Case Report

The Role of Real Time Elastography in the Diagnosis of a Patient with Liver Cirrhosis and Carcinoma of the Uncinate Process of the Pancreas - Case Study

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ABSTRACT: Hepatic cirrhosis represents the most advanced stage of any chronic liver disease characterized by progressive fibrosis. We report the case of a patient with carcinoma of the uncinate process of the pancreas and an occult form of liver cirrhosis. We concluded, based on the bioclinical profile, that the jaundice syndrome had an underlying mixed mechanism, obstructive and hepatic. Although, the clinical suspicion of pancreatic cancer was backed up by ultrasound, computed tomography and magnetic resonance imaging, we did not obtain, through these imaging investigations, any indicative features of liver cirrhosis. In order to further evaluate the presence of liver cirrhosis, we assessed liver stiffness using two non-invasive methods: Transient Elastography and Real Time Tissue Elastography (RTE). We observed highly suggestive features of liver cirrhosis only through RTE, although its diagnostic accuracy still needs large validation studies. Intraoperative assessment confirmed the diagnosis of liver cirrhosis, changing also the type of surgical approach and patient prognosis.

KEYWORDS: *liver cirrhosis, real-time tissue elastography, uncinate process carcinoma*

Introduction

Occasionally patients may present a clinically silent form of cirrhosis and absence of portal hypertension on ultrasound evaluation, making the diagnosis difficult. In order to rule out the presence of liver cirrhosis, a fibrosis assessment is mandatory, prognosis and treatment of the patient relying heavily on the outcome of this evaluation. Although liver biopsy (LB) is still considered the 'gold standard' for fibrosis assessment, it is an invasive method and not totally risk free. In this sense, many noninvasive methods were developed in order to replace LB, such as: transient elastography (TE) (Fibroscan), real-time tissue elastography (RTE) or Acoustic Radiation Force Impulse Elastography (ARFI)[1]. Although multiple studies determined cut-offs values for predicting liver cirrhosis with TE (14,5 kPa) and ARFI (1.7 m/s, AUROC 0.93), RTE is not currently a well-established method of diagnosis, more large-scale studies being needed to prove its applicability[2].

Case Report

We present the case of a patient, male, aged 50 years, from a rural environment, chronic alcohol consumer, with a chronic liver disease diagnosed 4 years ago, of witch type he cannot specify. He was admitted in February 2015 accusing yellow discoloration of the skin and sclera, weight loss (approximately 18 kg in 3 months), pain in right hypochondrium, postprandial bloating and loss of appetite.

Physical examination of the patient revealed the following aspects: sclero-tegumentary jaundice with a green cast, multiple spider angiomas in the territory of superior vena cava, normal cardio-respiratory functions, pulse rate of 88 per minute and blood pressure of 120/80 mmHg, sensitivity in the right hypochondrium, hepatomegaly with firm consistency, dark-colored urine.

Laboratory test showed GOT (glutamic oxaloacetate transferase) – 179 U/L (N<34U/L), GPT (glutamic pyruvate transaminase) – 167 U/L(N<55U/L), total bilirubin – 12 mg/dl(N 0.2-1.2mg/dl) with conjugated fraction 7,8 mg/dl(N<0.5mg/dl), AF (alkaline phosphatase) – 178 U/L(N 40-150 U/L), GGT (Gamma-glutamyl transferase) – 941 U/L(N 9-64U/L), total cholesterol – 153 mg/dl(N<200mg/dl), ESR (erythrocyte sedimentation rate) – 65mm/1h, 100mm/2h (N <20mm). The complete blood count showed a thrombocytopenia of 121,000/mm^3 (N

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150.000-440.000/mm^3). Blood clotting test showed a modified Prothrombin Index of 68 %(N >70%). Serological markers for hepatitis revealed a positive HBs antigen and the tumor-biomarkers showed an increased CA 19-9 (carbohydrate antigen 19-9) of 1000U/L (N<37U/L).

Ultrasound (US) examination findings: liver shows regular contours, of homogeneous structure without any noticeable lesions, left lobe 8cm, right lobe 20 cm, caudate lobe 7 cm, significant intrahepatic biliary tree dilatation (Fig. 1a) and a distended gallbladder of 11 cm (Fig. 1b) without the presence of gallstones; normal portal vein , with hepatopetal flow, CBD 10 mm; no ascites fluid; normal spleen; in the region of the head of the pancreas, the ultrasound showed a hypoechogenic structure (Fig .1c), imprecise delimited, of 3,5 cm; visible Wirsung duct in the pancreatic body. For a more accurate diagnosis the patient underwent CT scan and a MRI.

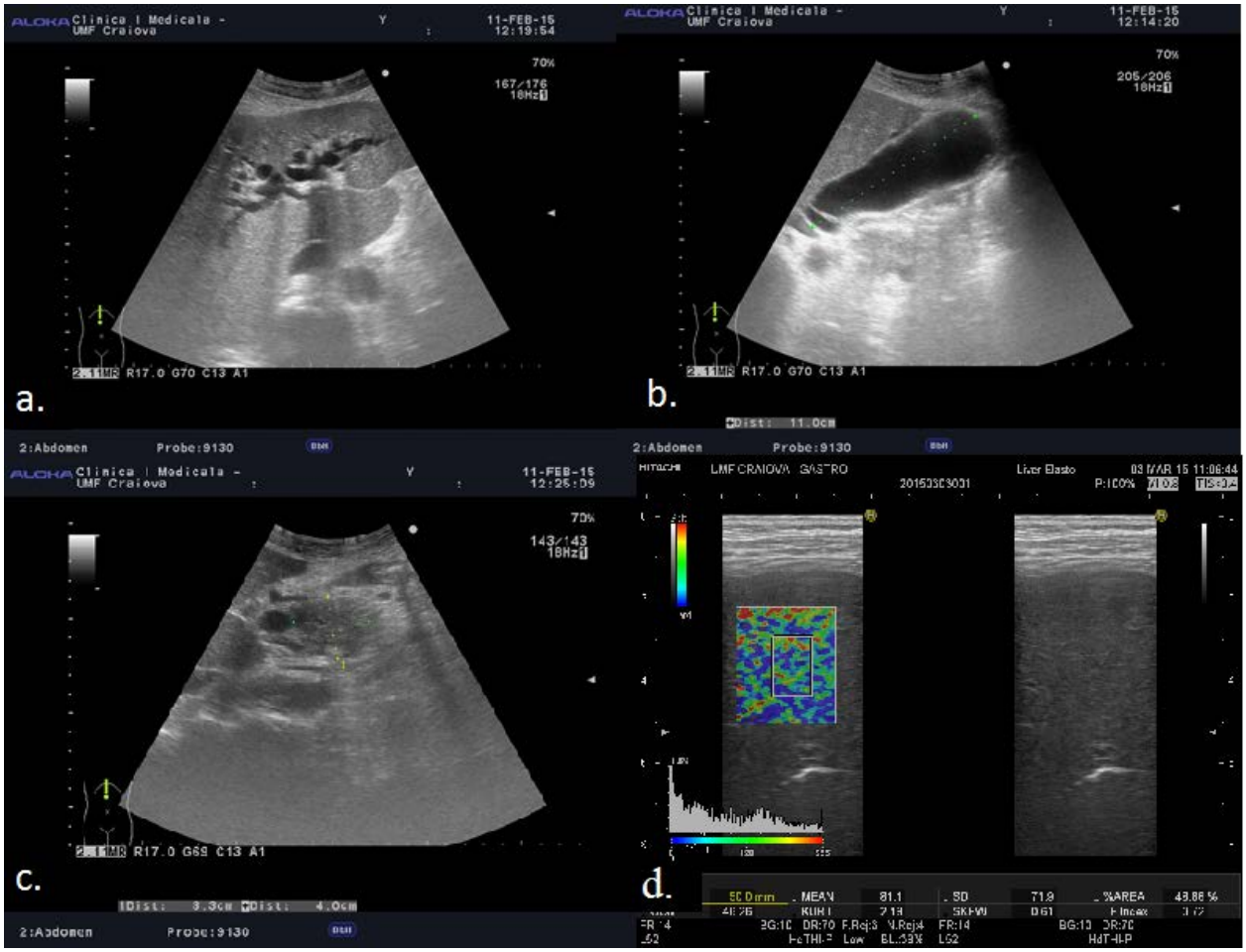

Fig.1. Ultrasound and RTE evaluation. [a] significant intrahepatic biliary tree dilatation; [b] distended gallbladder; [c] hypoechogenic structure in the region of the head of the pancreas; [d] RTE: hepatic tissue displayed a mosaic pattern, characterized by dominant blue area.

Computerized tomography (CT) revealed a mass located at the head of the pancreas encompassing the uncinate process, that is isodense with the pancreatic parenchyma (Fig. 2a) and slightly hypodense post-contrast (Fig. 2b), imprecise delimited, of 1,64/1,94 cm. More specific information about the location of the tumor were obtained through magnetic resonance imaging (MRI), which showed a soft-tissue mass located strictly at the uncinate process, 19/14,4 mm in size.

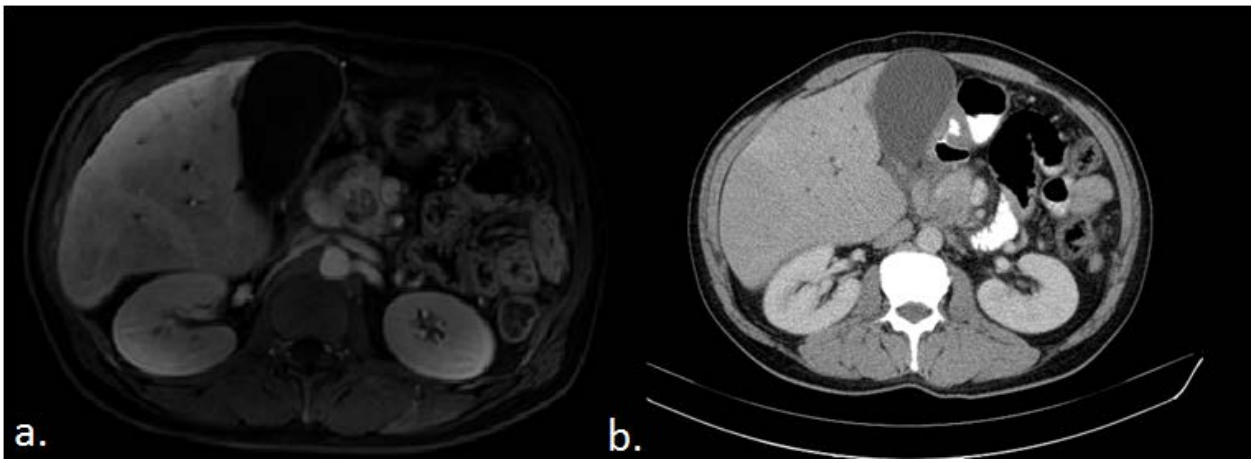

Fig.2. Computer tomography. [a] isodense mass located at the head of the pancreas encompassing the uncinate process; [b] pancreatic mass slightly hypodense post-contrast

Considering the history of alcohol consumption and present HBs antigen, additional investigations were needed in order to evaluate the exact nature of the hepatic disease. Upper gastrointestinal endoscopy (UGIE) did not identify esophageal varices. Neither CT nor MRI presented any features indicative of liver cirrhosis. Fibroscan evaluation measured a liver stiffness of 8 kPa, Matavir score F2, evocative for significant liver fibrosis. These results were inconsistent with the Real-Time Tissue Elastography (RTE) analysis. In RTE the hepatic tissue displayed a mosaic pattern, characterized by dominant blue area (Fig. 1d), with a LFI (liver fibrosis index) of 3.72, which is highly suggestive for liver cirrhosis.

Discussions

After the initial examination of the patient, based on the intense sclero-tegumentary icterus, pale colored stools and dark colored urine, a clinical diagnosis of obstructive jaundice with presumably malignant etiology (significant weight loss) was established. The laboratory findings backed up both presumptions, with high indicators of cholestasis and a very high CA 19-9 marker.

Cirrhosis is the final stage attained by various chronic liver diseases after years or decades of slow progression and is histologically characterized by fibrous septa between the portal fields. Diagnosis relies on its characteristic clinical findings, laboratory tests, imaging and fibrosis assessment studies. The typical findings in cirrhosis include: cutaneous signs of liver disease, a firm liver on palpation, signs of portal hypertension (variceal bleeding), or decreased detoxification capabilities of the liver (hepatic encephalopathy). Ancillary studies include abdominal US, UGIE (to demonstrate esophageal varices) and liver biopsy (indicated if the etiology of liver disease is unclear)[3]. In order to estimate the extent of hepatic fibrosis, non-invasive methods are preferred, such as: transient elastography (TE) (Fibroscan), real-time tissue elastography (RTE) or Acoustic Radiation Force Impulse Elastography (ARFI).

Studies on the use of TE for evaluation of fibrosis established different cut-off values for the diagnosis of cirrhosis, depending on the etiology: 12.5 kPa in HCV patients , 13.4 kPa in HBV patients, 10.3 kPa in NAFLD patients, 22.4 kPa in alcoholic steatohepatitis (ASH) and 17.3 kPa in cholestatic chronic diseases (primary biliary cirrhosis and primary sclerosing colangitis). The accuracy of ARFI elastography for assessment of liver fibrosis was also determined in a bicentric Romanian study and a meta-analysis published in 2013 with AUROC of 0.93 and 0.91, respectively. In the case of RTE, the recording method and analysis of data obtained was variable, depending on the published studies. Due to the inconsistent results in the published data, further studies should clarify the value of RTE, as well as the optimal cut-offs used to differentiate different stages of liver fibrosis[2].

The delayed diagnosis of liver cirrhosis in this case was due to the lack of evidence on initial imaging evaluation (US, CT scan, MRI, UGIE). The diagnostic sensitivity of these investigations, compared to histologically proven cirrhosis is satisfying (>80%) in the case of CT scan and MRI, but can be mediocre when it comes to the ultrasound performance (52%)[4]. For a more accurate diagnosis a transient elastography (Fibroscan) was performed which measured a Metavir score F2, evocative for significant liver fibrosis. Highly suggestive features of liver cirrhosis were

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obtained only through RTE, measuring a LFI (liver fibrosis index) of 3.72.

Morphologically, the cirrhosis caused by alcohol is characteristically of the „Micronodular" type, while the „mixed Micro-Macronodular" type is generally seen in cirrhosis caused by hepatitis B and C virus[5]. Intraoperative assessment of the liver morphology (Fig. 3) suggested chronic alcoholism as primary etiologic factor.

Fig.3. Intraoperative assessment of the liver showing micronodulary morphology and distended gallbladder

CA 19-9 (carbohydrate antigen 19-9) is a polysialylated Lewis blood group antigen. Elevated levels are found in 80% of cases of pancreatic cancer and 75% of cases of advanced colorectal cancer. However, it may also be present in serum in benign hepatic and biliary tract disease[6].

Ductal adenocarcinoma originates in 65% of cases in the head of the pancreas, in the isthmus, or in the uncinate process, in 15% of casese in the body and tail, while in 20% it can diffusely affect the whole gland. At the CT diagnosis, the tumor often shows small dimensions (<2 cm) if localized in the head or uncinate process than if it is localized into the body-tail (5–7 cm). Usually calcifications are not present[7]. Carcinoma of the uncinate process of the pancreas is considered to be rare, difficult to diagnose and particularly devastating. The current method of detection is computed tomography[8]. Compared with other parts of the pancreas, the uncinate process is more closely connected to the mesentery and is situated at some distance from the course of both pancreatic and bile ducts. This accounts for the lack of jaundice as a presenting feature[9]. In order for obstructive icterus to occur in uncinate process carcinoma, an invasion of the duodenal papilla needs to exist.

Surgical treatment can be grouped in radical and palliative procedures. Radical procedures include: pancreaticoduodenectomy, with or without preservation of pylorus, lymphadenectomy and reconstructive surgery. At diagnosis most patients already have locally advanced disease with vascular invasion and/or metastatic lesions, which rule out a curative surgical approach. In the minority of patients in whom radical surgery is possible, survival at 5 years is still 15–20%. For these reasons, palliation is the cornerstone of treatment for most patients with pancreatic adenocarcinoma. There are many palliative options: bilio-digestive derivations, chemotherapy, interventional radiology[10].

Staging is an essential part of the diagnostic work-up and key to the patient management. For this, we used the UICC (The Union for International Cancer Control) TNM (seventh edition) staging system. The tumor was classified T2 N0, stage IB. The staging system for the primary tumor reflects the surgical criteria for resectability of pancreatic cancer. Theoretically, Stages T1 and T2(present case) represent a resectable tumor [11], but clinical staging through the coding of T-N-M parameters does not always give a clear indication regarding the resectability of tumors in patients with a pancreatic neoplasm. For this purpose, a more reliable tumor staging assessment is the result of various procedures in which the preoperative diagnostic results are combined with surgical exploration [12].

Traditionally, cirrhosis has been considered a contraindication to major gastrointestinal surgery. Patients with cirrhosis have an increased risk of complications during surgery (bleeding because of portal hypertension and coagulopathy, liver dysfunction, and ascites, which often lead to sepsis), which is related to the severity of liver disease. Given its high surgery risk, the tendency is to opt for a palliative procedure if liver cirrhosis is confirmed [13].

The patient is set to undergo surgery and transferred to the Surgery Clinic. Considering the absence of portal hypertension and evidence of liver cirrhosis was lacking on initial ultrasound, CT scan and MRI, a radical

intervention was encouraged. After intraoperative assessment of the tumor, the micronodulary aspect of the liver confirmed the presence of cirrhosis and changed the surgical approach. The surgical team opts for a palliative intervention and carries out a cholecystectomy coupled with a biliodigestive anastomosis (*latero-lateral choledochoduodenostomy*).

Conclusions

We presented case of jaundice syndrome in a patient with uncinate process carcinoma and liver cirrhosis. Almost all preoperative imaging evaluations showed only signs of liver fibrosis, intraoperative assessment confirmed the diagnosis of liver cirrhosis, changing also the type of surgical approach and patient prognosis. The only suspicion of liver cirrhosis prior to the surgical intervention was the real time tissue elastography, but the diagnositic accuracy of this method still needs large validation studies to be proven.

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