Gastrointestinal

Mucinous carcinoma of the gallbladder with signet ring cells

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ABSTRACT

Most gallbladder carcinomas are adenocarcinomas, of which mucinous carcinoma (MC) is a rare pathologic subtype. Signet ring cells are seldom found in MCs. We report an extremely rare case of gallbladder MC with signet ring cells. This is the first radiological case report about this rare type of histologic entity with detailed discussion of imaging findings in the English literature. In addition to the features of MC, linitis plastica-like invasion, which is the key feature of signet ring cells, was confirmed by both imaging and histopathologic analysis. Furthermore, radiologists should know how the imaging findings of MC differ from those of other major subtypes of adenocarcinoma, as there is a risk of delays in diagnosis and underestimation of tumor spread.

Introduction

Gallbladder carcinoma is the most common type of tumor of the biliary tract, and adenocarcinoma is its dominant histologic type. Mucinous carcinoma (MC) is a rare pathologic subtype of adenocarcinoma, with stromal mucin deposition constituting >50% of the tumor necessary for its diagnosis [1]. MC accompanied by signet ring cells is extremely rare. The prognosis of patients with MC is considered to be very poor if poorly differentiated signet ring cells are dominant [2]. Radiological investigations are valuable for diagnosis of gallbladder carcinoma, but no previous reports in the English literature have discussed the details of imaging gallbladder MC with signet ring cells.

Case report

A 70-year-old woman with early-stage bladder cancer underwent a computed tomography (CT) examination for metastatic workup. There was local wall thickening in the fundal portion of the gallbladder and nodular calcification, which we suspected as being fundal-type adenomyomatosis and a gallbladder...
stone. Cystectomy was performed without any adverse events. Eleven months after imaging, although the patient had no symptoms or abnormal physical findings, a blood test revealed elevated levels of aspartate aminotransferase (95 IU/L), alanine aminotransferase (89 IU/L), alkaline phosphatase (2209 IU/L), and γ-glutamyl transpeptidase (587 IU/L).

Abdominal sonography showed a dilated intrahepatic biliary tract and calcification of the gallbladder wall. As a result of the calcification, it was not possible to observe the structure of the wall or the inside of the gallbladder. Dynamic contrast-enhanced CT revealed bilateral intrahepatic bile duct dilatation and remarkable calcification along the gallbladder wall. Although no obvious enhanced lesion was present in the gallbladder, a low-density nodule with slight calcification in the adjacent liver parenchyma suggested direct invasion by a gallbladder lesion (Fig. 1). There was a low-attenuating lobulated mass with calcification in the porta hepatitis and parapancreatic head area that was similar to the gallbladder lesion; lymph node metastasis was suspected (Fig. 2). T2-weighted imaging (T2WI) showed a hypointense, thickened gallbladder wall, consistent with calcification; the gallbladder lumen was hypointense-isointense on T1-weighted imaging (T1WI) and exhibited a heterogeneous hyperintensity on T2WI (Fig. 3A and B). Diffusion-weighted imaging showed that the lesion had a heterogeneous hyperintensity (Fig. 3C). Lymph node metastasis also showed as a hypointensity and hyperintensity on T1WI and T2WI, respectively.

Fine-needle aspiration biopsy was performed on the parapancreatic head lymph nodes, and signet ring cells were revealed. Although chemotherapy was initiated, the side effects were too severe for continuation of the regimen. Five months later, a CT scan revealed tumor invasion extending into the hepatic parenchyma and spread along biliary tract (Fig. 4). Peritonitis carcinomatosa was also revealed by CT. The patient died a few days after the final CT examination, and an autopsy was performed.

On macroscopic examination, the gallbladder was stiff and strongly adherent to the liver. The gallbladder lumen was occupied by a yellowish tumor, which had directly invaded the liver parenchyma. Tumor invasion was also found along the biliary tract (Fig. 5A). The microscopic structure of the gallbladder wall was destroyed by tumor invasion, and thick calcification was present. The tumor mainly consisted of abundant mucin and necrotic tissue, with tumor stroma spreading as a lattice structure, consistent with MC. Signet ring cells were evident and appeared to be floating in the mucous lake (Fig. 5B and C).

**Discussion**

The most common histologic type of gallbladder carcinoma is adenocarcinoma, which comprises 90% of all gallbladder carcinomas [3]. There are several histopathologic variants of adenocarcinoma, including the papillary, mucinous, squamous, and adenosquamous subtypes. Recent reports have indicated that MC is rare, comprising only 2.5%-5.5% of gallbladder carcinomas [3–5]. Stromal mucin deposition constituting >50% of the tumor is necessary for a diagnosis of MC [1]. Recently, the prevalence of signet ring cells among MC case has been reported as 33% [4]. Therefore, the present case is extremely rare pathologically. The prognosis of patients with MC is very poor if poorly differentiated signet ring cells are dominant [2]. There are no previous reports in the English literature on the details of imaging MC with signet ring cells.

Previous studies of MC have mainly been case reports, and imaging findings have varied [6–14]. Abdominal sonography has shown the tumor as a heterogeneous echogenic mass that results from calcification, necrosis, and the mucinous component. CT examination has shown focal or diffuse gallbladder wall thickness with water-like attenuation, reflecting the presence of mucin and necrosis. This finding is close to the...
corresponding one for adenomyomatosis, which involves cyst-like spaces in a thickened gallbladder wall. A previous review of gallbladder carcinoma stated that CT showed a poorly differentiated MC as a hypoattenuating mass in the gallbladder fossa with extension into the adjacent liver [14]. With the administration of contrast medium, MC exhibits no or weak enhancement during the delayed phase. Enhancement occasionally involves a septal structure that runs along the tumor stroma. In the present case, we could not find any enhanced areas in the tumor because the presence of abundant mucin and the reduced tumor stromal volume limited enhancement. Alternately, the thick calcification may have prevented detection of enhancement in the lesion. Calcification can be found in some instances of MC; because it occurs in the low-attenuation thickened gallbladder wall, it may mimic a gallbladder stone accompanied by adenomyomatosis [12]. Few studies have described magnetic resonance findings involving MC, but the tumors have been reported to appear hypointense on T1WI and show heterogeneous hyperintensity on T2WI [6]. These findings are consistent with the present case: the mucinous component seems to be responsible for this unique intensity. Here, diffusion-weighted imaging showed a hyperintense tumor appearance with high signal intensity on the apparent diffusion coefficient map.

Fig. 2 – Dynamic-enhanced computed tomography (CT) scan at the level of porta hepatis: precontrast (A) and delayed phase (B). Bilateral intrahepatic bile duct dilatation is present. There are multiple lymph node metastases accompanied by calcification in the porta hepatis (arrows).

Fig. 3 – Magnetic resonance imaging (MRI) at the level of gallbladder body: On T1-weighted imaging (T1WI) (A), the gallbladder lumen appears hypointensity to isointensity. On T2-weighted imaging (T2WI) (B), the gallbladder wall shows hypointensity that reflects the presence of calcification, and gallbladder lumen shows heterogeneous hyperintensity. The invasive lesion in the hepatic parenchyma shows a similar intensity to that of the gallbladder lumen (arrow). Diffusion-weighted image (C) of the lesion shows heterogeneous high intensity (arrow).

Fig. 4 – Non-contrast-enhanced computed tomography (CT): There is obvious tumor expansion and spread of calcification along Glisson’s sheath. A biliary tube is located in the biliary duct (arrow head).
A previous case report indicated that the features of signet ring cell carcinoma include linitis plastica-like invasion and poor prognosis [15–19]. In the present case, circumferential invasion of the gallbladder wall spreading along biliary tract suggested a signet ring cell component of MC.

In conclusion, the imaging features of MC, which shows a similar attenuation/intensity to bile and poor enhancement, may delay diagnosis and cause underestimation of tumor spread. When the gallbladder shows calcification, it is necessary to consider not only the possible presence of a gallstone but also that the calcification may be tumor-related. At the same time, linitis plastica-like invasion may suggest a signet ring cell component, which confers a very poor prognosis.

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Fig. 5 – (A) Photograph of a section of the gallbladder: The yellowish tumor occupies the gallbladder lumen (*). There is direct invasion into the liver parenchyma (black arrow) and tumor spread along the biliary tract is evident (white arrow). (B) Microscopic findings: Abundant mucin and necrosis are the main components. Some calcification is present (original magnification ×40; hematoxylin-eosin). (C) Signet ring cells can be seen floating in the mucus lake (original magnification ×400; hemotoxylin-eosin).
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