Superinfection of focal liver lesions after bile duct procedures

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KEYWORDS
Liver abscess; Biliary enteric anastomosis; Bile ducts; Focal liver lesion

Abstract
Objectives: Pyogenic liver abscess is a rare condition in the general population. The source of infection is most often biliary, and more rarely gastrointestinal via the portal tract, or even hematogenic. Other than in special contexts (scarring after radiofrequency ablation), focal liver lesions are not a usual risk factor for hepatic abscesses in patients with a history of bile duct procedures ( sphincterotomy, biliary stenting, biliary enteric anastomosis).

Materials and method - results: We report four cases of focal liver lesions (two patients with benign lesions of the biliary cyst type and two other patients with lesions due to pancreatic cancer) complicated by a superinfection in patients with a history of bile duct procedures. There were no predisposing factors other than a context of cancer or diabetes.

Conclusion: Superinfection of a focal liver lesion should be considered when there is a suggestive clinical picture and a change in the appearance of the lesion in patients with a history of bile duct procedures in a context of cancer or diabetes.

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Pyogenic liver abscess is a rare condition in the general population; its incidence is approximately 10–20 cases per 100,000 [1]. It consists of a collection of pus in stratified or destroyed hepatic tissue, and its etiology—when one is found—is primarily biliary or gastrointestinal, and sometimes promoted by immunosuppression or diabetes [2]. It has
now been firmly established that abscess formation in hepatic territory that has been treated with radiofrequency ablation or chemoembolization is promoted by the presence of a biliary enteric anastomosis [3–5]. However, we have found no articles in the literature illustrating the increased risk of spontaneous superinfection of preexisting focal liver lesions due to bile duct procedures. We present four cases of liver abscesses as complications of biliary cysts or liver metastases in patients with a history of bile duct procedures.

Case studies

Case no. 1

A 68-year-old man followed for adenocarcinoma of the head of the pancreas was treated by cephalic duodenopancreatectomy and biliary enteric anastomosis. Two years later, during adjuvant chemotherapy, a metastatic lesion appeared in segment 2 and then another in segment 5, revealed by an MRI of the liver. Three months later, the patient was taken to the emergency room for morphine-resistant violent right hypochondrial pain, accompanied by an inflammatory syndrome on the laboratory work-up with a C-reactive protein (CRP) of 42 mg/L (normal range < 6 mg/L) and hyperleukocytosis of > 10,000/mmm^3. The abdominopelvic CT scan showed that the segment 5 lesion had increased in size, with liquefaction in the center (Fig. 1). An ultrasound-guided needle biopsy confirmed the infection, as the specimen contained numerous impaired polymorphonuclear leukocytes, multidrug sensitive Escherichia coli, and Streptococcus anginosus. Antibiotic therapy was adjusted based on the sensitivity testing (tazocillin, switched to a combination of amoxicillin and levofoxacin) and administered for 3 weeks, with a rapidly favorable clinical outcome.

Figure 1. Case 1. A 68-year-old man followed for pancreatic adenocarcinoma, treated by cephalic duodenopancreatectomy, with liver metastases. Abdominopelvic CT scan with injection of contrast product. Hypodense fluid-filled lesion with ring-pattern contrast uptake.

Case no. 2

A 73-year-old man underwent cephalic duodenopancreatectomy and biliary enteric anastomosis for adenocarcinoma of the head of the pancreas. The postoperative course was complicated by a pulmonary embolism and deterioration of the patient’s condition. The adjunctive chemotherapy was postponed. A follow-up abdominopelvic CT scan showed multiple hypodense hepatic images with a metastatic appearance.

The patient was admitted through the emergency room shortly afterward for marked sepsis with a fever of 40 °C, leukocytes of 40 G/L (normal range < 10,000/mm^3), and a CRP of 192 mg/L. Empirical antibiotic therapy with tazocillin and gentamycin was started immediately. The MRI of the liver (Fig. 2) clearly showed that at least two of the hepatic lesions had increased in size, and had hyperintense fluid content on T2-weighted images, and ring-pattern enhancement on the sequences following injection of gadolinium. The blood cultures were positive for Klebsiella and Enterococcus. The needle biopsy of one of the hepatic lesions corroborated both the Enterococcus superinfection and the presence of tumor cells, thus confirming the metastasis of pancreatic adenocarcinoma. The antibiotic therapy was adjusted to a combination of imipenem, vancomycin, and amikacin, which resulted in partial regression of the inflammatory syndrome (CRP 132) and apyrexia. Unfortunately, the patient progressed to cachexia and death a few weeks later.

Case no. 3

A male patient was followed for adenocarcinoma of the head of the pancreas, revealed by pruritus, deterioration of the patient’s condition, weight loss of 14 kg, and repeated septic episodes of the angiocholitis type. While awaiting the preoperative workup, a biliary stent was placed endoscopically, which improved the cholestasis and the infectious syndrome. The patient also had numerous single biliary cysts. The hepatic MRI performed during an episode of angiocholitis (Fig. 3) showed that some of the biliary cysts had changed, with a fluid/fluid level and marked peripheral contrast uptake. The CRP was initially 43 mg/L. A blood culture grew E. coli. Antibiotic therapy was initiated with amoxicillin and clavulanic acid, resulting in improvement in the patient’s condition (+6 kg) and normalization of the CRP. The clinical outcome was also favorable with antibiotic therapy, with regression of the radiologic images, a decrease in the size of the complicated cysts, and disappearance of the ring-pattern contrast uptake.

Case no. 4

A 68-year-old diabetic woman was followed for inoperable adenocarcinoma of the pancreas treated palliatively with a simple biliary enteric bypass. During the initial workup, two single biliary cysts were discovered. Chemotherapy was then initiated with Gemzar. After one line of chemotherapy, the patient was hospitalized for severe sepsis, but no portal of entry was found. The patient was febrile with a CRP of 50, but no hyperleukocytosis. The only etiological explanations were an outright change in appearance on the CT scan (Fig. 4) of one of the biliary cysts, which increased
in size, with peripheral contrast uptake, and blood cultures positive for *E. coli*. Antibiotic therapy was initiated with imipenem and amikacin. An ultrasound-guided draining procedure was performed, which produced fluid that was purulent with numerous polymorphonuclear leukocytes, but sterile, probably due to the broad-spectrum therapy that had been initiated several days earlier. After 6 weeks of treatment with imipenem, the clinical outcome was favorable, with regression of the clinical, laboratory, and radiologic picture. The follow-up CT scan after 3 weeks of treatment showed that the size of the biliary cyst had markedly regressed, but retained a thick wall.

**Discussion**

We report four cases of patients who each had a history of a bile duct procedure and experienced a septic episode associated with a hepatic abscess during follow-up. All of these infectious hepatic lesions developed with a preexisting focal liver lesion, whether benign or malignant. This type of spontaneous complication is not typical and has not reported in the literature.

The physiopathology of hepatic abscesses is well known. They are typically of biliary or gastrointestinal origin. The biliary origin is more common and caused by a lithiasic disease, endoscopic retrograde catheterization or malfunction of a biliary stent or a biliary enteric anastomosis. The abscess may also develop due to proximity, from contact with cholecystitis or, more rarely, contact with perforated diverticulitis or a tumor of the right colon. Many gastrointestinal diseases (diverticulitis, appendicitis, chronic inflammatory disease of the digestive tract, etc.) can lead to portal bacteremia followed by formation of a hepatic abscess, not to mention neoplastic lesions or colon polyps [6], which are routinely looked for by coloscopy during the infectious episode.

The radiological presentation [7,8] of such pyogenic abscesses is typically the discovery of a fluid-filled or heterogeneous multi-compartmental lesion, with peripheral

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**Figure 2.** A 73-year-old man treated by cephalic duodenopancreatectomy for adenocarcinoma of the pancreas. MRI of the liver showing the increased size of the hyperintense lesions on T2-weighted images and ring-pattern contrast uptake. MRI of the liver: a: T2-weighted axial sequence; b: T1-weighted axial sequence and fat saturation after injection of gadolinium.

**Figure 3.** A 72-year-old man treated by biliary stenting for adenocarcinoma of the head of the pancreas. MRI of the liver: T2- and T1-weighted sequence with fat saturation and injection of gadolinium. a: Increased size and fluid/fluid level of certain cysts; b: Ring-pattern contrast uptake on sequence with injection.
contrast uptake or with the characteristic "double target" sign on the rim of the abscess associated with enhancement of the healthy adjacent parenchyma due to inflammatory phenomena. The presence of air in the lesion is unusual but suggestive. On the MRI, the ADC is low, contrary to a simple cyst [9].

We report four cases where a bacterial superinfection occurred within a preexisting hepatic lesion, biliary cyst, or liver metastasis and was more difficult to diagnose both clinically and radiologically, particularly in the case of liver metastases with a necrotic center. It required the help of laboratory tests, which reflected the bacterial sepsis with neutrophilic polynucleosis, elevated CRP, and blood cultures sometimes positive for gastrointestinal microorganisms. Slice imaging studies have shown the fluid transformation of the center of the lesion and ring-pattern enhancement of their peripheral tissue portion. It was easier to identify the superinfection of a biliary cyst when there was a change in the appearance of a known cyst and its contents, as well as unusual contrast uptake by its walls. However, drainage was most often necessary in order to obtain proof of superinfection. This was presumably fostered in two cases by a course of chemotherapy and in one case by a poor nutritional state. Finally, it should be pointed out that all these patients had colonization of their biliary tract with gastrointestinal microorganisms due to the presence of either a biliary enteric anastomosis or a biliary stent.

In general, superinfection of a biliary cyst is quite rare, occurring in 1% of cases compared with a hemorrhagic complication (2–5%) [8,10], and is especially found with voluminous cysts or in patients with hepatorenal polycystic disease in whom immunosuppression is more common due to the renal failure that is often associated with it. In these patients, the origin of the superinfection is diverticulosis, a polyp, or colon cancer [11].

Abscess formation in a liver metastasis is an even rarer event nowadays and one that was the subject of articles in the literature more than 30 years ago [12]. Large series [13], especially reported superinfections of liver metastases in the presence of uncontrolled cholangitis. The current problem is rather one of making a differential diagnosis versus an area of central tumor necrosis, often associated with persistent fever. In that case, the diagnostic aspiration of the center of the lesion is decisive [14].

It is difficult not to draw a parallel with what is seen in cases of radiofrequency ablation or chemoembolization in the presence of a biliary enteric anastomosis, complicated by a liver abscess in the treated territory in 22–44% of cases [3–5]. Prescribing preventive antibiotic therapy does not completely exempt the patient from this type of complication. Furthermore, the risk of superinfection of a scar from radiofrequency ablation or chemoembolization outside of such a context is very low (approximately 0.2–1.9% [3,4,15–18]. Likewise, the (risk of) formation of an isolated hepatic abscess in the presence of a biliary enteric anastomosis or biliary drain does not exceed 10% (between 0.1 and 7% of cases) [19–21]. The suspected physiopathology is ischemic necrosis of the hepatic parenchyma in contact with the focus of destruction of tissue and bile ducts, almost always with bacterial colonization, whether after a sphincterotomy [22], biliary enteric anastomosis [23], or biliary stenting [24]. It is therefore legitimate to think that it is this mechanism that was at cause in our four clinical cases, promoting development of bacterial colonization in the vulnerable hepatic parenchyma, in a context of immunosuppression and impaired general health.

**Conclusion**

Chronic contamination of the bile ducts by gastrointestinal microorganisms in patients with a history of a bile duct procedure (biliary enteric anastomosis, biliary stenting, wide sphincterotomy, etc.) is a risk factor that promotes the occurrence of hepatic abscesses, and that risk is multiplied.
by a factor of 3 or 4 after hepatic radiofrequency ablation or chemoembolization. Superinfection of benign or malignant focal liver lesions (biliary cysts, metastases, etc.) has rarely been reported but should be considered in case of sepsis and a change in the appearance of the lesion in question in this type of context, especially when there is a decline in the immune defense, such as in patients with diabetes or treated with chemotherapy.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References