

Ciliated Foregut Cyst of the Gallbladder. A Diagnostic Challenge and Management Quandary

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ABSTRACT

Ciliated foregut cysts are rare anomalies due to aberrant embryological development. Only a small number of gallbladder ciliated foregut cysts have been reported. We report the case of a 29-year-old woman presenting with epigastric pain associated with diarrhoea and vomiting, who was found to have raised serum bilirubin levels and abnormal liver function tests. Following a diagnostic pathway including abdominal ultrasound, magnetic resonance cholangiopancreatography and endoscopic ultrasound the gallbladder cyst was provisionally diagnosed to be a cyst arising from the cystic duct or a duplicated gallbladder. A laparoscopic cholecystectomy was carried out and histopathology identified a ciliated foregut gallbladder cyst. The postoperative course was uneventful. In this report we offer what we believe to be an optimal diagnostic pathway and therapeutic strategy for this rare congenital cyst.

INTRODUCTION

Ciliated foregut cysts are rare anomalies due to aberrant embryological development. They are usually located above the diaphragm [1]. They can also arise in relation to the pancreas, upper digestive tract and the liver. However, very few cases have so far been reported regarding the gallbladder [1-6]. We present the case of a young woman with a ciliated foregut cyst of the gallbladder whose clinical presentation, biochemical and radiological findings posed a diagnostic challenge. Postoperative histopathological findings proved informative and raised questions as to the management of this rare condition with embryology not well understood.

CASE REPORT

A 29-year-old Caucasian woman presented to the

gastroenterology department of a nearby hospital with a 2-week history of symptoms of acute onset. The initial symptoms were severe epigastric pain radiating to her chest and subsequently associated with rigors, vomiting, diarrhoea and pale, loose stools. In view of the abnormal liver function tests (aspartate aminotransferase AST, 218 IU/L, alanin aminotransferase ALT, 579 IU/L) and elevated serum bilirubin (61 μ mol/L), a provisional diagnosis was made of acute hepatitis of unknown cause. Subsequently, serology was found to be negative for hepatitis B and hepatitis C. Abdominal ultrasound (US) showed no thickening of the gallbladder wall. However, a cystic mass was noted, containing solid elements, adjacent to the neck of the gallbladder, possibly representing a choledochal cyst. On magnetic resonance cholangiopancreatography (MRCP) there appeared to be a pouch connected to the cystic duct, containing debris, suggesting either a diverticulum or a duplication of the gallbladder.

The patient subsequently sought an opinion from a gastroenterologist at our hospital. On clinical examination the patient was found to have severe pruritus. A repeat abdominal US was carried out in our hospital, and this showed a 2.3cm choledochal cyst in segment V of the liver adjacent to the gallbladder, with hypoechoic features. The gallbladder was shown to have a 4mm polyp but no gallstones and no intra or extrahepatic bile duct dilatation.

At this stage she was referred for assessment by the hepatobiliary surgical team. She was still unwell with nausea, fatigue, dark urine and yellow sclerae. Blood tests revealed a raised bilirubin level of 47 μ mol/L and abnormal liver

function tests with ALT at 759 and AST at 203 IU/L. She was admitted to hospital for re-hydration with intravenous fluids and underwent an endoscopic ultrasound (EUS) to rule out a connection between the cyst and the bile duct. The EUS clarified that the common bile duct was smooth, with no debris and without any cyst originating from it and the liver was normal without an obvious intrahepatic cyst. Additionally, a high resolution MRCP (Figs. 1,2) was conducted which demonstrated a 2.2 cm cyst, not in the liver but adjacent to the gallbladder which could either represent a cyst arising from the cystic duct or represent a duplicated gall bladder. The patient's jaundice and cholestatic symptoms were attributed to a pressure effect and probable passing of debris from the cyst to the main biliary system leading to a degree of cholangitis and also contributing to obstruction from the cyst on the common bile duct, responsible for a temporary liver injury with abnormal liver function tests. At the time that the MRCP was performed in our hospital, the bilirubin levels had started to decrease and the images did not demonstrate any bile duct dilatations. This finding added to the hypothesis of intermittent obstruction of the common bile duct with debris and subsequent hepatic injury with raised liver function tests. Following this diagnosis, it was decided to perform laparoscopic cholecystectomy with a view to removing the cyst. The operation and subsequent recovery were uneventful. The histopathology was as follows: in microscopic examination, the ovoid cyst, with a size of almost 3 cm, containing gelatinous grey material, was lined by respiratory type epithelium with a thin smooth muscle wall and clearly separated from the gallbladder mucosa and located just outside the muscularis propria (Figs. 3-6). A very unusual, and perhaps unique finding was the presence of a tiny 0.5 mm focus of salivary gland type acini within the wall (Fig. 7). The patient's symptoms were resolved following laparoscopic cholecystectomy with the removal of the cyst and the bilirubin and liver function tests returned to normal values.



Fig. 1. Sagittal view of MRCP image demonstrating a 2.2 cm cystic lesion adjacent to the gallbladder appearing as extraparenchymal. The common bile duct at the time of this scan appeared to be of normal calibre.

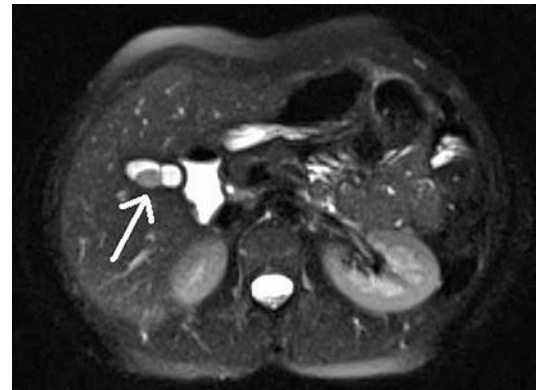


Fig. 2. Axial view of MRCP image demonstrating the cystic lesion adjacent to the gallbladder (arrow).

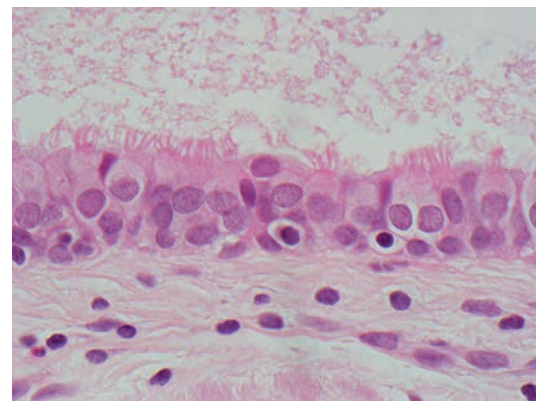


Fig. 3. At high magnification the ciliated cells are clearly seen with some smaller intercalated cells (H&E x1000).

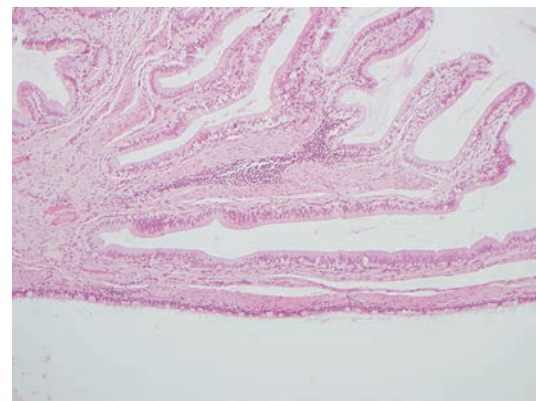


Fig. 4. A low power view of the complex columnar cell-lined gallbladder mucosa at the top of the field, and at the lower edge a single layer of ciliated epithelium (H&E x100).

DISCUSSION

Gallbladder cysts, first described by Wiederman in 1797, are rare and classified as acquired, neoplastic or congenital [2, 7]. Ciliated foregut cysts are uncommon congenital cysts, arising from the remnant of the embryonic foregut and usually located above the diaphragm, presenting either as a bronchial or oesophageal cyst [6]. When located below the diaphragm, they are usually found in the liver, where they are known as ciliated hepatic foregut cysts (CHFUs). More than 60 cases of CHFUs have been reported [8, 9]; extrahepatic cysts are exceedingly rare.

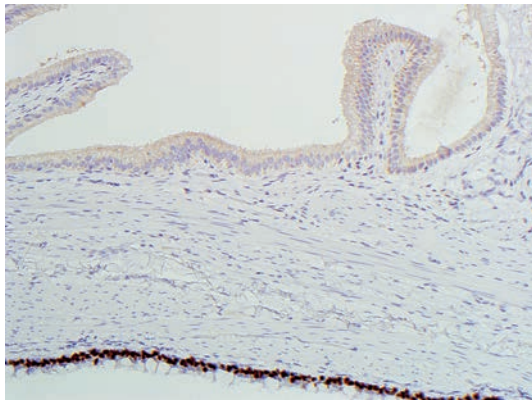


Fig. 5. p63 immunohistochemistry demonstrates strong nuclear expression in the ciliated epithelium in contrast to the gall bladder mucinous epithelium (x200).

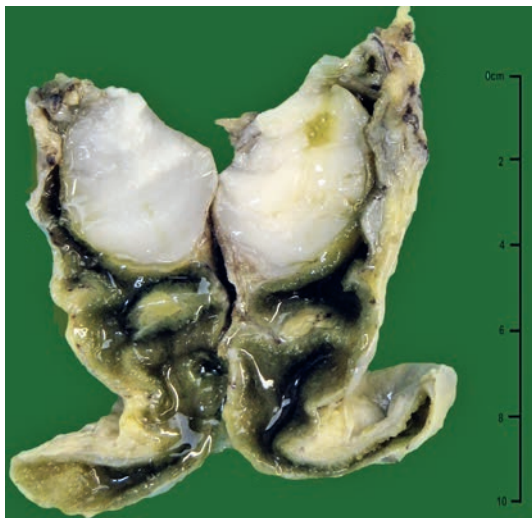


Fig. 6. Macroscopic aspect of the cyst.

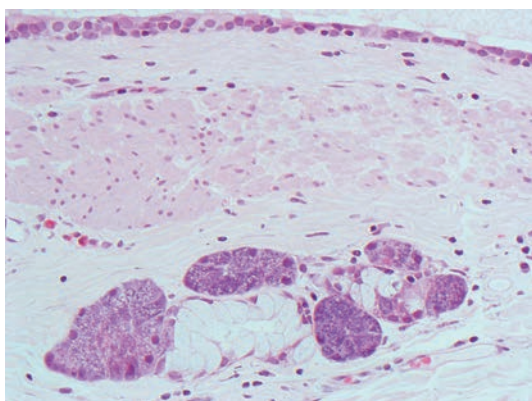


Fig. 7. A small focus of mixed zymogenic and mucinous cells resembling a salivary gland acinus (H&E x630).

The embryological development of the gallbladder and extrahepatic biliary tract are intimately related to the development of the liver. Thus no account of gallbladder development would be adequate without at least a brief consideration of hepatic embryology. Towards the end of the 2nd week of development, the primitive gut is formed by a process of transverse and cephalo-caudal infolding of the embryonic plate. At this stage the gut may be described as comprising foregut, midgut and hindgut which are all

continuous one with another. The foregut may be described as being formed by the pharyngeal gut and postpharyngeal gut. The latter gives rise to the oesophagus, stomach and proximal portion of the duodenum in addition to the pancreas and liver [10, 11].

The primordium of the liver first appears in the middle of the 3rd week of embryological development as an endodermal outgrowth from the ventral aspect of the very distal end of the primitive foregut. In reaching the septum transversum the hepatic diverticulum grows within the ventral mesogastrium; a structure which later gives rise to the lesser omentum and falciform ligament of the liver. The cephalad end of the hepatic diverticulum gives rise to the liver, while the caudal end of the diverticulum remains relatively narrow and gives rise to the bile duct [10, 11].

While the hepatic cells continue to proliferate in the septum transversum, the bile duct gives rise to a small diverticulum from its ventral aspect. This diverticulum develops into the gallbladder and cystic duct. The lower respiratory tract (comprising the larynx, tracheo-bronchial tree and lungs) is also derived from the foregut. Highly selective cellular differentiation within the endoderm of the respiratory diverticulum as well as in the upper part of the pharyngeal gut results in the larynx, nasopharynx and tracheobronchial tree possessing an epithelial lining that is characterised by the presence of ciliated columnar cells admixed with mucus-secreting tall columnar cells (goblet cells). The precise molecular mechanisms underlying this specific and selective epithelial differentiation within the foregut endoderm are not completely understood. Nevertheless, it is hypothesised that it is the induction of the very same molecular mechanism in aberrant locations within the foregut that is the cause of the congenital ciliated cystic lesions that are encountered from time to time in the liver, pancreas and least commonly within the wall of the gallbladder [10, 11].

In 1995 Kakitsubata et al first published a case of a patient with a gallbladder cyst lined by a single layer of ciliated columnar epithelium with a fibro-muscular wall. However, it was not until 2000 that the term ciliated foregut cyst of the gallbladder was introduced by Nam et al [3, 6], who presented a case of this rare condition. Further case reports were published by Hirono et al and Muraoka et al [1, 4]. Interestingly there is only one report of a hepatic ciliated foregut cyst communicating with the gallbladder [10].

Our case highlights the diagnostic challenges posed by this rare condition. Both US and high resolution MRCP demonstrated conflicting results making it impossible for us to establish an exact diagnosis preoperatively. Although on US the cyst seemed to be intrahepatic, on MRCP it was obvious that the cyst was not located in the liver and that its origin was possibly from the cystic duct or the gallbladder itself. Also the bile duct was not related to the cyst. The latter was confirmed by EUS. We would wish to suggest that the optimal approach to diagnosis should include a high resolution MRCP, which appears to be superior to other modalities in indicating the precise origin of the cyst.

The other important question, should such a cyst be found on imaging, is whether the ideal management approach is surveillance with regular imaging or a surgical excision.

Muraoka et al in their case report in 2003 recommended either minimally invasive surgery or close observation [1]. However, one could argue that as we are still not fully aware of the biological behaviour of this type of cyst due to its rarity and a possible malignant potential cannot be fully excluded, a surgical removal of the cyst along with the gallbladder with a laparoscopic technique would seem a more appropriate management pathway. Hepatic ciliated foregut cysts have been known on occasion to undergo malignant transformation [8, 13], and although hepatic cysts comprise a different entity, one should always bear in mind the possibility of similar changes in gallbladder ciliated cysts as well. As a pre-malignant behaviour cannot be entirely excluded with our current available knowledge and especially if the patient is young and symptomatic, as was the case in our patient, we would recommend minimally invasive surgical intervention.

CONCLUSION

We should be aware of the fact that the biologic behaviour of this very rare cystic lesion is not yet thoroughly clarified. It can demonstrate a significant diagnostic challenge and in our experience, high resolution MRI offers the most reliable and detailed imaging pathway. Also a surgical removal in the form of laparoscopic cholecystectomy would be the preferred therapeutic approach as we cannot exclude its potential for neoplastic transformation and consequently cannot be confident enough to manage the condition conservatively with regular follow-up.

Conflicts of interest. None to be declared.

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