CASE REPORT OPEN ACCESS

A patient with primary biliary cirrhosis and ulcerative colitis with progression to primary sclerosing cholangitis and colorectal cancer: A case report

Rui-Hua Shi, Bo Hao, Shun-Fu Xu, Qi-Yun Tang, Jian-Xia Jiang

ABSTRACT

Introduction: Ulcerative colitis (UC) is a chronic inflammatory disease of the colon characterized by intermittent exacerbations and remissions. It can be associated with primary biliary cirrhosis (PBC) or primary sclerosing cholangitis (PSC) and complicated with colorectal cancer (CRC). We describe a complicated case of associaton of PBC and chronic UC, eventually progressed to PSC and CRC. Case report: A 41-year-old female was diagnosed as PBC based on liver biopsy 10 years ago, and then UC was diagnosed too. Now symptoms of jaundice and abdominal pain aggravated. At last PSC and CRC were conformed. Conclusion: Prolonged Inflammatory bowel disease (IBD) accompanied with PSC in a patient has high risk of CRC. More exploration is needed to gain insight into relationship between IBD, PBD, PSC and CRC.

Keywords: Primary biliary cirrhosis, Ulcerative colitis, primary sclerosing cholangitis, colorectal cancer.

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Shi Rui-Hua, Hao B, Xu Shun-Fu, Tang Qi-Yun, Jiang Jian-Xia. A patient with primary biliary cirrhosis and ulcerative colitis with progression to primary sclerosing cholangitis and colorectal cancer: A case report. International Journal of Case Reports and Images 2012;3(12):11–15.

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doi:10.5348/ijcri-2012-12-229-CR-3

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Received: 10 January 2012
Accepted: 10 July 2012
Published: 01 December 2012

INTRODUCTION

Primary billiary cirrhosis (PBC), primary sclerosing cholangitis (PSC), ulcerative colitis (UC) and colorectal cancer (CRC) are common diseases. PBC is marked by the slow progressive destruction of the small bile ducts (bile canaliculi) within the liver. When these ducts are damaged, bile builds up in the liver (cholestasis) and over time damages the tissue. This can lead to scarring, fibrosis and cirrhosis. PSC is a chronic liver disease caused by progressive immune-mediated inflammation and subsequent fibrosis of the bile ducts of the liver with the development of multiple strictures due to an intrinsic liver disease. The underlying cause of the inflammation is believed to be autoimmunity. Both PBC and PSC can be induced by autoimmune reactions. There are multiple similarities between these two diseases that may cause confusion or misdiagnosis, especially at the onset stage, including symptoms of fatigue, abdominal discomfort, pruritus and weight loss [1]. Diagnosis of PBC and PSC needs to be confirmed by liver biopsy.

UC is a chronic inflammatory disease of the colon characterized by intermittent exacerbations and remissions. It may be complicated with colon cancer or autoimmune-related extracolonic problems. It is not rare that PBC can be associated with UC and in such association occurrence of these diseases may not have particular order [2, 3]. Burnevich et al. reported that 24.1% of PBC patients has extrahepatic manifestations including UC [4]. It has also been reported that PBC can happen after proctocolectomy for ulcerative colitis [2].

There are many evidences that UC can be associated with PSC. Approximately, three quarters of patients with PSC have inflammatory bowel disease (IBD), e.g. UC or Crohn's disease [5] and 2–7.5% patients with UC have PSC [6–9]. It is, generally, accepted that approximately 5% of patients with UC will have the associated PSC.

We describe a complicated case of association of PBC and chronic UC, eventually progressing to PSC and CRC. Some special common mechanisms may be involved in the pathogenesis of these diseases.

CASE REPORT

A 41-year-old female was admitted with complaints of abdominal pain diarrhea and high fever for five days. The patient was diagnosed with PBC 10 years ago based on pathological examination of liver biopsy. Three years later, a colonoscopy examination proved a diagnosis of UC (Figure 1A). Symptoms including jaundice, pruritus and diarrhea persisted throughout the next seven years during which cholecystolithiasis developed in 2003 and relapsed in 2007. Four months before admission, the patient underwent hysterectomy and resection of right ovarian cyst along with right ovarian appendage in a local hospital. Rectovaginal fistula and rectal stenosis occurred one month after surgery. A metal stent was placed into the rectum. X-ray exhibited partial intestinal dilation with intermediate obstruction (beading). Magnetic resonance cholangiopancreatography (MRCP) showed typical appearance of PSC like diffuse strictures of both intrahepatic and extrahepatic bile ducts with dilation of the intervening areas and multiple bile duct stones in the common bile duct (Figure 1B–C). Severe abdominal pain and increasing skin icterus accompanied with high fever led us to take the patient for surgery. The laboratory test results of the patient are given in Table 1. A total colectomy and ileostomy were performed.

Peroperative findings: During surgery significant adhesions were observed in abdominal and pelvic cavity. Nodular cirrhosis of liver and splenomegaly was found. Biopsy from left external lobe of liver was taken for pathological examination. Ascending colon, cecum and small intestine were dilated with thickening and swelling of bowel wall. A hard mass of 3x3x3 cm invading the submucosa was found in ascending colon near the hepatic flexure which was causing intestinal obstruction. Distal colon and upper part of rectum were thickened and stiff.

Pathological results and final diagnosis: Histopathological examination of colon showed mucosal atrophy with loss of crypts and distortion of the mucosal architecture. Some of the crypts were shortened and branching. Transmucosal inflammation with basal plasmacytosis, lymphocytosis and eosinophilia were evidenced by the presence of neutrophils infiltrating the walls of some crypts. Thickening of mucosa muscularis layer and hyperplasia of fibrotic and fatty tissue in the submucosal layer indicated late stage of ulcerative colitis (Figure 2A). Grade II colonic adenocarcinoma was found which was invading all the layers of colon from epithelium to serosa to the surrounding connective tissue (Figure 2B). Lymph nodes metastasis was found positive in one out of 10 lymph nodes. The final diagnosis was UC concomitant with PSC complicated by colonic adenocarcinoma, liver cirrhosis, hypersplenism, post-cholecystectomy, post-hysterectomy, and post-unilateral adnexectomy. The patient was regularly followed-up and was given Pentasa, 1 g, qid, po; UDCA 250 mg, bid po. and UDCA without discomfort.

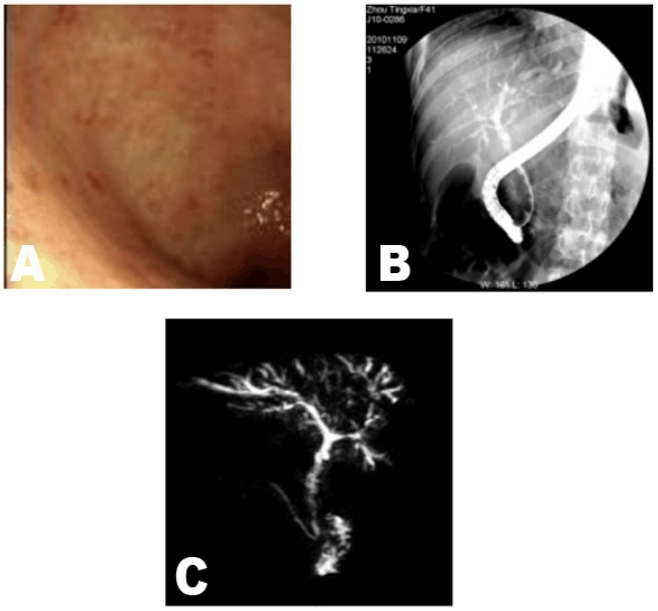

Figure 1: (A) Colonoscopy picture used for diagnosis of UC in 2004, (B) image of MRCP that showed multiple bile duct stone in the lower part of common bile duct, (C) Retrograde cholangiopancreatography showed that both intra- and extra-hepatic bile duct, exhibited segmental and diffused stenosis and expansion, which conforms with the diagnosis of PSC. Stones were shown in common bile duct.

DISCUSSION

We reported a complicated, multi-disease case with long-duration of clinical manifestations. Although certain diseases discussed here may be an isolated event,

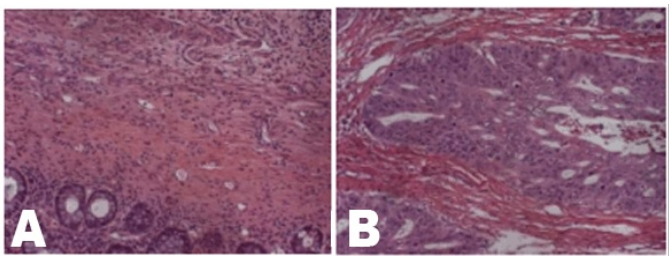

Figure 2: Pathologic sections for UC and CRC diagnosis. (A) Section from colon tissue showed late stage of UC, (H&E, x200) (B) Section of colon neoplasms that invaded whole layer of submucosa (H&E, x200).

Table 1: Laboratory test reports of the patient.

Lab examination	Results
Blood routine test	WBC 2.6x10^3/μL, NE 66.00%, RBC 2.70x10^6/μL, Hb 7.7 g/dL, PLT 99x10^3/μL
Urine routine test	Bilirubin 2+
Electrolyte	Ca^{2+} 2.13 mmol/L, P^{+} 0.38 mmol/L, Mg^{2+} 0.47 mmol/L
Biochemical markers	Albumin 2.71 g/dL, SGPT 80.4 U/L, SGOT 115.8 U/L, GGT 167.6 U/L, ALP 1205.8 U/L, Bilirubin (total) 341.0 mol/L, Bilirubin (indirect) 185.10 mol/L, Alb/Globulin 0.8
Coagulating function	PT 17.9 s, APTT 59.6 s, Fibrinogen 60 mg/dL, PT-INR 1.65, TT 25.5 s
ESR and CRP	ESR 7 mm/1st h, CRP 60 mg/L
Immunoglobulin and complement anti-ENA antibodies	IgG 295 mg/dL (7.0–16 mg/dL), C3 0.5x10^3 μg/mL (0.9–1.8x10^3 μg/mL), anti-ENA antibodies was negative
Tumor markers	CEA 19.54 ng/mL (0–4.3 ng/mL), CA19.9 76.33 U/mL (0–39 U/mL)

most of the diagnoses reported in literature have shown a pattern of more or less interconnection with a common mechanism for disease progression.

Liver biopsy clearly indicated that the onset of all symptoms in this case started from PBC and progressed to UC and further to PSC. It is unclear whether PBC can directly progress to PSC. Not many cases of PBC progression to PSC have been reported. Jeevagan et al. reported one case recently in which PBC and PSC were diagnosed in the same patient but failed to clarify whether it is just an overlapping phenomenon or progression of one disease to another [10]. In a large study in Sweden with 1500 UC patients, it was found that 5% patients had increased serum alkaline phosphatase and 3.7% had evidence of PSC [11]. The same study showed that 95% patients who had PSC were found to have UC. In another study, 48/336 (48%) patients with UC had evidence of hepatobiliary pathology and 4% patients with UC had PSC [12]. In our case, the patient received ERCP twice for removing stones in the bile duct. It is reported that cholecystolithiasis was found in 23/41 (56%) UC patients, of which 7/23 (30%) were missed on cholangiography and detected only by cholangioscopy [13]. Major investigations for stone detection include CT scan, sonography and cholangiogram. Endoscopic therapy can provide drainage of bile ducts, removal of stones and/or temporary relief from obstruction [14].

After the prolonged duration of UC, the possibility of colorectal carcinoma should be highly suspected. The patient was found to have CRC during the surgical operation, which had already invaded through the whole layer including the serosa and showed lymph node metastasis.

UC-PSC shows unique colonoscopy features and are associated with more frequent colorectal neoplasm development and poor prognosis [15]. The overlap of UC and PSC constitutes a higher risk of developing colorectal dysplasia/carcinoma than UC patients without PSC. Prolonged disease duration of IBD is another important risk factor for CRC [16]. Eaden's meta-analysis has shown that the risk for CRC in UC patients is 2% at 10 years, 8% at 20 years and 18% at 30 years of disease duration [17]. The onset of CRC was significantly younger in patients with IBD and PSC [7]. Terg R et al. analyzed the prevalence of PSC in 1,333 patients with UC and the risk for developing colon cancer. Seven out of 39 (18%) patients with PSC developed colorectal carcinoma compared with 2/78 (2.6%) in the control group (p=0.006). The cumulative risk of colorectal carcinoma was 11% and 18% after 10 and 20 years in the PSC group compared with 2% and 7% in the control group, respectively (p=0.002) [9]. It is highly recommended to have early and/or regular colonoscopy screening for IBD patients with or without PSC.

CONCLUSION

Prolonged inflammatory bowel disease, accompanied with PSC is not an uncommon disease that has high risk of CRC. Close follow-up of patient with regular colonoscopy for neoplasm detection will help in the early diagnosis and extension of life span. Additional research studies such as prospective studies are needed to gain insight into disease evolution and relationship between IBD, PBC, PSC and CRC. Additionally, exploring when CRC screening should begin in IBD and PSC patients would be a relevant topic.

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Acknowledgements
The research was supported by the Science Foundation of Nanjing Science & Technology Bureau of China (Grant. No. 2010ZD220) and the National Natural Science Foundation of China (Grant No. 81101800/H1617).

Author Contributions

Rui-Hua Shi – Substantial contributions to conception and design, Acquisition of data, Drafting the article, revising it critically for important intellectual content, Final approval of the version to be published
Bo Hao – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Final approval of the version to be published
Shun-Fu Xu – Substantial contributions to conception and design, Acquisition of data, Revising the article critically for important intellectual content, Final approval of the version to be published
Qi-Yun Tang – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Final approval of the version to be published
Jian-Xia Jiang – Substantial contributions to conception and design, Analysis and interpretation of data, Drafting the article, revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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