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Indetermined Biliary Filling Defects: Sequential Approach Using Ultrasound, MRT and Cholangioscopy (Case Report)

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1. Abstract

Indetermined intrahepatic biliary obstruction and filling defects can be a clinical challenge not only to determine the origin, but also to solve the problem when clinical symptoms prevail. Optimal interventional algorhythms and innovative endoscopic procedures are required. In the current case report, transcutaneous sonography with high resolution, followed by magnetic responance cholangio-pancreaticography (MRCP) and subsequent peroral cholangioscopy were sequentially performed. A symptomatic patient is presented with unclear but symptomatic biliary filling defects in the left liver lobe that had been persistent for several years after cholecystectomy had been performed 12 years ago. Peroral SPY-glass cholangioscopy in combination with electrohydraulic lithotripsy was used and proved to be highly effective in immediate diagnosis and interventional therapy of intrahepatic bile duct stones and the long term problem was immediately solved without signs of infection.

2. Key Messages

1. Although computed tomography is one of the most commonly used diagnostic tools for undetermined biliary filling defects and segmental cholestasis, it is frequently unable to detect intrahepatic stones.
2. High-resolution transabdominal ultrasonography followed by MRCP represent the most sensitive method in the diagnosis of intrahepatic bile duct stones.
3. Single-use cholangioscopes in combination with localized and centered eletrohydraulic therapy are safe, and highly effective in the therapy of intrahepatic filling defects lesions, should be routinely available in high volume centers.

3. Introduction

Segmental intrahepatic cholestasis in the liver, especially when prevalent over years, can often be explained by cystic dilation of the bile ducts, with or without the formation of intrahepatic bile duct stones (cholelithiasis). Also, segment cholestasis in the liver may also results as a consequence of cholecystectomy since in some cases, clips or electrocoagulation may lead to the destruction of the bile tree, especially in the left liver lobe. With a prevalence of 15-20% in the adult population in Germany, cholelithiasis is a common clinical picture, especially when cholecytolithiasis in present [1-3]. While gallbladder stones can often be detected with a good sensitivity of >95% and a specificity of almost 100% by sonography [4], the sensitivity of transabdominal ultrasound for choledocholithiasis, especially in the intrahepatic region, ranges only at about 70% and a specificity of 90% [5]. Despite increasing prevalence, intrahepatic stones occur much less frequently overall and require further specific diagnostic methods since transcutaneous sonography often fails. Thus, correct diagnose and treatment of the strictures or filling defects within the

biliary tracts requires optimal interventional strategies and modern technical possibilities [6, 7]. However, intrahepatic carcinoma and malignant strictures within biliary tract often also present frequently with only slight clinical symptoms and thus may be delayed in clinical practice [8], and patients often report right-sided upper abdominal pain and increased cholestasis parameters in the laboratory, suggesting an obstruction of the outflow tract without clearly visible tumors in CT scans or ultrasound techniques [9]. Still, in both cases (various malignant and benign causes), both groups require immediate diagnostic algorhythms such as sonography, followed by subsequent MRT or CT Scanning [9, 10], and this sequence will be discussed herein. Also, the patient case is presented to illustrate the increasing importance attached to efficient clinical practices of cholangioscopy as a sensitive diagnostic and therapeutic strategy for the classification and treatment of these causes conditions.

4. Patients History

A 76-year-old man presented with upper abdominal pain that had been progressive for several days. Cholecystectomy had been performed 12 years ago, and a CT scan was performed afterwards without any consequences. Anamnestic questions revealed that that had been early CT scans with the assumption of biliary obstruction and slight elevation of liver enzymes; however, due to the scarcity of symptoms the further diagnostic procedures had not been performed. At the day of submission to the hospital, symptoms were more severe in pain scale of 7/10, associated with acute postprandial pain, with punctum maximum in the right upper abdomen and epigastrium. There were no prior B-symptoms in terms of night sweats, involuntary weight loss, or fever. The travel history showed no relevant incidents. Ramipril, Metoprolol, and Allopurinol were relevant medications with possible liver affections. Allergies were denied. There was also a history of expired Herpes Zoster disease, an axial hiatal hernia, a 12-mm left renal cyst. The CT scan which had been performed 12 years ago at the times of cholecystectomy was not immediately available upon admission, but was ordered for the further procedures as a print out.

5. Diagnostics and Therapeutic Procedures

Clinically, the patient presented in a slightly reduced general condition due to the symptoms. Physical examination revealed evident tenderness in the epigastric region with a soft abdomen. There was no pain on percussion over the renal bearings and spine, and there was no evidence of edema. Upon admission, there were laboratory findings of increased cholestasis parameters (gamma-GT: 88 U/l, alkaline phosphatase: 146 U/l), accompanied by slightly increased inflammatory parameters (C-reactive protein: 3.3 mg/dl (normal range <0.5mg/dl), ESR: 28 mm/1h, leukocytes: 13.57/nl).

The following transcutaneous abdominal ultrasonography initially showed a hepatic duct dilated to 10 mm in a state after cholecystectomy, an intrahepatic cholestasis and a polycyclic filling defect in segment III of the liver, with otherwise unremarkable remaining organs. Due to the excellent visibility in ultrasound, hepaticolithiasis was suspected as the main differential diagnose. For further clarification of the clinical findings with the accompanying inflammatory parameters, a chest X-ray was performed, which showed no remarkable findings. EGD showed no signs of gastritis except for the known large axial hernia.

6. Results of Radiological Examinations

6.1. MRT, CT and ERCP-Imaging Procedures (Figure 1)**:** Since dilated bile ducts, especially in combination with a history of cholecystectomy, was be considered as the differential diagnosis of cholangiocarcinoma or bilioma [11], an MR cholangiopancreatography (and not a CT scan) was performed next to exclude it and to visualize a biliary stricture and unclear filling defects. This showed a smooth-edged liver with homogeneous parenchyma, but an extension of the intra- and extrahepatic biliary system, especially of the ductus hepaticus sinister. Furthermore the MRT scan shows localized and focal findings of left intrahepatic obstruction most likely in the area of the S2/S3 segment (Figure 1A). The ductus hepaticus communis ranged at 11mm at its widest point and is well marked to the papilla vateri. There was no evidence of calculi and no evidence of malignancy. Except for isolated enlarged paraaortic lymph nodes (8mm), and at the hepatic hilus (16mm), there was no evidence of pathologically increased or enlarged lymph nodes. Following detailed clinical evaluation, it turned out that the patient had a CT scan almost 10 years ago. As shown in figure 1B, the previous CT scan that had been performed immediately after CHE in the year 2008, revealed retrospectively a diffuse hypodensity in the left lobe of the liver in segments II and III, presumably the early onset of intrahepatic cholestasis. However, it has to be emphasized that this CT scans did not offer a sufficient sensitivity and specificity to exclude or proof the presence of gall stones. Consecutively, (figure 1C), the following ERCP showed biliary dilation of the ductus hepaticus communis to 11mm, dilation of the left bile duct at 10mm, and also space occupying lesions in segment 2 and segment 3 of the bile tree. The downstream bile ducts, especially in the right hepatic branches were not dilated. To improve the outflow of bile, a 12cm/7-charrier double pigtail catheter was inserted, and cholangioscopy as planned to determine the nature of the dilation and the space occupying lesions.

Next, Spy glass cholangioscopy and electrohydraulic lithotripsy (EHL) was performed ((Cholangioscopy and EHL, illustrated in (Figure 2a-d)), yielding in the final diagnose and treatment. Under visual spyglass imaging, the intrahepatic hilus and the Ductus hepaticus dexter and sinister could be visualized properly. (Figure 2a) First, no stricture was detected in the left or righ duct. With deeper approach to segment II and III in the left liver lobe, there were 3 stones found In the left ductus hepaticus, so hepatolithiasis could finally be diagnosed (Figure 2b). Next, by using Electrohydraulic Lithotripsy (EHL) centered under visual control of a Spy-glass cholangioscopes, the stones were successfully removed, resulting in the discharge of

the stones and further sludge via the papilla during irrigation (Figure 2c). The following control ERCP showed a decreasing trend of cholestasis under contrast medium (Figure 2d). After a post interventional course without complications, the left intrahepatic cholestasis was completely regressed in the control ultrasonography and patient was dismissed.

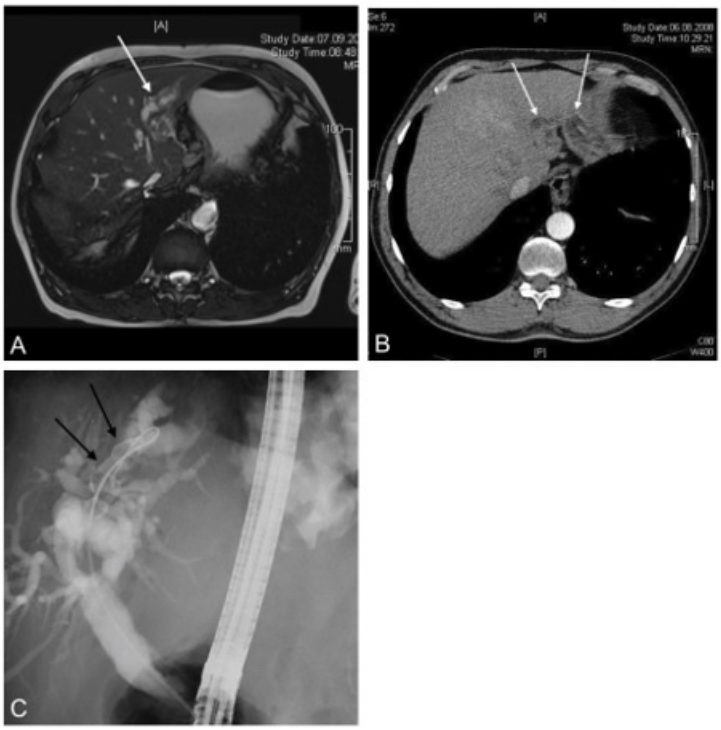

Figure 1(A): MRCP scan of the patient in T2 amplification showing the intrahepatic ductal system. The left biliary system its dilated most likely in the area of the S2/S3 segment and a filling defect is visualised (arrow);**1(B):** Abdominal CT-Scan (2008) with contrast medium in atrial phase with focus on the left liver. Diffuse hypodensity in segment 2 (arrows), suggesting intrahepatic cholestasis but bile duct stones cannot be detected; **1(C):** Endoscopic retrograde cholangiography image oft the biliary tree. It shows multiple filling defects in the S2/S3 segment (arrows) next to a guide wire with dilated ductus hepaticus communis up to 11mm in a state after cholecystectomy.

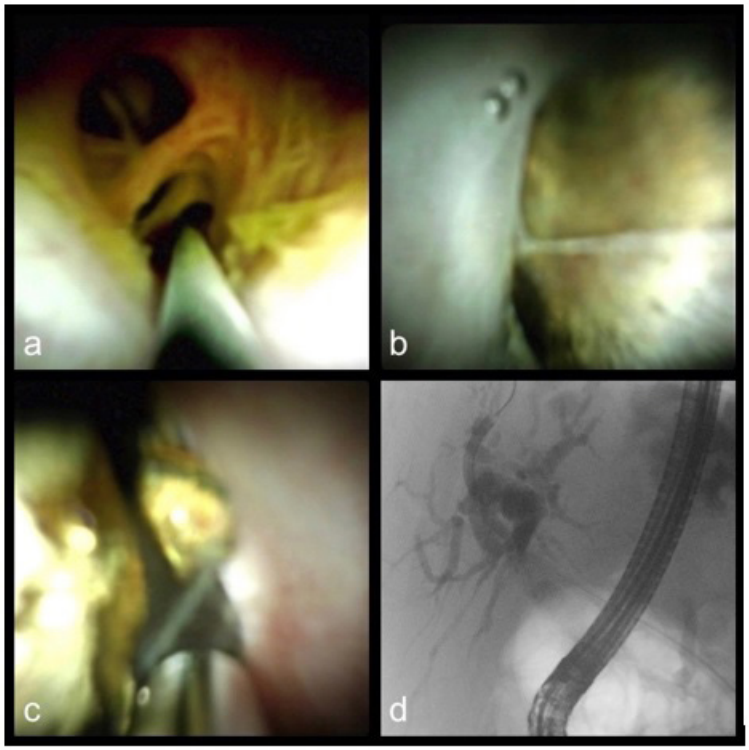

Figure 2: Peroral transpapillary cholangioscopy using spyglass visualization. (a) Visualization of the hilus of intrahepatic bile ducts and the guide wire, which is located in the left hepatic bile duct;
(b) Visualization of one bile duct stone in the left hepatic bile duct; (c) The tip of the EHL sonde is placed in front of the lowest stone under visual guidance; (d) Endoscopic retrograde cholangiography image with decreasing trend of cholestasis indicating removal of the stone.

7. Discussion

Differential diagnose of undetermined segmental cholestasis with filling defects can range from benign diseases (such as stones with or without stricture formation), or malignant such as intrahepatic cholangiocarcinoma [12]. Indetermined intrahepatic filling defects, however, require a reasonable strategic diagnostic algorithm, which is presented in the case report here. Here, a piloting diagnose was made by non-invasive transcutaneous sonography with high resolution, known tob e diagnostic tool of 1st choice. Ultrasound is known to detect choledocholithias with a sensitivity of 70-80% [5], however, specificity remaines below 70% [12, 14, 15]. Therefore, sonography was followed by MRCP in a second step to achieve a precise visualization. MRCP allows a more precise differentiation of various cholangiopathies than ultrasound in regard to intrahepatic filling defects, and may offer a differentiation between benign and malignant structures. A benign genesis would be most likely indicated by a smoothly limited, short-path stricture without wall thickening. In MRCP. In the diagnosis of coledocholithiasis, MRCP has a sensitivity of 90%, a specificity of 88%, and an accuracy of 89% [16] [12, 17]. MRCP, with a sensitivity of 97%, is clearly superior to this procedure to commonly used ultrasound techniques [14, 15].

Consecutively, ERCP is the most important diagnose and treatment of choice not only due to the diagnostic findings, but also with an interventional approach to choledocholithiasis. ERCP is commonly performed to extract stones, to perform biopsies of intraductal lesions, and place stents. Almost 90% of stones in the choledochal duct can be extracted endoscopically [17, 18]. In the context of ERCP, stone extraction can be performed by inflatable balloon catheter or with special basket catheter systems [19, 20, 21]. In approximately 5-10% of intrahepatic bile duct stones, however, extraction cannot be performed via the described standard stone removal techniques due to complicated stone localizations, for example intrahepatic or in smaller side branches.

Peroral cholangioscopy allows this more precise diaignosis and treatment, and may thus be regarded as a true gold standard when it comes tot he evaluation of unclear intrahepatic biliary filling defects and strictures [22]. It should be routinely available when symptomatic patients are being treated. Also, endoscopic visualization of the bile duct strictures and biopsy sampling is possible, so that an exact differentiation of bile duct adenomas, intraductal malignant tumors, polypoid lesions, biliary pappilomatosis or IgG4 dependent cholangiopathy is present [23].

An important study using re-usable cholangioscopes by Prinz et.al previously investigated the use of a shorter mother-baby system (S-POCS) with regard to functionality and manageability in cases of suspicious bile duct strictures or fixed filling defects in the bile duct [23]. A total of 76 patients with indeterminate strictures and filling defects, which usually represent a challenge for diagnostic and therapeutic endoscopy, were examined using the short baby scope. In all cases, the insertion of the cholangioscope into the biliary system and intrahepatic side branches was without complications. In 5 patients, intrahepatic bile duct stones that were inaccessible by conventional methods were successfully removed using visually guided laser lithotripsy [23]. Re-usable cholangioscope are still used, however, in most hospitals, the use of the devices has been limited due to the fear of possible infection with Klebsiella species following perfusion of the biliary tract with solutions.

Currently, peroral video cholangioscopy (POCS) is performed with a *single use* Mother-Baby-System (MBSS) in which an ultra-thin endoscope is inserted transpapillary through the instrumentation channel of a duodenoscope due to the high frequency of cholangitis when cholangioscopy is performed. Current standard is the use of single-use cholangioscopes, provided by Boston-Scientific Inc. and termed as Spy-glass systems [24]. Using Spy-glass system in the current patient, initially inspection allowed to describe the correct anatomy of the left and right biliary segments liver. Stones were detected in segment 2 and 3, and EHL tips were placed in front of the stones under visual guidance. Immediately, stones could be easily destroyed up to the periphery in the bile ducts of segments II, III and IV, no further cystic formation of the bile duct was found, and patient could be dismissed immediately. It has to be emphasized that EHL can only be performed under continuous flushing with sodium chloride; however, no bacterial infection or signs of cholangitis were observed. Thus, single use cholangiogscope may currently be regarded as a first choice of treatment to guarantee the highest degree of safety, and therapeutic success during the intervention. Use of Single-Use ERC device may also be considered in the near future during these clinical cases.

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