Incidentally Discovered White Subcupsular Liver Nodules during Laparoscopic Surgery: Biliary Hamartoma and Peribiliary Gland Hamartoma

Bílé subkapsulární jaterní uzly objevené náhodně během laparoskopické operace: žlučové hamartomy a peribiliární žlázový hamartom

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Summary
During routine laparoscopic surgery, the surgeon may encounter the presence of small white subcapsular liver nodules, either solitary or multiple. The lesions may mimic liver metastasis and in many cases are not demonstrated in the preoperative ultrasound or computed tomography. The aim of this article is to familiarize the laparoscopic surgeon with the incidental discovery of these nodules which represent the two types of intrahepatic benign bile duct proliferations and include biliary hamartomas, which are usually multiple benign malformations of the intrahepatic bile ducts, and peribiliary gland hamartoma, which is usually solitary and consists of a benign epithelial tumor of the liver derived from bile duct cells.

Key words
bile ducts – liver – surgery – adenoma – von Meyenburg complexes – hamartomas

Souhrn
Během rutinní laparoskopické operace se může chirurg setkat s přítomností malých bílých subkapsulárních jaterních uzlů, ať už solitárních nebo mnohočetných. Tyto léze mohou napodobovat jaterních metastáze a v mnoha případech nejsou prokázány předoperačním ultrazvukem nebo počítačovou tomografií. Cílem tohoto článku je seznámit laparoskopického chirurga s náhodným objevem těchto uzlíků, které představují dva typy intrahepatálních benigních malformací žlučových cest a zahrnují žlučové hamartomy, které jsou obvykle mnohočetné nezhoubné malformace intrahepatických žlučovodů, a peribiliární žlázový hamartom, který je obvykle solitární a skládá se z benigního epiteliálního nádoru v játrech odvozeného od buněk žlučových cest.

Klíčová slova
žlučové cesty – játra – chirurgie – adenomy – von Meyenburg útvary – hamartomy

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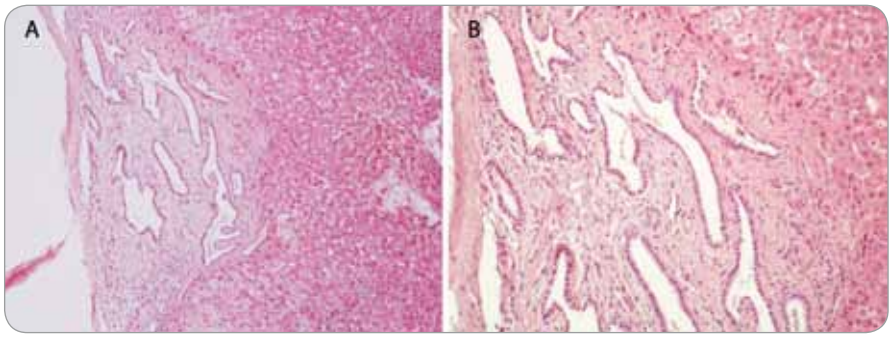

Fig. 1. The hepatic nodule appear as a focal disorderly collection of bile ducts and ductules surrounded by abundant fibrous stroma (Hematoxylin and Eosin A: ×100, B: ×200).

Introduction

Biliary hamartomas (BH) are rare benign malformations of the intrahepatic bile ducts which are usually multiple (also called von Meyenburg complexes) [1,2] while peribiliary gland hamartoma (PGH) is a rare benign epithelial tumor of the liver derived from bile duct cells, which is usually solitary [3]. Both lesions are usually found incidentally during surgery or at autopsy and represent the two types of intrahepatic benign bile duct proliferations [1,3,4]. We report two cases of white subcupsular liver nodules found incidentally during laparoscopic cholecystectomy which proved to be a biliary hamartoma and a peribiliary gland hamartoma.

Case Report 1

During routine laparoscopic cholecystectomy in a 38 year old male, multiple subcapsular nodules were noticed on the liver surface, which preoperative ultrasound and computed tomography failed to depict. A biopsy specimen was obtained. Histopathological examination showed small, irregular dilated ducts that are embedded in a fibrous stroma and confirmed the diagnosis of biliary hamartoma (Fig. 1A, B).

Case Report 2

During routine laparoscopic cholecystectomy in a 62-year old female, a nodule of the left lobe was noticed on the liver surface, which preoperative ultrasound failed to depict. A biopsy specimen was received. Histopathological examination showed numerous, tortuous bile ducts in a fibrous stroma with moderate chronic inflammation and established the diagnosis of peribiliary gland hamartoma (Fig. 2A–C).

Discussion

Biliary hamartomas (BH) are also known as von Meyenburg complexes, bile duct hamartomas, hepatic hamartoma, microhamartoma, cholangioadenoma, minute bile duct adenomas, multiple adenomas, adenomata, fibroadenomata and intracapsular aberrant bile ducts [5]. BH are benign biliary malformations, usually discovered during autopsy or incidentally during surgery, with an incidence between 0.6 and 5.6% [6]. BH may be located intraparenchymally or subcapsularly and are usually multiple well circumscribed small (usually less than 1 cm) focal lesions scattered throughout both liver lobes, while solitary lesions can also occur [1,5].

The pathogenesis of BH remains speculative but they are generally considered to be developmental disorders rather than true neoplasms and represent ductal plate malformation of the small interlobular ducts [1,5,6]. BH are related to other congenital disorders, including Caroli's disease, polycystic liver disease, congenital hepatic fibrosis, mesenchymal hamartomas, bile duct atresia and autosomal recessive polycystic kidney disease [5,6]. Failure of embryonic bile ducts involution is one of the most common theories while a disruptive or ischemic factor during bile duct lamina remodeling has also been proposed [1,6]. BH are divided into three classes depending on the degree of bile ducts cystic dilatation within the lesions: 1) predominantly solid, 2) intermediate lesion with both solid and cystic foci and 3) predominantly cystic [1]. BH do not seem to predispose to malignant transformation, although in a few cases there was a coexisting cholangiocarcinoma [6,7]. Also, another classification divides BH in two types: 1) BH connected to the draining bile ducts, and 2) BH without any connection to the bile ducts [8].

Macroscopically, BH are small white to green round to irregular nodules, usually well-defined but without true capsule [1,5]. Microscopical examina-

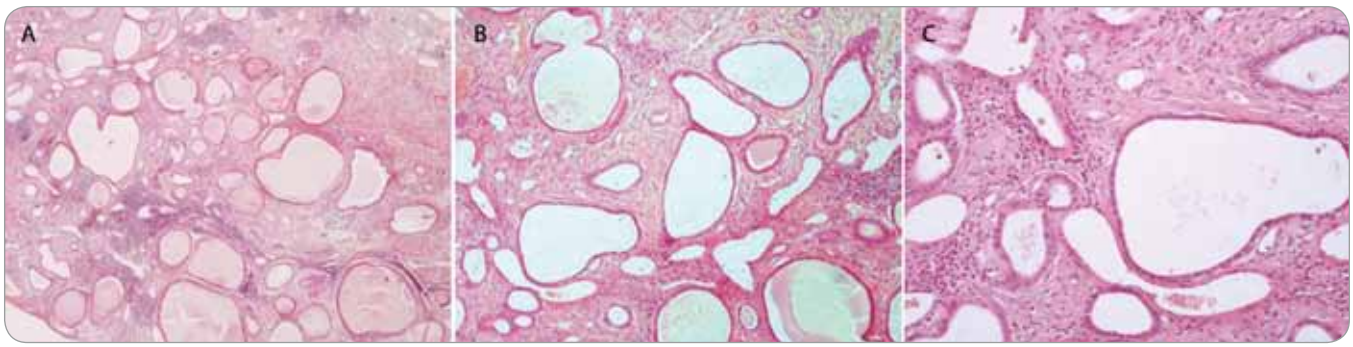

Fig. 2. A subcapsularly lesion of liver consist of dilated bile ducts with in fibrous stroma (Hematoxylin and Eosin A: ×40, B: ×100, C: ×200).

tion reveals proliferation of small irregular, disorganized or dilated, bile ducts lined by normal cuboidal to low columnar epithelium, without cellular atypia, embedded in abundant fibrocollagenous stroma containing proteinaceous fluid and sometimes inspissated bile [1,2,5,6,9]. BH in most cases do not communicate with the biliary system but communication with the normal terminal bile ducts in the adjacent portal trial can also be noted [1,5,6].

In a minority of cases, BH can be seen by imaging techniques [7]. Ultrasound of BH demonstrates small discrete hypoechoic, hyperechoic and mixed echoic nodules [1,6]. Computed tomography shows multiple irregular hypodense cystoid lesions without enhancement uniformly distributed in the liver [1,6]. Magnetic resonance imaging reveals hypointense lesions on T1-weighed images and strongly hyperintense lesions on T2 weighed images [1,2,6].

BH are almost always asymptomatic; only a few cases have been reported to cause jaundice, fever, epigastric pain and cholangitis [10]. In asymptomatic patients, no treatment or follow-up is necessary [10].

Differential diagnosis of BH includes PGH liver metastases, hepatic cysts, microabscesses, dilated bile ducts and primary sclerosing cholangitis [1,2,8].

PGH is also known as intrahepatic bile duct adenoma, cholangioma, benign cholangioma, cholangioadenoma and simply bile duct adenoma [2,11,12]. PGH is a rare benign epithelial hepatic tumor originating from bile duct cells usually discovered incidentally at autopsy or laparotomy with an incidence 1.3% [3, 11]. PGH is most commonly located on the liver surface or subcapsularly and is a well circumscribed small lesion (usually less than 1 cm) usually solitary, but may also present as multiple nodules throughout the liver [3,11,13].

The pathogenesis of PGH is still unclear but it is considered a reactive process to a focal bile ductular injury caused by trauma or inflammation rather than a true neoplasm based on immunohistochemical studies [3,11,12]. In PGH because of absence of appropriate mesenchymal epithelial signaling, the acini and tubules fail to organize into a mature gland draining into a bile duct [3,13]. PGH has benign behavior and show limited growth potential but cases of suspected malignant transformation have been reported [3,11,12].

Macroscopically, PGH is small, white to gray or tan, firm, flat or slightly elevated, well defined but without true capsule [3,11]. Microscopic examination demonstrates confluent proliferation of disorganized mature ductules and peribiliary gland acini lined by low columnar or cuboidal cells containing light colored transparent cytoplasm, without cellular atypia and with low mitotic activity, in a connective tissue stroma showing varying degrees of chronic inflammation and collegenization [3,11]. PGH does not usually invade the portal tract but in some cases portal vein and arterioles are lost [11].

PGH may not be seen by imaging techniques and is difficult to detect due to small size and peripheral location [3,11]. Ultrasound shows an echogenic nodule with or without a hypoechoic rim. Computed tomography demonstrates hyperdense areas within the lesion and magnetic resonance imaging usually reveals hypointensity in T1-weighed images and hyperintensity in T2 weighed images but hyperintensity both on T1 and T2 as well as hyperintensiity both on T1 and T2 has been reported [3,11,12]. Also, in contrast, enhanced CT and MRI PGH show delayed or prolonged enhancement [11,12].

PGH is asymptomatic and no symptoms or signs are attributed to the lesion [11]. It can occur at any age but the mean age of presentation is 55 years and presents no sex predilection or maybe a slightly male predominance [3,11].

Differential diagnosis of PGH includes BH, mesenchymal hamartoma, metastatic liver tumor, inflammatory pseudotumor, cholangiocarcinoma, hepatic abscess, hepatic granuloma, epithelioid hamangioendiotheloma and tuberculosis [3,11,12]. PGH is distinguished from BH microscopically by the lack of intraluminal bile and the compact nature of its proliferation without cystic changes [3,12]. Macroscopically, diagnosis of both lesions is difficult. An intraoperative biopsy should be performed in all cases of incidental finding during an abdominal operation, which would give the definite diagnosis.

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