

Isolated granulomatous hepatitis-A histopathological surprise mimicking cholangiocarcinoma in ulcerative colitis

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ABSTRACT

A 63-yr-old woman, known case of ulcerative colitis, was diagnosed with sclerosing cholangitis 2 years back. She was admitted for investigation of abdominal discomfort, fatigue with elevated alkaline phosphatase and deranged liver function test. Imaging studies (computerised tomography and magnetic resonance imaging) demonstrated a normal biliary tree with focal hepatic lesion which was showing features of cholangiocarcinoma. Ultrasound guided biopsy of the lesion surprisingly revealed non caseating granulomata. Granulomatous hepatitis occurs in less than 1 percent of cases of inflammatory bowel disease. A clinical diagnosis of isolated granulomatous hepatitis was established as the lesion remained stable on follow up and no other cause for it was identified on further investigation. Although the differential diagnosis of focal hepatic lesion in patients with ulcerative colitis with sclerosing cholangitis is wide, granulomatous hepatitis presenting as focal mass lesion mimicking cholangiocarcinoma has never been described previously.

Key words. MRI. Sclerosing cholangitis. Inflammatory bowel disease. Hepatic mass. Extraintestinal manifestation.

INTRODUCTION

The most common hepatobiliary manifestation of ulcerative colitis (UC) is primary sclerosing cholangitis (PSC). Cholangiocarcinoma is one of the serious complications of PSC which can arise at any stage of PSC and can present either as intraductal tumor in the biliary tree or as a liver mass. In a known patient of UC and PSC, any suspicious hepatic mass on imaging raises the possibility of cholangiocarcinoma and needs exclusion. We herein report a case presenting with vague clinical and biochemical picture, which on imaging raised the possibility of cholangiocarcinoma but on biopsy turned out to be granulomatous hepatitis.

To our knowledge, this is the first case of isolated granulomatous hepatitis in ulcerative colitis presenting as focal hepatic mass lesion mimicking cholangiocarcinoma and turned out to be granulomatous hepatitis as histopathological surprise.

CASE REPORT

63 years old female patient with 10 year history of ulcerative colitis presented with mild abdominal discomfort and fatigue to The Ottawa Hospital, Canada. No history of bloody diarrhea and fever was present. Two years ago in March 2010, she was diagnosed as having primary sclerosing cholangitis based on her clinical presentation with mild intermittent jaundice, elevated alkaline phosphatase and magnetic resonance imaging (MRI) showing mild irregularity of biliary radicles. Clinical examination was unremarkable except mild tenderness in right upper quadrant. Her current biochemical profile evaluation revealed elevated alkaline phosphatase 510 IU/L, Hb 11.4 g/dL, WBC 8X 10⁹/L, AST 67 IU/L, ALT 128 IU/L, γGT 463 IU/L, albumin 4.1 g/dL, globulin 3.5. Serological tests for Hepatitis A, B, C, and HIV ELISA were negative.

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Manuscript received: March 11, 2012.

Manuscript accepted: May 25, 2012.

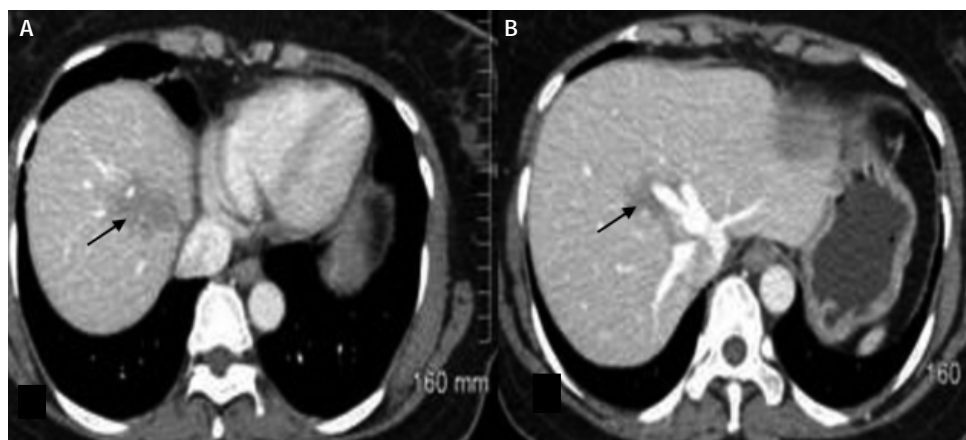


Figure 1. (A and B). Contrast enhanced computerized tomography of abdomen showed ill-defined hypodense lesion with irregular margins (arrow) in segment VIII of right lobe of liver near hepatic vein confluence.

She was previously well controlled with mesalamine and intermittent steroids for flare ups in the past. On further work up, Ultrasonography (USG) revealed ill-defined heterogeneous area in segment 8 without any intrahepatic biliary dilatation of liver which was not conclusively evaluated. She underwent computerized tomography (CT) which showed irregular hypodense lesion in segment 8 near hepatic venous confluence (Figure 1). Unfortunately, triphasic CT evaluation for definite tissue characterization was not performed at this time and with cholangiocarcinoma as potential suspect in known PSC patient, it was decided to undertake dynamic MRI with contrast for further evaluation.

Dynamic MRI revealed an ill-defined irregular area measuring approximately 3.5 x 2.8 cm in segment VIII of liver adjacent to middle hepatic vein (Figure 2). The lesion was hyperintense on T2 weighted images and poorly visualized on T1 weighted images. It showed peripheral enhancement with progressive central filling on delayed images. No other lesion was seen and no dilatation of biliary radicles was present. Given the patient's history of UC and PSC in presence of a focal lesion in liver showing delayed enhancement and mild diffusion restriction, the possibility of cholangiocarcinoma was considered and patient underwent USG guided biopsy. On USG, lesion was difficult to visualize, so using hepatic vein and inferior vena cava as vascular landmarks the iso to hypoechoic area in segment VIII was targeted.

Biopsy showed numerous well formed non necrotizing epithelioid granulomata within hepatic lobules (Figure 3). They were composed of epithelioid cells admixed with lymphocytes and neutrophils so a

diagnosis of granulomatous hepatitis was established. In addition, liver also showed expanded portal tracts with no significant fibrosis and lymphocytic/histiocytic infiltrates. No evidence of malignancy was seen. Special stains for fungal organisms (PAS and Grocott) and acid fast-mycobacterium (Ziehl Neelson) were negative. As biopsy confirmed the lesion in question to be an inflammatory lesion, patient was put up on close follow up and repeat MRI till 24 months showed stable lesion. Patient was reassured of the benign nature of the findings and further future clinical and imaging follow up were planned as needed.

DISCUSSION

Inflammatory bowel disease (IBD) is often associated with extraintestinal manifestations affecting multiple organs with hepatopancreatobiliary manifestations representing one of the most common occurrences. PSC is the most common association of IBD with approximately 70-80% of patients with PSC having IBD and 1.4-7.5% of patients with IBD develop PSC during course of their disease.¹ PSC is more frequently associated with UC than Crohn's disease (CD). Cholangiocarcinoma is found synchronously with the diagnosis of PSC in 20-30% and within 1 year in 50%. During later follow-up, the yearly developmental rate of cholangiocarcinoma is 0.5-1.5%.² In a study comparing the various techniques in the diagnosis of cholangiocarcinoma, CT and MRI had higher sensitivity than US.³ In patients who have suspicious mass on imaging, endoscopic retrograde cholangiopancreatography (ERCP) with cytology brush or CT- or US-guided biopsy of the mass is needed to be pursued to confirm the diagnosis.³

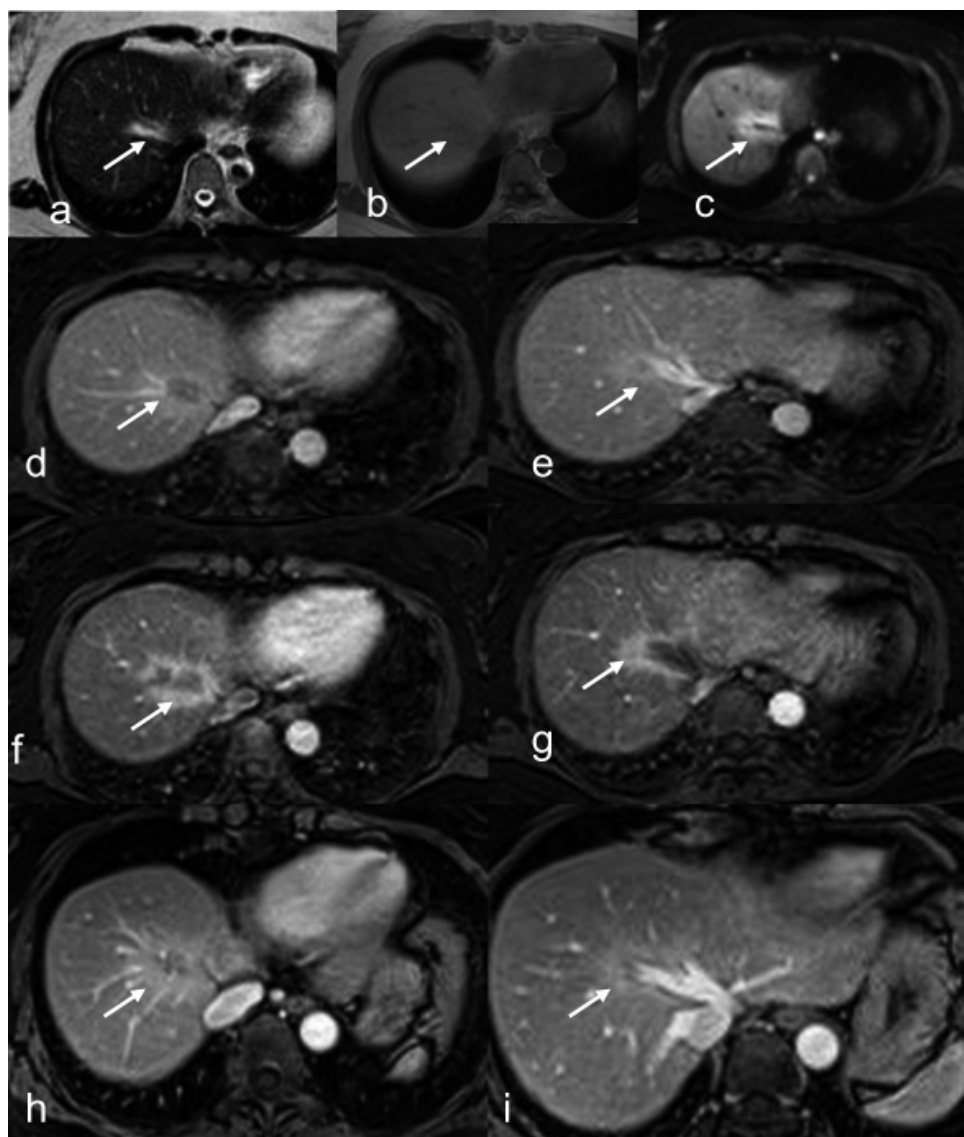


Figure 2. Magnetic resonance imaging showed ill-defined irregular lesion (arrow) in segment VIII of liver adjacent to middle hepatic vein. The lesion is hyperintense on T2 weighted, poorly delineated on T1weighted as iso to hypointense lesion (**a** and **b**). It shows diffusion restriction (**c**). Dynamic post contrast images reveal peripheral early enhancement which on sequential delayed images showed centripetal filling in (**d** to **i**).

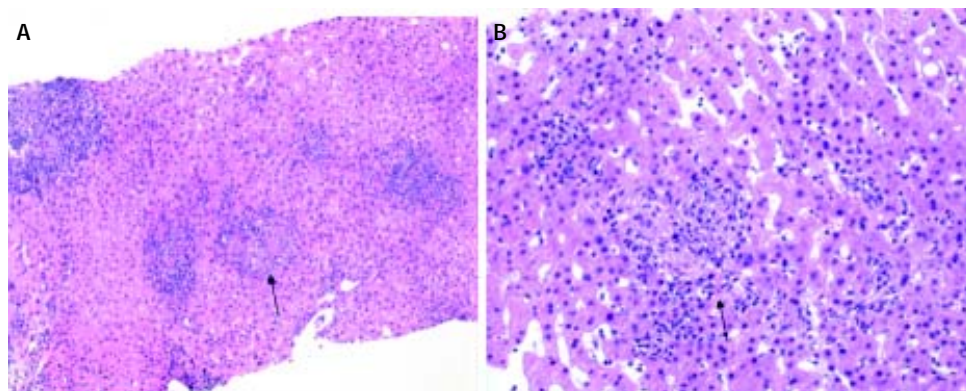


Figure 3. Low power 10x (**A**) and medium power 20x (**B**) photomicrograph of liver biopsy specimen reveal granuloma (arrow) composed of epithelioid histiocytes with a collar of lymphocytes.

At CT, cholangiocarcinoma with underlying PSC is often seen as hypoattenuating mass or thickened bile duct wall. The lesion may be associated with capsular retraction, satellite nodules and encasement of the vessels.⁴ On MRI, the mass-forming cholangiocarcinoma shows an irregular margin with high signal intensity at T2-weighted imaging and low signal intensity at T1-weighted imaging. The peripheral and the delayed enhancement may be more prominent at MRI than CT.

Our patient was a known case of ulcerative colitis with primary sclerosing cholangitis and on imaging showed features which are well described in intrahepatic cholangiocarcinoma such as irregular margins, hypoattenuation on CT, T2 hyperintensity, irregular peripheral enhancement with central hypointensity and delayed central enhancement on dynamic MR. Prebiopsy presumptive diagnosis of cholangiocarcinoma was made and patient underwent USG guided biopsy of the lesion which turned out to be granulomatous hepatitis. Multiple mimickers of cholangiocarcinoma on imaging are previously known like primary sclerosing cholangitis, recurrent pyogenic cholangitis, acquired immunodeficiency syndrome cholangiopathy, autoimmune pancreatitis, inflammatory pseudotumor, Mirizzi syndrome, xanthogranulomatous cholangitis, sarcoidosis, chemotherapy-induced sclerosis, hepatocellular carcinoma, metastases, melanoma, lymphoma, leukemia, and carcinoid tumors.⁵ To our knowledge this is the first case of granulomatous hepatitis mimicking cholangiocarcinoma on imaging.

Granulomatous hepatitis is defined as an inflammatory liver disease associated with granuloma formation in the liver. Granulomas on liver histology are seen in association with IBD, occurring in less than 1% of the patients.¹ They occur more frequently in patients with CD than UC. Classically they present as an isolated elevation in alkaline phosphatase with or without evidence of cholestasis as in our index case. The most common cause of granulomatous hepatitis in the setting of IBD is secondary to medications, particularly sulfasalazine. Other causes in IBD are isolated extraintestinal manifestation or other granulomatous infections.¹ On reviewing literature, we could find only one case report in which granulomatous hepatitis due to Mesalamine has been reported in a patient of ulcerative colitis.⁶ Although our patient was also on mesalamine therapy, this was unlikely etiology in our patient considering its long term use for over 10 years. The presence of granulomatous hepatitis on

pathology was thought isolated idiopathic extra-intestinal manifestation in our case.

Granulomatous hepatitis on imaging typically shows diffuse nodular liver involvement which is hypoattenuating on CT. Both caseating and non caseating types are known. The differential diagnoses on imaging for multiple non caseating granulomas are regenerative nodules in liver cirrhosis and for caseating granulomas are hypovascular metastases. Caseating granulomas show intermediate and high signal on T2-weighted, low signal on T1-weighted images where as noncaseating granulomas reveal intermediate signal on T1, and T2-weighted images.^{7,8} However we could not find any previous case report in which granulomatous hepatitis presented as a focal lesion with or without associated UC and PSC as in our patient.

To conclude, in a known patient of UC and PSC, any suspicious hepatic mass on imaging raises the possibility of cholangiocarcinoma and needs tissue diagnosis by biopsy which will clinch the diagnosis in the patients and may throw surprising results as in index case. Importance of diagnosing benign entities like granulomatous hepatitis as potential imaging mimicker for cholangiocarcinoma should also be recognized in future, considering the significant implications in the management and its psychological impact on the patient.

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