Singapore.⁴ Concomitant PSC in UC is reported to be associated with increased risk of rapid progression of PSC, and malignancy including colon carcinoma as well as hepatobiliary carcinoma.

CASE REPORT

We report a case of a 26-year-old woman who is an alpha zero thalassemia carrier diagnosed with UC during her second pregnancy. She initially presented with chronic diarrhoea and weight loss for 6 months' duration at 12 weeks' period of amenorrhoea (POA). Colonoscopy showed a rigid colon with loss of colonic folds and extensive pancolitis. Histopathological examination (HPE) of colon biopsy samples showed active colitis with chronicity changes, in keeping with active ulcerative colitis. She was then commenced on a course of oral prednisolone, oral and suppository mesalazine and her symptoms were subsequently well controlled. Her pregnancy was uncomplicated and she delivered a healthy baby girl.

A colonoscopy was then repeated 3 months postpartum for increased frequency of diarrhoea more than 20 times per day, with blood in stool, which responded partially to increment in dose of prednisolone and commencement of Azathioprine. It showed pancolitis with marked erythema, absent vascular pattern, erosion, markedly friability, worse at right colon and caecum consistent with Mayo 3 score (Fig. 1). Histologically, the biopsied bowel samples showed active ulcerative colitis with concomitant cytomegalovirus (CMV) colitis. She was then admitted for a 2 week course of intravenous Ganciclovir. While in the ward, we noticed that her alkaline phosphatase (ALP) level rose from 192 to 358IU/L, with concurrent rise in gamma-glutamyl transferase (GGT) 292U/L. Her antinuclear antibodies (ANA) and antimitochondrial antibodies (AMA) was negative. She however declined for a liver biopsy. Physical examination was otherwise unremarkable. Azathioprine was withheld in view of worsening cholestasis. A clinical suspicion of PSC was made. Ultrasound of hepatobiliary system showed features suggestive of fatty liver without biliary duct abnormality. Magnetic resonance cholangiopancreatography (MRCP) performed revealed beaded appearance of the right and left intrahepatic ducts with focal narrowing seen at the ducts (Fig. 2). As these changes are suggestive of PSC, she was subsequently started on oral Ursodeoxycholic acid (Ursofalk) 250mg bd. Her ALP improved from 358 to 199IU/L within 3 weeks of initiation of treatment. Meanwhile, she was still having active ulcerative colitis. Her diarrhoea and bleeding per rectal have worsened to more than 6 times per day. She was then subsequently worked up for biological therapy. Her chest X ray was clear and her serum Quantiferon Gold test was negative. After discussion, patient agreed to be started on subcutaneous Adalimumab (an anti-tumor necrosis factor (TNF)-alpha monoclonal antibody). A repeat colonoscopy 3 months after

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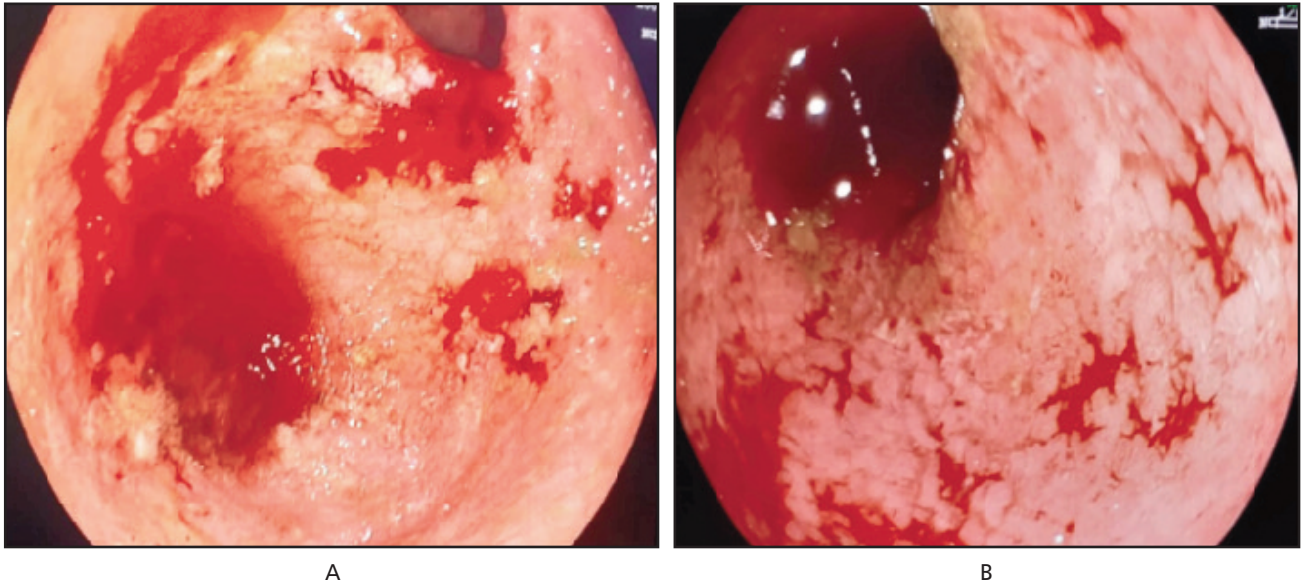


Fig. 1: Pancolitis with marked erythematous (A), friable bowel walls (B) noticed during colonoscopy.

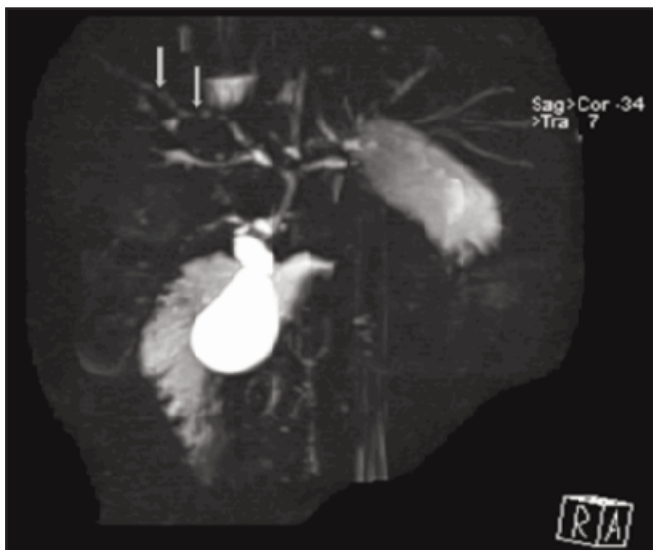


Fig. 2: Beaded appearance of cystic duct, right and left intrahepatic ducts (arrows) diagnosed during MRCP.

starting Adalimumab showed an improvement of the pancolitis (Mayo score 1). During her last clinic review, which was 8 months after the PSC diagnosis was made, her liver function test had normalized with her latest ALP value of 62IU/L. She is otherwise asymptomatic.

DISCUSSION

In this case UC was diagnosed during pregnancy, via colonic biopsy which was done to investigate chronic diarrhoea. UC in pregnancy is associated with higher risk of exacerbation of disease, especially if conception occurring at a time of active disease. UC is also linked with adverse pregnancy outcomes including preterm delivery, small for gestational age (SGA)

infant, increased neonatal intensive care unit admission, and low APGAR (Appearance, Pulse, Grimace, Activity, Respiration) score. Fortunately, pregnancy in our patient was uneventful and disease control on the other hand was able to be achieved with prednisolone and mesalazine.

Postpartum, UC is at high risk of relapse. In this case, UC relapsed with increasing frequency of diarrhoea. Oral prednisolone dose was increased to 30mg od (0.5mg/kg), T Azathioprine 50mg od was commenced on top of oral mesalazine 2g bd and suppository mesalazine 1g od. Disease symptoms are refractory to thiopurines, with only partial response despite on the mentioned treatment. Thus, colonoscopy was scheduled to exclude other causes of persistent symptoms including coexistent cytomegalovirus (CMV) or *Clostridium difficile*-associated disease. Repeated colonic biopsy showed active ulcerative colitis with concomitant CMV colitis. Colonoscopy showed pancolitis with right colon and caecum affected more severely.

We noticed her liver function test (LFT) was deranged with predominantly cholestatic picture when the patient was admitted to the ward for treatment of concomitant CMV colitis. Azathioprine was withheld. Ideally, other secondary causes of cholestasis should be excluded, including infection, immunodeficiency, ischaemia, pancreatic disease, or immunoglobulin (IgG4) related conditions.

PSC is the most common liver disease specific to IBD, especially UC.^{3,4} PSC can present with intermittent and nonspecific symptoms such as malaise, pruritus, fever, night sweats, and right upper abdominal quadrant pain, which may be masked by those of underlying IBD. High clinical awareness for PSC among patients with UC is needed as this disease is commonly asymptotically. PSC is usually picked up as an incidental finding of abnormal liver function test (LFT) as shown from this case report.

Ultrasound HBS showed no calculi and no dilatation of the biliary system. Nevertheless, ultrasound is usually undiagnostic of PSC. Thus, MRCP was subsequently done to look for the co-existence of PSC. MRCP has a sensitivity and specificity of 80% and 87% respectively in diagnosing PSC.⁵ In this case, MRCP showed few typical features of PSC, mainly beaded appearance of cystic duct, right and left intrahepatic ducts, as well as strictures of proximal right intrahepatic and left hepatic duct. Liver biopsy was not done as its role is limited in altering the management after.⁶

The management of IBD and PSC includes retardation and reversal of the disease process and prevention of complications of the disease. The management of UC and PSC is almost similar to management of UC alone. Ursodeoxycholic acid (UDCA) has been demonstrated to improve liver function tests by decreasing serum bilirubin, ALP and GGT. UDCA may be particularly considered in high-risk groups, for example those with strong family history of colorectal cancer, previous colorectal neoplasia or longstanding extensive colitis. Recommended dose of UDCA is 13-15mg/kg/day. However, there is limited data for the use of UDCA in reducing time to liver transplantation, cholangiocarcinoma, or death. In this case, we started our patient on oral UDCA 250mg bd, corresponding to 11mg/kg/day.

The presence of PSC in an IBD patient dramatically affects prognosis. It increases the risk of rapid progression of PSC, and malignancy including colon carcinoma, cholangiocarcinoma as well as hepatocellular carcinoma. Surveillance colonoscopy with biopsies is recommended at one to two years' intervals from the time of diagnosis of PSC in patients with UC. The median survival for patients with PSC from the time of diagnosis to death or time of liver transplantation is estimated to be 10-12 years. However, PSC with UC might progress fast, requiring liver transplant earlier

than expected. Intractable pruritus, recurrent cholangitis, and cholangiocarcinoma are among the indications for liver transplantation in PSC patients. Referral to a liver transplant center for assessment should be considered when the Model for End-Stage Liver Disease (MELD) score is >12. Post liver transplantation 5-year survival rates close to 85%.⁴

CONCLUSION

It is important to monitor liver function test frequently among patients with UC. PSC should be kept in mind as one of the important differentials during the work-up of UC patients with cholestasis as PSC might be asymptomatic. MRCP should be part of the investigation as early diagnosis might prevent further complications of the disease.

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