Villous adenoma of the common hepatic duct: the importance of contrast-enhanced ultrasound and endoscopic retrograde cholangiopancreatography for relevant diagnosis. A case report and review of the literature.

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Abstract
Adenomas are frequently encountered in the lower digestive tract but are rarely diagnosed in the biliary tree. We report a case of villous adenoma of the common hepatic duct. A 58-year old male was admitted with a four week history of intermittent upper right quadrant pain. Gray scale and contrast-enhanced abdominal ultrasound showed a mass inside the common hepatic duct with arterial enhancement and slow wash-out during the late venous phase. Subsequent endoscopic retrograde cholangiopancreatography and intraductal ultrasound confirmed the presence of the lesion. The final histopathological examination showed villous adenoma of the common hepatic duct with high-grade dysplasia. Contrast enhanced ultrasonography used in conjuncture with endoscopic retrograde cholangiopancreatography can help in differentiating biliary tumors.

Keywords: common hepatic duct, villous adenoma, ultrasound, contrast-enhanced ultrasound, endoscopic retrograde cholangiopancreatography

Introduction
Benign biliary tumors are seldom encountered. Adenomas are frequently seen in the colon and rectum but are rarely diagnosed in the biliary tree. Benign tumors of the extrahepatic biliary tract are rare, making up for approximately 6% of all extrahepatic tumors [1]. Papillomas and adenomas comprise two thirds of these lesions, followed by myoblastomas, neural tumors, fibromas, hamartomas and leiomyomas [2]. They are more frequently located close to the ampulla of Vater, but some of these tumors might have originated in the duodenal mucosa, thus being falsely considered biliary tumors.

Clinically, these benign tumors can mimic an ampullary tumor, with a fluctuating jaundice, which may be due to the valve-like effect of the tumor. Most cases are not diagnosed until surgery [3]. To our knowledge, only one other case of extrahepatic biliary villous adenoma diagnosed via contrast-enhanced ultrasonography (CEUS) was previously reported [4].

We present a case of villous adenoma of the common hepatic duct diagnosed by CEUS and endoscopic retrograde cholangiopancreatography (ERCP). We emphasize the importance of CEUS as a novel technique in diagnosing and differentiating bile duct strictures.

Case report
A 58-year-old male presented with a four week history of intermittent upper right quadrant pain not related to food intake. His appetite was normal, without weight-loss. He had a history of choledocholithiasis 2 years previously, when a successful ERCP with extraction of cal-
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Physical examination revealed no jaundice. Abdominal examination revealed no organomegaly, palpable mass or tenderness.

The laboratory tests revealed serum alanine aminotransferase of 56 U/l (reference values 0-40 U/l) and gamma-glutamyl transpeptidase of 192 U/l (reference values 11-50 U/l). The patient tested negative for both hepatitis C antibodies and hepatitis B antigen. Serum CA 19-9 and CEA were within the normal range.

Imaging evaluation started with conventional grayscale abdominal ultrasound (US). It revealed fatty liver, dilated intrahepatic biliary tree and a mass inside the common hepatic duct with no posterior acoustic shadowing. The maximal diameter of the common bile duct at the hepatic hilum level was 11 mm. No hepatic or pancreatic focal lesions were identified. Thus, CEUS was subsequently performed using a General Electric LOGIQ E9 imaging system. The EFSUMB recommendations [5] were respected: 1.6 ml contrast agent (Sonovue – Bracco SpA, Milan, Italy) was injected, followed by a 10 cc bolus of saline. A mechanical index of 0.10 was used. The exploration was continuous for 5 minutes using a longitudinal section plane in the long axis of the common bile duct. The followed mass inside the common hepatic duct showed arterial enhancement, starting at 15 seconds after contrast-agent injection, with slow wash-out during the late venous phase (around 120 seconds) (fig 1a-b).

Magnetic resonance cholangiopancreatography (MRCP) was performed, showing the thickness of the common hepatic duct walls, up to about 3 mm, which extended approximately 2 cm in length.

Based on these findings, the possibility of choledochoolithiasis was excluded and a diagnosis of cholangiocarcinoma was suggested. Nonetheless, serum total immunoglobulin (Ig) G and IgG4 were taken, given the possibility of an IgG4 cholangiopathy, both being within the normal range. Rheumatoid factor, antinuclear antibodies and p-ANCA were also negative.

Having a high suspicion of cholangiocarcinoma, an ERCP was performed using an Olympus TJF-145 duodenoscope, which confirmed the presence of a mass inside the common hepatic duct (fig 1c). In order to explore the biliary anatomy, we performed an intraductal ultrasound (IDUS) with a miniature probe (Olympus UM-2R, 12 Mhz), inserted through the working channel of the duodenoscope. This revealed a semi-circumferential isoechoic thickening of the mucosal layer of the common hepatic duct to about 2-3 mm, extending to about 20 mm, with no apparent invasion of the submucosa (fig 1d). Multiple biopsies were taken.

The histopathology report of the endoscopic specimen showed a villous adenoma of the common hepatic duct with high-grade dysplasia. No stromal invasion was identified in the sample (fig 1e).

The patient was referred to surgery, which was refused for the time being, due to personal reasons. Subsequently, he was lost to follow-up by being unreachable.

Discussions

Villous adenomas are benign epithelial lesions with malignant potential which can occur at any site in the gastrointestinal tract. They are usually encountered in the rectum and colon, less frequently in the small bowel and...
very rarely in the biliary tree [6]. They are produced by a proliferation of the surface epithelium in the pattern of densely packed, thin, delicate fronds which are joined at their bases. Considering that intestinal adenomas can follow an adenoma-carcinoma sequence, it can be assumed that biliary adenomas could follow the same sequence, thus recommending the complete resection of all lesions. Tumoral size and the number of lesions seem to influence the rate at which carcinoma is found [3]. In recent years, only a few villous adenomas with different grades of dysplasia have been reported [4,6-8].

Two cases of biliary tract polyps associated with intestinal polyps have been published [9,10]. It has been proposed that bile duct adenomas are part of the spectrum of generalized gastrointestinal polyposis [11]. In our case, colonoscopy was not performed but gastroscopy revealed no tumors in the stomach or duodenum.

Abdominal ultrasound is frequently used as a primary imaging procedure in cases with abdominal discomfort, pain or jaundice and may reveal the biliary tumor as an endoluminal mass, more or less well-defined, with no posterior acoustic shadowing or it may show biliary tract dilatation as an indirect sign of biliary duct obstruction. Color and power Doppler techniques may provide additional information about the vascularization of the lesion, while CEUS can thoroughly characterize the tumoral mass, improving the sensitivity of abdominal US in the diagnosis [12]. An arterial hyperenhancement with subsequent washout is typical for lesions of a neoplastic nature. However, CEUS has not been extensively used for diagnosing extrahepatic biliary lesions, its major role in this regard being in distinguishing between tumor and debris or stone without obvious acoustic shadowing [2]. In our case, CEUS showed hyperenhancement during the arterial phase and slow washout, suggesting it was a vascularised lesion and excluding other diagnosis.

When US shows dilatation of the biliary tree, with no signs of an endoluminal mass, MRCP must be carried out. The diagnostic sensitivity, specificity and accuracy of MRCP in differentiating benign and malignant biliary tract strictures were 81%, 70% and 76% respectively, as shown by Park et al [13]. In 2009 Sai et al demonstrated that MRCP followed by endoscopic ultrasound (EUS) was highly sensitive (90%) and specific (98%) for the early diagnosis of extrahepatic bile-duct carcinoma [14].

When US or EUS shows localized bile duct wall thickening, ERCP should be conducted with intraductal US (IDUS) and forceps biopsy [15]. In our case, given that both MRCP and US showed an endoluminal mass suggestive of a neoplastic lesion, we chose to follow up with an ERCP.

Regarding ERCP, malignancy is suspected when a long (>10 mm), asymmetrical and irregular stricture is found after injection of the contrast agent into the biliary tract. In contrast, benign lesions tend to appear as short, regular and symmetrical strictures. Using these criteria, Park et al reported a sensitivity, specificity and accuracy of 74%, 70% and 72% for ERCP in differentiating benign and malignant biliary tract strictures [13]. Interestingly, our patient presented with a long stenosis; however, no histopathological signs of malignancy were reported.

When the findings of ERCP are equivocal, transpapillary IDUS can be performed in order to detect localized wall thickening. US imaging of the biliary tract uses a miniature probe (2.0-2.4 mm in diameter), generating high frequencies (15-20 MHz), therefore providing high-resolution and high fidelity images of the bile ducts. Varadarajulu et al showed that IDUS is an easy procedure, offering unique advantages in the evaluation of patients with indeterminate findings at ERCP [16]. Stavropoulos concluded that IDUS is a valuable adjunct to ERCP in the characterization of biliary strictures, increasing its accuracy from 58% to 90% [17]. In our case, IDUS demonstrated that the lesion did not extend beyond the bile wall hence, the diagnosis of a benign tumor or an early cancer was suggested.

Transpapillary bile forceps biopsy is not widely used as a routine diagnostic method because of technical difficulties, the bile duct being narrower with lesser space for opening the forceps. However, Kitajima et al, using a Howell introducer were able to easily collect multiple tissue samples, reporting a sensitivity and specificity rate of 57% and 100% respectively in diagnosing bile duct cancer [18].

Endoscopic brush cytology from the biliary duct system still has an important diagnostic role, as shown by Eiholm et al [19]. However, Sugiyama et al compared transpapillary biopsy to brush cytology, showing that it had a superior level of sensitivity for malignancy (81% vs. 48%), recommending that it be performed routinely at initial ERCP for patients with a stricture or filling defect of the extrahepatic bile duct [20].

Recently, the SpyGlass system (Boston Scientific Co., Natick, MA, USA) was introduced, which allows for single-operator, direct visualization cholangioscopy for detection and treatment of strictures throughout the pancreatico-biliary system [21]. Even more recently, Nevanethan et al indicated that the measurement of specific oxidized phospholipids products may help to distinguish cholangiocarcinoma from other biliary strictures, enhancing the endoscopic diagnosis of indeterminate biliary strictures [22].

To our knowledge, only one other case of extrahepatic biliary villous adenoma diagnosed via CEUS was previ-
ously reported. This case further goes to prove that CEUS is of maximum importance in characterising the nature of lesions of the biliary tree. Although an extremely rare entity, adenomas should be considered in the differential diagnosis of small tumorous lesions in the common hepatic duct.

In conclusion, as showing in our case, CEUS used in conjecture with ERCP can help in the differential diagnosis of neoplasms of the biliary tree.

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References