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MASS-FORMING INTRAHEPATIC CHOLANGIOCARCINOMA PRESENTING WITH PAINFUL OBSTRUCTIVE HEMOBILIA

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We report a very rare case of acute obstructive hemobilia caused by bleeding of a mass-forming intrahepatic cholangiocarcinoma in a 75-year old man. The prompt complete emergency diagnosis was made by ultrasound and confirmed by MDCT. The features of hemobilia and intrahepatic cholangiocarcinoma are briefly reviewed.

Key-word: Bile ducts, neoplasms.

We report a rare case of hemobilia diagnosed in a 75-year old man presenting at the emergency room with the classic triad of Quincke associating right upper quadrant pain, jaundice and maelena. The full diagnosis of massive biliary obstruction by a long clot due to bleeding of an mass-forming intrahepatic cholangiocarcinoma was made during emergency ultrasound examination completed by MDCT. The features of hemobilia and intrahepatic cholangiocarcinoma are briefly reviewed.

Case report

A 75-year old man was admitted in the emergency department with complaints of acute colicky pain in the right upper quadrant, associated with jaundice and a history of maelena.

Laboratory tests showed a marked cholestasis with total bilirubin level at 71,7 mgr/L (nl < 12 mg/L), direct (conjugated) bilirubin level at 45,8 mgr/L (nl < 3 mgr/L), aspartate aminotransferase (AST or GOT) at 76U/L (nl < 40 U/L), alanine aminotransferase (ALT or GPT) at 151 U/L (nl < 41U/L), alkaline phosphatase (ALP or PAL) at 557 U/L (nl < 270 U/L) and gammGT (GGT) at 373 U/L (nl < 50 U/L).

Emergency abdominal ultrasound of the right upper quadrant (Fig. 1A) was immediately performed and showed a 6 x 5 x 3 cm moderately hypoechoic tumoral mass in the S3 hepatic segment. This mass was responsible for a proximal diffuse ductal dilatation in the S3 hepatic segment (Fig. 1B).The dilated ducts were clearly seen converging to the mass and a biliary tumor was immediately suspected. Three centimetric small satellites tumors were found in the vicinity of the main lesion.

The elective cause of the mechanical painful jaundice was attributed to the presence of a very long serpiginous clot extending from the main left hepatic biliary tree – just distally from the main tumor – to the bottom of the distal intrapancreatic choledocus (Fig. 1C-F). This long clot was not only responsible for the dilatation of the entire left biliary tree but also for an indirect global dilatation of the contralateral right biliary tree (Fig. 1D & 3B). This dilated right biliary tree appeared free from clot but contained echogenic retained bile.

Complementary abdominal MDCT was immediately performed. Unenhanced scan confirmed the presence of a long fresh and spontaneously hyperdense blood clot extending from the left hepatic lobe to the bottom of the pancreatic choledocus (Fig. 2). It was responsible for a global dilatation of the hepatic biliary tree. Contrast enhanced series (Fig. 2C, 2D, 3A) confirmed the presence of a 6 x 5 x 3 cm hypodense mass with peripheral enhancement developing in the S3 hepatic lobe and causing intralobar hepatic duct dilatation. The three satellites tumors already demonstrated during ultrasound were confirmed in the left lobe.

The imaging staging was completed by hepatic MRI and 18F-FDG PET/CT (not illustrated) which results were exactly comparable and failed to provide further information.

The retained clinical and imaging diagnosis was that of an mass-forming intrahepatic cholangiocarcinoma confined to the left hepatic lobe. The lesion was spontaneously bleeding, causing painful acute obstructive mechanical jaundice. The administration of Clopidrogel (Plavix) to the patient for previous coronary bypass was considered a main predisposing factor for obstructive hemobilia.

A partial left hepatectomy (resection of the S2 & S3 segments) was performed. Three of the eleven removed hilar nodes were histological found metastatic. Gross anatomy confirmed a 6 x 5 x 3 cm multilobulated firm but largely necrotic whitish mass surrounded by dilated biliary ducts in a fibrotic stroma (Fig. 3C).

Histologically (Fig. 3D) the mass consisted of a proliferation of circumvoluted ductal structures sometimes taking a cribriform appearance. The ductal structures were lined with one or more layers of cells whose nuclei were moderately variable in size, with compacted chromatin and prominent nucleoli. Mitoses were relatively frequent and the neoplastic cells were distributed in a highly fibrotic modified stroma containing variable amounts of inflammatory cells. The final histological diagnosis was that of a moderately differentiated intrahepatic cholangiocarcinoma.

The postoperative period was uneventful and no additional chemotherapy was judged necessary during the multidisciplinary oncologic consultation. The patient is presently doing well and free of recurrence 36 months after surgery.

Discussion

Hemobilia is caused by an anomalous communication between the splanchnic circulation and the biliary tree (1-3). In the past the main causes of hemobilia were accidental trauma (38,6%), followed by gallbladder stones (14,9%), inflammation (13%), vascular disorders (10,7%) and tumors (6,2%) (2). Overtime there has been a shift in the etiology of hemobilia and the main cause is actually iatrogenic, of which needle biopsy or percutaneous intervention – such as

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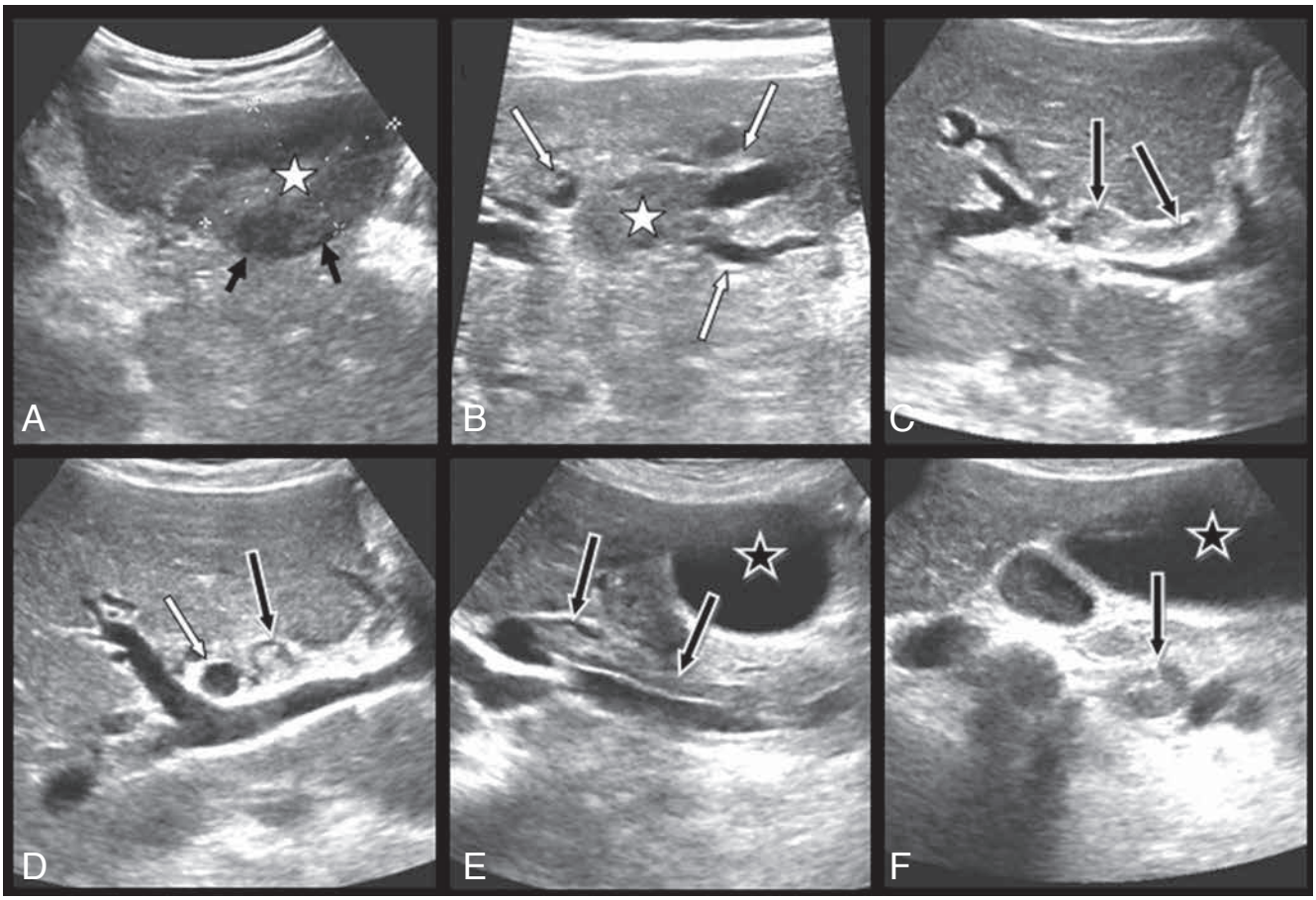

Fig. 1. — Six selected views of the right upper quadrant ultrasound illustrate the full diagnosis of a S3 slightly hypoechoic tumoral mass (white star on A & B) surrounded by a hypoechoic rim (small black arrows on A) and being responsible of a retrograde dilatation of the S3 biliary thee (white arrows on B). It is prolonged by a very long clot obstructing the entire biliary tree from the hile (black arrows on C & D) to the bottom of the pancreatic choledocus (black arrows on E & F). Simultaneous dilatation of the right biliary tree is seen (white arrow on D) (black star: gallbladder).

transhepatic cholangiography – account for the main part and are related to a more and more increasing practice (2, 4). Stones in the gallbladder or in the biliary tree may also cause direct mucosal damage or may erode the cystic artery leading usually to minor bleeding (2). Nevertheless acalculous cholecystitis may also lead to hemobilia due to the high pressure induced. Cholangitis, parasite diseases (ascariasis or hydatid disease) and hepatic abscesses are other possible causes of hemobilia. Malignancies of the liver (hepatocarcinoma, cholangiocarcinoma and metastases), of the pancreas and biliary tract, especially in advanced stages, may also cause hemobilia by direct invasion of surrounding vessels (2). Finally vascular diseases comprising polyarteritis nodosa, aneurysms of the hepatic artery but also coagulopathies (i.e. Bernard-Soulier syndrome, idiopathic thrombocytopenic purpura, hemophilia and treatment with anticoagulants) have been implicated in the induction of hemobilia (2-3).

Cholangiocarcinoma presenting with hemobilia is an extremely rare event and to our best knowledge there have been only three or four previous descriptions (3, 4-7) essentially in Southeast Asia were the disease is more prevalent. In the reported case the administration of Clopidrogel (Plavix) to the patient for previous coronary bypass was considered an associated predisposing factor for obstructive hemobilia.

The most common symptoms associated with hemobilia are jaundice (30%), biliary colic (52%), and gastrointestinal hemorrhage (73%) (2-4). These three symptoms are referred to as Quincke's classic triad of hemobilia. This complete triad was found in our patient but only occurs in approximately 22% - 37,9% of symptomatic patients (2-5). Hemobilia usually concerns minor bleeding and stops spontaneously in most cases. In cases of very active bleeding, the blood flows rapidly into the duodenum and the patient usually presents with maelena or hematemesis. In contrast, a slow bleeding tends to form clots and preferentially may cause biliary obstruction because the blood does not mix with bile and forms separate layers due to the difference in gravity and surface tension (2).

The currently available diagnostic modalities for hemobilia include esophagogastroduodenoscopy, side- view endoscopy, abdominal MDCT, ultrasonography, and angiography (2). Although CT angiography is very helpful to detect the bleeding point and mass lesions, it does not indicate the amount and rate of bleeding. An endoscopy has many advantages in that endoscopy can demonstrate fresh blood around the ampulla of Vater and exclude the other bleeding sites in the gastrointestinal tract. ERCP plays important roles in the diagnosis of hemobilia. The rate and amount of bleeding can

Fig. 2. — Coronal oblique MPR (A) and axial (B) views of the unenhanced CT illustrate the presence of a fresh long spontaneously hyperdense extending from the left hepatic lobe to the bottom of the pancreatic choledocus (black arrow). Coronal oblique (C & D) obtained from contrast enhanced CT illustrate the massive global dilatation of the entire biliary tree (white arrow on C) and the long clot occupying the entire length of the extrahepatic bile duct (black arrows on D).

be directly estimated and opacification of the biliary tree can reveal the causes of hemobilia, the type and site of filling defects, and degree of bile duct dilatation (2).

In the report case the patient presented with the Quincke's classic triad but his dominant symptom was nevertheless an extremely acute colicky pain in the right upper quadrant associated with jaundice. For this reason ultrasound was first performed as the recommended initial emergent imaging test in patients with signs and symptoms of hepatic, gallbladder or biliary disease as well as right upper quadrant pain (8-9). The full imaging diagnosis was directly made by this first line imaging modality and the other imaging modalities (MDCT, MRI and PET/CT) which were performed to complete the preoperative staging didn't reveal fundamental additional data.

Cholangiocarcinoma accounts for 3% of all gastrointestinal cancers and is the second most common primary malignancy of the liver (5, 10). It accounts for approximately 15-20% of all primary liver cancers (11). The prevalence and mortality of intrahepatic cholangocarcinoma are continuously increasing the highest prevalence being found in Southeast Asia (10-11). On the contrary, the prevalence of cholangiocarcinoma of the gallbladder and extrahepatic cholangiocarcinoma seems to remain rather constant or decrease (10).

Recognized risk factors for cholangiocarcinoma all share the common feature of chronic biliary inflammation (10-12). Schistosomiasis and hepatolithiasis are common risk factors in eastern Asia, whereas primary sclerosing cholangitis, liver cirrhosis, alcohol-related liver disease, and diabetes are relatively common risk factors in Western countries (10). Various viral infections, anomalies and/or malformations of the biliary tract, biliary-enteric drainage procedures and environmental or occupational toxins also constitute risk factors (10, 12).

Based on gross anatomic morphologic characteristics, cholangiocarcinoma are classified into mass-forming, periductal infiltrating and intraductal grow type (10, 12). Traditionally, extrahepatic bile duct cancer has been classified as nodular, sclerosing, or papillary, corresponding to the mass-forming, periductal infiltrating, and intraductal growth types of intrahepatic cholangiocarcinoma, respectively (10, 12-13). This classification is useful for the interpretation of the imaging findings and for the differential diagnosis but also for prediction of dissemination, prognosis and planning of surgery (10).

The reported case was a typical intrahepatic mass-forming cholangiocarcinoma (MFC) where a homogenous mass with irregular but well-defined margin is found with a frequent dilatation of the biliary intrahepatic tree at the periphery. This type of intrahepatic cholangiocarcinoma is the most common representing 60% of all intrahepatic cholangiocarcinomas (11, 13). During ultrasound MFC is homogenous well-defined mass with irregular but well-defined margin and presenting with a peripheral hypoechoic rim – as found in the reported case – in about 33% of cases. Tumors larger than 3 cm are usually hyperechoic and tumors less than 3 cm are rather hypo- or isoechoic. In the reported case the echogenicity appeared heterogeneous but predominantly hypoechoic (10, 13). Typical CT features of the mass-forming type of cholangiocarcinoma include homogeneous attenuation, irregular peripheral enhancement – as illustrated in our case – with gradual centripetal enhancement on much delayed phase – phase not performed in the reported case – (10-12). The degree of delayed enhancement is closely related to the proportion of fibrous stroma. Capsular retraction, the presence of satellite nodules – as found in our patient – and vascular encasement without the formation of a grossly thrombus are other possible features. The MR imaging features of mass-forming cholangiocarcinoma are similar to its CT features (10).

At gross examination, mass-forming cholangiocarcinoma is characterized by a homogeneous sclerotic mass with an irregular lobulated margin, typically in the absence of hemorrhage or central necrosis. The tumor is firm and whitish gray because of its large amount of fibrous stroma (13). Histologically the viable

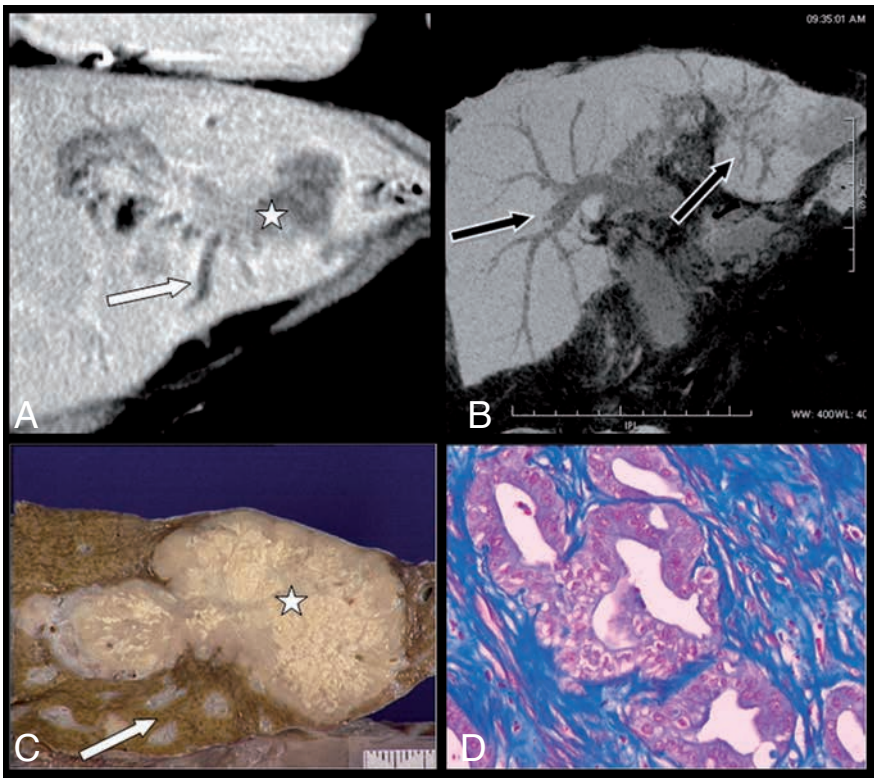

Fig. 3. — Coronal contrast enhanced CT view (A) of the S3 segment illustrates the presence of a polylobulated hypopense mass with peripheral enhancement (white star). The S3 bile ducts are dilated (white arrow). Very thick global coronal MIN (minimal intensity projection) view (B) illustrating the entire dilatation of the hepatic biliary tree (black arrows). Corresponding gross anatomy (C) of the whitish tumoral mass (star). The dilated bile ducts are clearly visible (white arrow). Photomicrograph (D) illustrating the characteristic of cholangiocarcinoma with neoplastic glands distributed in a well highlighted highly fibrous stroma (blue color in the Masson's trichrome stain).

tumor cells are usually located at the periphery of the tumor. The central portion of the tumor is composed of a variable degree of fibrosis with necrosis and scattered tumor cells.

The differential diagnosis concerns tumors with abundant fibrous stroma such as hepatocarcinoma (HCC) with cirrhotic stroma, sclerosing HCC or combined HCC-cholangiocarcinoma but also various tumor with abundant fibrous stroma, embryonal sarcoma and neuroendocrine carcinoma (10, 12).

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