Journal of Crohn's and Colitis (2013) 7, e61–e65

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SHORT REPORT

Dysplasia and colorectal cancer in a patient with ulcerative colitis and primary sclerosing cholangitis: A case report and a short review of the literature

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Received 5 September 2011; received in revised form 1 April 2012; accepted 3 April 2012

KEYWORDS
Ulcerative colitis;
Primary sclerosing cholangitis;
Dysplasia and colorectal cancer

Abstract

Primary sclerosing cholangitis is a chronic progressive disorder which involves the medium size and large ducts in the intrahepatic and extrahepatic biliary tree. The great majority of cases have underlying inflammatory bowel disease, mainly ulcerative colitis. A higher risk of colorectal cancer has been described among ulcerative colitis patients with primary sclerosing cholangitis. Here we report a case of a primary sclerosing cholangitis in a young male with a newly diagnosed ulcerative colitis presenting with colonic dysplasia. Surveillance for colorectal cancer should be strongly recommended in this group of patients.

1. Introduction

Primary sclerosing cholangitis (PSC) is a chronic progressive disorder of unknown etiology that is characterized by inflammation, fibrosis and structuring of medium size and large ducts in the intrahepatic and extrahepatic biliary tree.[1,2] The great majority of cases have underlying inflammatory bowel disease (IBD), mainly ulcerative colitis (UC); the prevalence may be as high as 90% when rectal and sigmoid biopsy are routinely obtained. Conversely, it has been estimated that PSC occurs in approximately 5% of UC patients and 3% of

Abbreviations: PSC, primary sclerosing cholangitis; UC, ulcerative colitis; CRC, colorectal cancer; IBD, inflammatory bowel disease; CD, Crohn's disease; 5-ASA, 5-amynosalicilates; LGD, low-grade dysplasia; HGD, high-grade dysplasia; UDCA, ursodeoxycholic acid.

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1873-9946/$ - see front matter © 2012 Published by Elsevier B.V. on behalf of European Crohn's and Colitis Organisation.
doi:10.1016/j.crohns.2012.04.005

Crohn's disease (CD) patients.[3,4] A higher risk of colorectal cancer (CRC) has been described among IBD patients with PSC.[5] Chemoprevention and surveillance for CRC have been strongly recommended in this group of patients.

2. Case report

A 26 year-old male presented to the hepatology outpatient clinic with abdominal pain and bloody diarrhea. The patient had been diagnosed with PSC/autoimmune cholangiopathy 10 years ago. The liver biopsies at diagnosis showed infiltration of the bile ducts by lymphocytes with degeneration of the epithelial cells of the bile ducts. He was on methylprednisolone 8 mg per 24 hours, ursodeoxycholic acid (UDCA) 15–20 mg/kg per 24 hours and azathioprine 50 mg per 24 hours. The laboratory results showed a cholestatic pattern of abnormal biochemical tests with moderate increases in serum aminotransferase levels (aspartate transaminase: 180 U/L, alanine transaminase: 210 U/L), an elevation of alkaline phosphatase (730 U/L), γ-glutamyl transferase (750 U/L) and serum bilirubin (2 mg/dL). The ultrasound showed no data of portal hypertension. An ileocolonoscopy was performed; from the anus to cecum, the colonic mucosa had erythema, edema and superficial ulcers. The patient was diagnosed with UC with moderate to severe activity (Fig. 1a). The patient was then referred to the IBD Unit. The dose of methylprednisolone was increased to 0.8 mg/kg per 24 hours, and the dose of azathioprine to 2.5 mg/kg per 24 hours. Oral and topic 5-amynosalicilates (5-ASA) were added to the treatment. High-grade dysplasia (HGD) with severely active inflammation was observed in two of the biopsies taken during the endoscopy. The biopsies were reviewed by the pathologist; as there was a severely active inflammation, the biopsies were finally classified as indeterminate for dysplasia. We decided to treat the endoscopic and histological inflammation, and to repeat the colonoscopy short later on.

The Mantoux test, and the serology for HCV and HIV were negative in this patient. Anti-HBs were positive (due to previous vaccination). The chest X-ray was normal. In October 2009 the treatment with infliximab 5 mg/kg was started. Cotrimoxazole was added to the treatment for the prevention of *Pneumocystis jiroveci* infection, due to the immunesuppression. The patient had an excellent response to the therapy and he was in remission after the second induction dose of infliximab. In December 2009, after the three induction doses of infliximab (at 0, 2 and 6 weeks), a colonoscopy was performed. The colonic mucosa was slightly friable, but without ulcers or erosions, with a great improvement compared with the previous endoscopy. No dysplasia was observed in any of the multiple random biopsies that were taken.

The patient remained in remission with azathioprine 2.5 mg/kg, infliximab 5 mg/kg every 8 weeks, 5-ASA 4 g per 24 hours and 5-ASA foam. He maintained methylprednisolone 8 mg per 24 hours, calcium, vitamin D and UDCA for the treatment of the PSC and co-trimoxazole. In October 2010, after a year of combination therapy (azathioprine plus infliximab), a colonoscopy was performed to decide if the patient could be left with azathioprine monotherapy. The colonic mucosa was completely normal (Fig. 1b), although the random biopsies showed multifocal low-grade dysplasia (LGD) (Fig. 2). The diagnosis of LGD was confirmed by a second pathologist; therefore a colectomy was recommended to the patient, and he accepted.

3. Discussion

The increased risk of CRC in UC has been recognized for decades, although the estimates of the magnitude of that risk vary considerably in the literature.[6] Several studies have recognized PSC as a risk factor for CRC in UC patients; however, this has not been proven in all studies (Table 1). Soetikno et al. performed a meta-analysis and they described an odds ratio of 4.09 (95% confidence interval, 2.89–5.76) when compared patients with UC and PSC to UC patients without PSC.[5] This finding has led to the recommendation of closer surveillance in this unique high risk subset of UC patients.

The mechanism by which PSC induces CRC remains unclear. It has been hypothesized that alterations in the bile salt pool and a high concentration of bile acid in the colon may, at least partially, be responsible for the increased risk.[7] This hypothesis would explain the preponderance of right-sided cancers

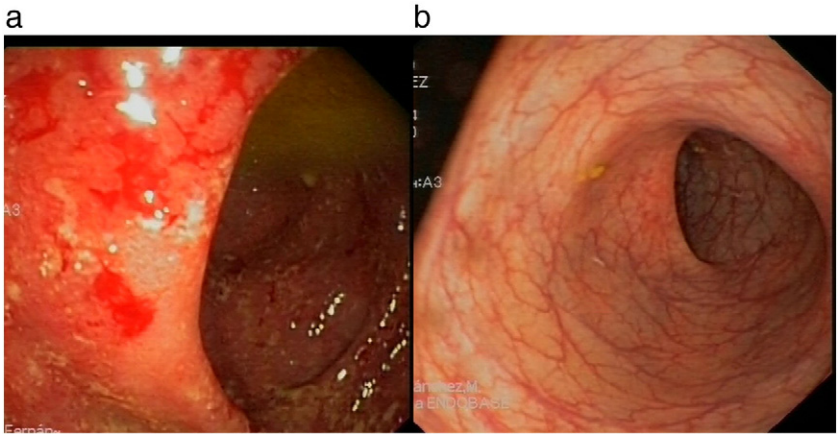

Figure 1 Endoscopic response to the treatment with infliximab: a) at diagnosis, the mucosa had erythema, edema, spontaneous bleeding and superficial ulcers; b) after 1 year of combination therapy (azathioprine plus infliximab), the mucosa was completely normal. However, biopsies showed multifocal low-grade dysplasia.