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clinical practice

Primary sclerosing cholangitis in patient with celiac disease complicated by cholecystic empyema and acute pancreatitis

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SUMMARY: **Primary sclerosing cholangitis in patient with celiac disease complicated by cholecystic empyema and acute pancreatitis.**

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Background. *The association of celiac disease and sclerosing cholangitis is a well known, although unusual, pathologic feature of autoimmunity.*

Methods. *A 64 year old patient presenting with sub-acute cholangitis and pancreatitis, treated with cholecystectomy and endoscopic sphincterotomy. The post-operative course, complicated by cholestatic jaundice, and subsequent clinical complications are described, showing how the diagnosis of sclerosing cholangitis was outlined after the Endoscopic Retrograde Cholangio-Pancreatography (ERCP) and confirmed by liver biopsy. Long term treatment with Ursodeoxycholic acid has gradually normalized bilirubin values, while cholestasis enzymes are gradually decreasing. After 18 months bleeding from oesophageal varices ensued, which was controlled through endoscopic ligation.*

Conclusions. *The diagnosis of primary sclerosing cholangitis should be taken into account when cholangitis is associated with other immunity derangements and segmentary dilatations of the intra-hepatic bile ducts, but no dilatation of the main bile duct is noticed at imaging or endoscopy. Recovery of hepatic function should be always attempted before bringing the patient to surgery, in order to avoid post-operative hepatic decompensation.*

KEY WORDS: Sclerosing cholangitis - Celiac disease - Cholecystitis - Pancreatitis.

Introduction

The association of primary sclerosing cholangitis (PSC) and celiac disease has been reported for the first time in 1988 (1), strongly suggesting an immunologic connection between these two diseases. Abnormalities of liver function have been frequently found as extra-intestinal manifestations of celiac disease, especially hypertransaminasemia as an expression of non specific reactive hepatitis (celiac hepatitis), reverting to normal after 6-12 months of strict gluten-free diet, while autoimmune liver disease does not usually improve with diet (2). On the other hand, celiac disease has been found in 2-3% of patients with PSC and serological evidence of celiac disease has been detected in 3% of patients undergoing screening tests for end-stage autoimmune liver disease (3).

In 2005 a research in the UK primary care database showed a threefold increase in risk of PSC in patients with diagnosis of celiac disease (4).

Case report

We report the case of a 64 year old male patient, with a history of celiac disease, previous thyroidectomy for toxic nodular goiter, gallbladder stones and a recent episode of acute pancreatitis and cholecystitis, with pain and fever, treated with medical therapy, with spontaneous partial resolution.

In July 2011 the patient was hospitalized in our Institution with sub-acute cholangitis, with jaundice (total bilirubin 5.6mg%) and fever, mildly elevated cytolysis enzymes: (ALT 130 U/l, AST 110 U/l), slight elevation of amylase and lipase, and severely altered cholestasis enzymes: ALP 996 U/L, GGT 709 U/L. Ultrasound showed signs of gallbladder inflammation, with thickened gallbladder walls and biliary sludge and stones, and mildly dilated common bile duct. An ERCP with endoscopic sphincterotomy was performed, with a diagnosis of sub-stenosing papillitis, but no biliary stones were found in the common bile duct.

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The subsequent course was marked by increase of bilirubin up to 9.2 mg/dL (direct 5,9 mg%). The patient was given Ursodeoxycholic acid and one month later was hospitalized again to undergo elective cholecystectomy.

Upon admission the patient was still jaundiced (total bilirubin 6.3mg%, direct bilirubin 3.8mg%, ALP 863 U/L and increased CA 19-9, 226 U/ml). Ultrasound examination confirmed severe cholecystitis, spots of liver steatosis and absence of dilatation of intra and extra-hepatic bile ducts.

Contrast CT-scan (Figure 1) confirmed acute cholecystitis, with marked thickening of the gallbladder walls, minimal intra-parietal fluid areas and multiple calcifications. The liver parenchyma showed diffuse inhomogenous hypodense areas, with edema and inflammation all around segmentary portal branches and areas of increased vascular staining in the early arterial phase (Figure 2).

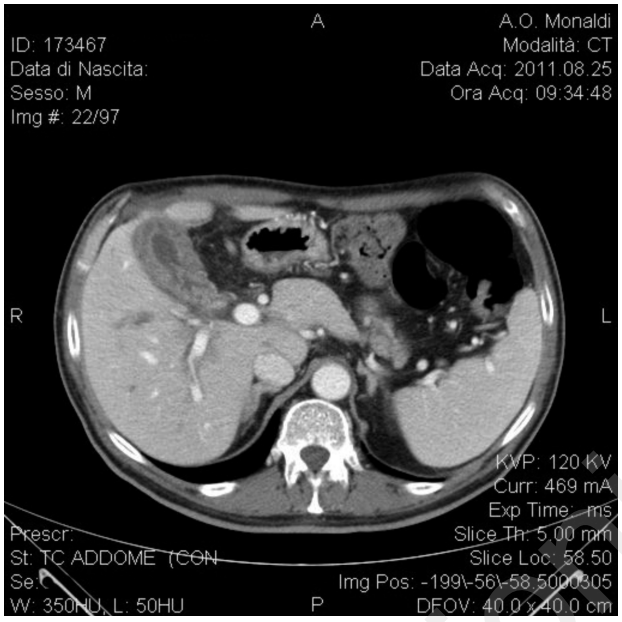

Fig. 1 - CT scan showing thickened gallbladder walls.

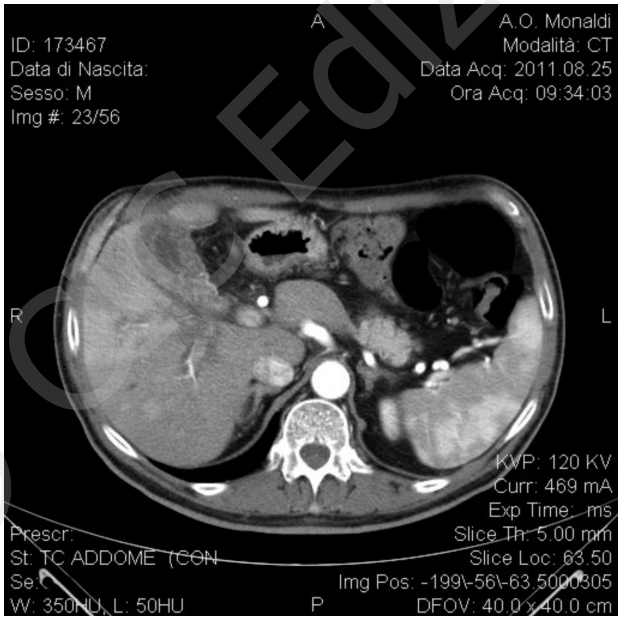

Fig. 2 - CT scan showing inhomogeneous parenchymal enhancement at the early arterial phase.

After few days the patient underwent laparoscopic surgery. The liver was found to be sclerotic with irregular surface, the gallbladder was buried by dense adherences, a tear in the wall gave exit to puruloid fluid and stones. Because of an uncertain anatomy of the hilar structures, the procedure was converted to the open approach, but while performing anterograde dissection of the gallbladder profound bleeding from the hepatic bed ensued, and the procedure had to be interrupted, after a tentative suture of a sclerotic cystic stump remnant, while performing hepatic bed tamponade with collagen sponges, fibrin glue and mass sutures. Liver biopsy was finally performed.

The post-operative course was marked by increased jaundice, with bilirubin spiking to 17 mg%, and a trend to slow decrease, leading to RMI and further ERCP, to rule out possible iatrogenic bile duct ligature (Figure 3). ERCP showed an intact thin main bile duct, with signs of sclerosing cholangitis, bare intra-hepatic biliary tree, and a leak of contrast through the remnant of the cystic duct.

The biopsy showed signs of early biliary cirrhosis, with lymphocyte and granulocyte infiltration of peri-portal septa.

The patient was discharged after 16 days with a total bilirubin of 9.6mg% (direct 5.6 mg%) ALP 826 U/l, GGT 1037 U/l, slightly elevated amylase and lipase values, with a prescription to take Ursodeoxycholic acid 18 mg/kg/d, vit D, vit K, and gastric protection with omeprazole.

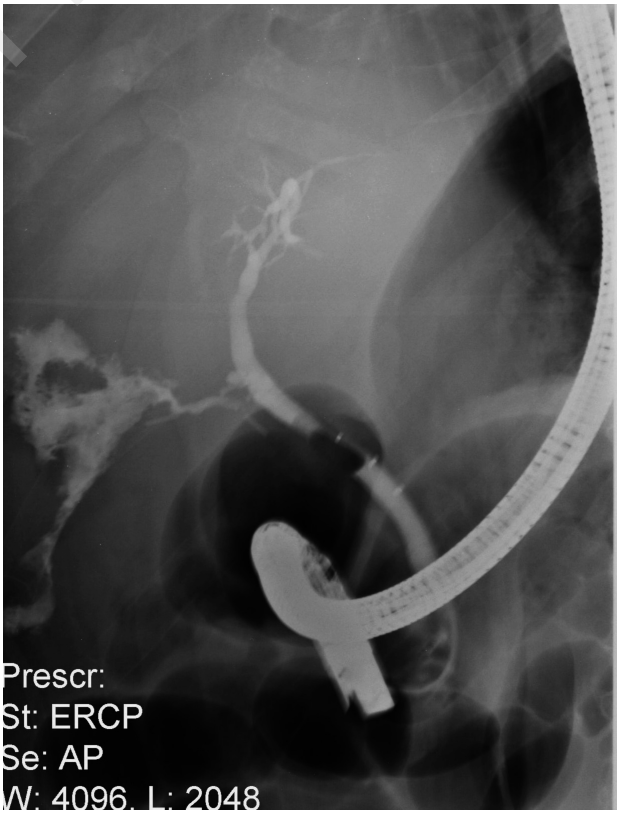

Fig. 3 - Post-operative ERCP showing non dilated CBD, with bare intra-hepatic bile tree; extravasation of the contrast media through the remnant of the cystic duct. A balloon was inflated in the CBD, to provide better visualization of the intra-hepatic bile ducts.

Follow-up

After three months, chemistry values had significantly improved: bilirubin had decreased to 4.0 mg% (dir. 2.50 mg%), ALP to 491 U/l, GGT to 618 U/l, auto-antibodies (ANA, AMA, ASMA, anti-LKM) were found to be negative, transglutaminase antibodies were present.

Jejunal biopsy was compatible with the diagnosis of celiac disease; RMI showed inhomogeneous enhancement of the hepatic parenchyma with areas of tissue hypoperfusion (Figure 4) and segmentary dilatation of the intra-hepatic bile ducts (Figure 5), compatible with primary sclerosing cholangitis.

Clinical course was uneventful until January 2013, when bilirubin gradually returned to normal values, but the patient suddenly showed melena and anemia; an upper GI tract endoscopy revealed oesophageal varices with signs of recent bleeding; endoscopic ligature was performed, with fast recovery of haematological parameters.

At present, clinical conditions are stable and there are no signs of liver decompensation.

Therapy with beta-blockers was added, to reduce portal pressure and prevent further bleeding episodes.

Present data are: alb. 2,8 g%, Hb 10,5 g%, glucose 116 mg%, bil 0,8 mg%, gGT 144U/l, ALP 406U/l, INR=1.

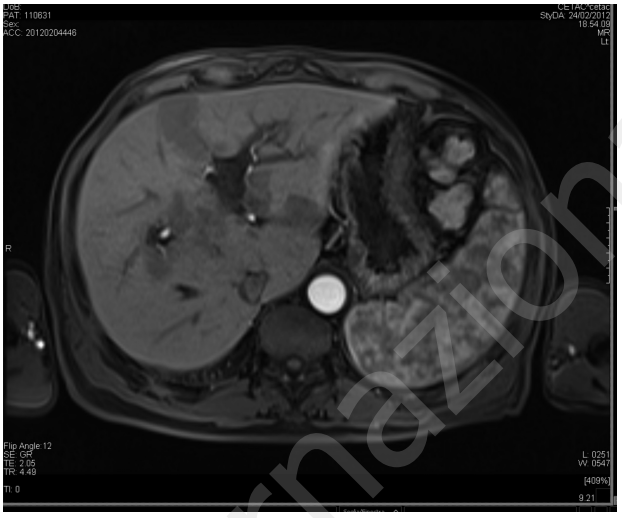

Fig. 4 - RMI showing inhomogeneous enhancement of the hepatic parenchyma, with areas of vascular hypoperfusion.

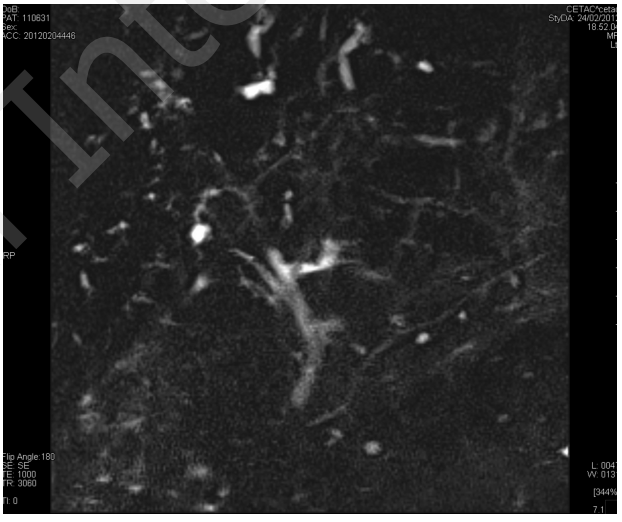

Fig. 5 - RMI showing irregular segmental dilatation of the intra-hepatic bile ducts.

Discussion

Sclerosing cholangitis (PSC) is an autoimmune disorder of the bile ducts, marked by dominant cholestatic biochemical profile, mainly affecting male population, leading to cholestasis, caused by multifocal stricturing of intra or extra-hepatic bile ducts, and progressive liver insufficiency (5-7). There is a strong association with inflammatory bowel disease, because of the common autoimmune etiology (8).

In our case, PSC was associated with long standing celiac disease, which is a well known autoimmune inflammation of the intestinal villi, in response to gluten intolerance (9).

The association of underlying sclerosing cholangitis, subsequent calculous acute sclerotic cholecystitis and acute pancreatitis is an example of uncommon related pathologies.

Cholecystectomy in patients with PSC can become heavy surgery, and a stressful procedure for the patient, especially when gallbladder walls are severely inflamed and sclerotic, and can be associated with a high morbidity; every effort should be done to improve liver function prior to surgery (14).

Cholangiocarcinoma was suspected because of elevation of tumor marker CA 19-9 (11), but was subsequently ruled out by the regression of jaundice, the progressive decrease of cholestasis enzymes (12), and the absence of a dominant stricture of the bile ducts at ERCP imaging. For the same reasons placement of an endoscopic biliary stent was not attempted and just endoscopic sphincterotomy was performed, to enhance biliary flow into the duodenum (6-13). In spite of this, it took more than one and half year of medical therapy with Ursodeoxycholic acids, (11-15) for bilirubin to return to normal levels. However, amelioration of cholestatsis did not prevent development of portal hypertension and bleeding of oesophageal varices. Recently hypoalbuminemia developed, determining mild ascites, with prompt response to albumin administration and diuretic therapy.

The usually progressive course of PSC seems to have been slowed down in this case, in spite of the acute presentation, by the good results of surgical and endoscopic therapy; the gradual decrease of cholestatic enzymes was a good prognostic factor (12) and the associated celiac disease was completely controlled by dietetic regimen.

Authors disclosures
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