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CORRELATIVE IMAGING IN GALLBLADDER CARCINOMA

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Gallbladder carcinoma is a relatively rare malignant epithelial neoplasm, arising from gallbladder mucosa. It is the fifth most common gastrointestinal malignancy and the most common biliary tract cancer. Early diagnosis remains difficult, because clinical symptoms are sparse and non-specific, often resulting in advanced stage disease at the time of diagnosis. The most common feature of gallbladder carcinoma on different imaging modalities is focal wall thickening, associated with a large eccentric tumor mass. In this case we report the imaging characteristics of gallbladder carcinoma on ultrasound, MDCT and ^{18}F-FDG PET/CT.

Key-word: Gallbladder, neoplasms.

Gallbladder carcinoma (GBCA) is a relatively rare malignancy with bad prognosis. Is was first described in 1777 by deStoll (1), and is the most common malignant neoplasm of the biliary tract and the fifth most common gastrointestinal cancer. Patients with GBCA have usually advanced disease at the time of diagnosis. GBCA is associated with porcelain gallbladder and chronic inflammation, secondary to gallstones. Ultrasonography is often the first step to the diagnosis. CT and MRI are used for further characterization of the gallbladder lesions and metastatic survey. ^{18}F-FDG PET/CT is useful in diagnosing ambiguous primary lesions, uncovering distant disease and detecting residual disease after cholecystectomy. In this report, we present these imaging findings in 4 patients with gallbladder carcinoma.

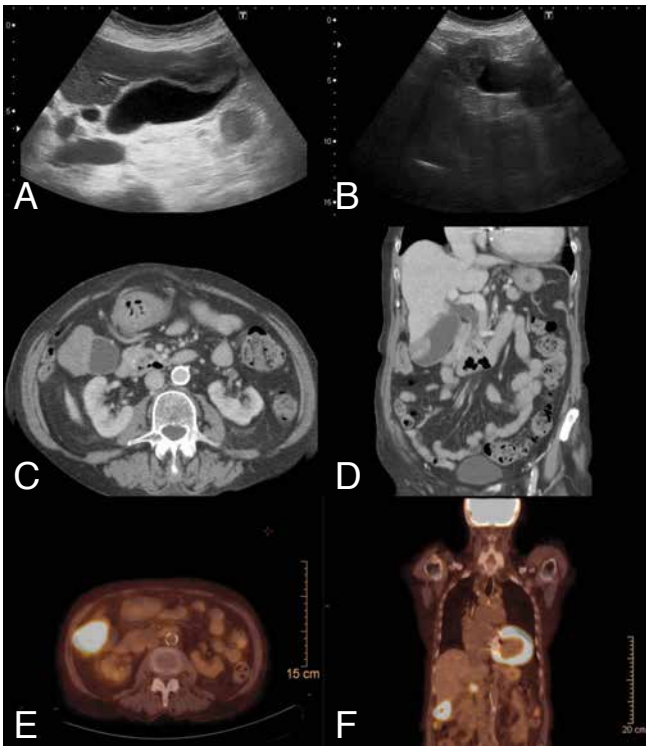


Fig. 1. — Sagittal (A) and coronal (B) ultrasound image reveals a hypoechogenic mass adjacent to the wall of the gallbladder. Axial (C) and coronal (D) multiplanar reformatted computed tomography images after IV contrast injection displays a contrast-enhancing mass adjacent to the wall of the gallbladder, with possible local invasion of the liver parenchyma. Axial (E) and coronal (F) FDG-PET/CT images show a solitary hypermetabolic focus at the fundus of the gallbladder, corresponding to the contrast-enhancing mass adjacent to the wall of the gallbladder.

Case reports

An 82-year-old woman was admitted to our hospital with congestive heart failure. Abdominal history included diverticulosis, diverticulitis, cholangitis, pancreatitis, and a partial colectomy for an ileocaecal adenoma. Seven years earlier, there was an increased CA19.9 without signs of malignancy on ^{18}F-FDG PET/CT or US-endoscopy. The patient had no abdominal pain. Physical examination revealed a flexible abdomen with normal peristalsis. Blood sample demonstrated increased levels of alkaline phosphatase, gamma-glutamyl transferase, lactate dehydrogenase (LDH), and lipase. Abdominal ultrasound (Fig. 1A and B) revealed a hypoechogenic mass adjacent to the gallbladder wall. This finding was further investigated by CT. A contrast-enhanced (80 cc non-ionic iodinated contrast medium, Ultravist®, Bayer HealthCare Pharmaceuticals) multidetector CT scan of the abdomen (Fig. 1C and D) demonstrated a suspicious, contrast-enhanced mass adjacent to the wall of the gallbladder and possibly locally invading the liver. Non-contrast enhanced ^{18}F-FDG PET/CT (Fig. 1E and F) confirmed a mass lesion with hypermetabolic characteristics at the fundus of the gallbladder and suggested local invasion of the liver parenchyma. Surgery was no option due to the important comorbidity of the patient. Palliative chemotherapy was pro-

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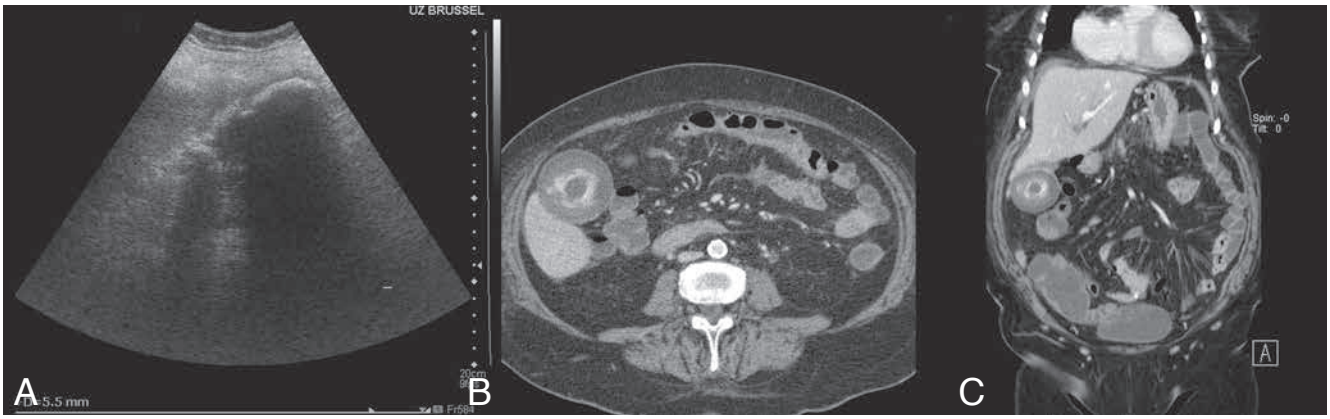


Fig. 2. — Ultrasound (A) image shows an enlarged gallbladder with thickened wall and gallstones. Axial (B) and coronal (C) multiplanar reformatted computed tomography images after IV contrast injection displays a hydrops of the gallbladder with thickening of the wall and enclosed gallstones. One of the gallstones is impacted in the neck of the gallbladder. The liver is surrounded by free fluid. An acute cholecystitis was diagnosed.

posed, if the patient would become symptomatic due to tumor progression. Follow-up was organized, and two years later the patient died due to cardiovascular disease.

An 83-year-old woman was admitted to the emergency department of our institution with abdominal pain since 10 days, fever and hypotension. The pain was initially continuous and located in the right hypochondrium, subsequently migrating to the right fossa region. Medical history included gastric ulcers, gallstones, diverticulosis, chronic renal insufficiency, and appendectomy. Physical examination revealed a tense, diffusely sensitive abdomen. Blood sample demonstrated increased levels of C-reactive protein, alkaline phosphatase, gamma-glutamyl transferase, and lipase. Abdominal ultrasound (Fig. 2A) revealed an enlarged gallbladder with thickened wall and gallstones. The gall A contrast-enhanced (80 cc nonionic iodinated contrast medium, Ultravist®, Bayer HealthCare Pharmaceuticals) multidetector CT scan of the abdomen (Fig. 2 B and C) confirmed a hydrops of the gallbladder with thickening of the wall and enclosed gallstones. One of the gallstones is impacted in the neck of the gallbladder. The liver is surrounded by free fluid. An acute cholecystitis was diagnosed. A laparoscopic cholecystectomy was performed. Pathological analysis revealed an adenocarcinoma of the gallbladder. Due to the chronic renal insufficiency, chemotherapy could not be started. Two weeks after surgery the patient died due to septicemia.

An 80-year-old woman was admitted to the nuclear medicine department of our hospital for a follow up of a carcinoma of the anal canal. Abdominal history included a squamous cell carcinoma of the anal canal treated by abdominoperineal resection and radiotherapy and an appendectomy. The patient had no abdominal pain. Physical examination revealed a painless abdomen with normal peristalsis. Contrast enhanced ^{18}F-FDG PET/CT (Fig. 3A, B, C and D) showed a mass lesion with hypermetabolic characteristics at the gallbladder with invasion of the liver. Diagnosis of a solitary metastasis was suggested and a partial hepatectomy with resection of the gallbladder was performed. Pathological analysis revealed a primary gallbladder carcinoma. Adjuvant chemotherapy was initiated and during one year follow-up, a liver metastasis of the gallbladder carcinoma was diagnosed and treated by radiofrequency ablation.

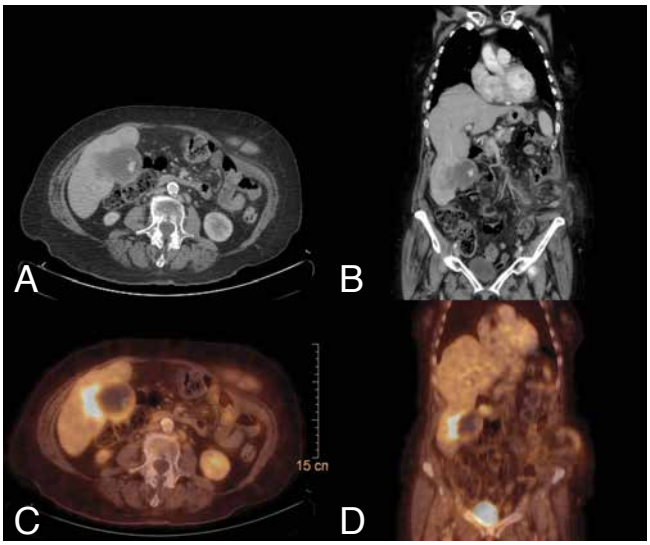


Fig. 3. — Axial (A, C) and coronal (B, D) FDG-PET/CT images show a mass lesion with hypermetabolic characteristics at the gallbladder with invasion of the liver.

A 65-year-old woman was admitted to our hospital with progressive dyspnea. Medical history includes arterial hypertension, choledocolithiasis treated by sphincterotomy and stenting, and diabetes with a recent leg amputation (4 months ago). Blood sample showed increased inflammatory markers and liver enzyme values. A chest X-ray demonstrated bilateral pleural effu-

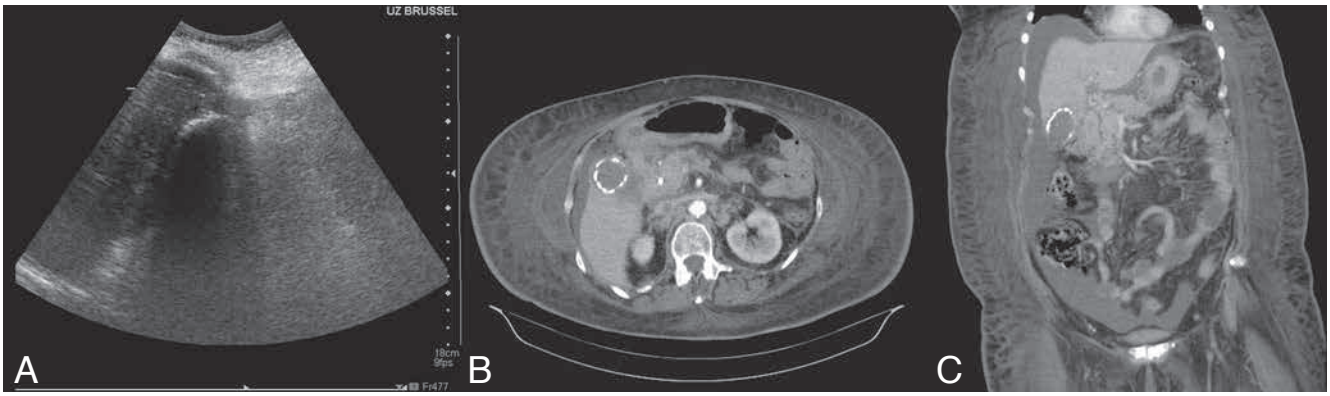


Fig. 4. — Ultrasound (A) image shows a porcelain gallbladder. Axial (B) and coronal (C) multiplanar reformatted computed tomography images after IV contrast injection displays a porcelain gallbladder, a hypodense liver lesion, abdominal and retroperitoneal adenopathies, peritoneal metastases, and ascites.

sion. A pleural puncture showed a chylothorax with metastatic cells. Additional blood samples showed an elevated CA 125 level. Abdominal ultrasound (Fig. 4A) showed a porcelain gallbladder. Further investigation by contrast-enhanced (80 cc non-ionic iodinated contrast medium, Ultravist®, Bayer HealthCare Pharmaceuticals) multidetector CT scan of the abdomen (Fig. 4B and C) confirmed a porcelain gallbladder, a solitary hypodense liver lesion, abdominal and retroperitoneal adenopathies, peritoneal metastases, and ascites. The patient died 15 days after hospitalization. Autopsy established macroscopically a gallbladder filled with gallstones. The wall was thickened and contained a mass with central necrosis. Microcopy confirmed the presence of a gallbladder carcinoma.

Discussion

Gallbladder carcinoma is a relatively infrequent neoplasm in most Western countries. The most common incidence rates have been reported in women from India, Chile, Pakistan and Ecuador. GBCA is up to 3 times higher among women than men (2).

GBCA is found incidentally in 1-3% of cholecystectomy specimens and in 0.5%-7.4% of autopsies (3).

Gallstones are identified as the major risk factor, being present in 60% to 90% of cases (4). Obesity is also associated with an increased risk of GBCA (5). A strong association has been described with mixed bacterial and Salmonella infections (6) and porcelain gallbladder (7). Anomalous pancreatobiliary ductal junction (APDJ) is a rare congenital anomaly considered to be an etiological factor in the development of GBCA, especially in young women without stones (8).

The clinical presentation of GBCA remains unspecific and may include abdominal pain, weight loss, fever, and jaundice (9).

Sonography is often the first imaging technique (10). CT and MRI are widely used for further characterization of potentially malignant gallbladder lesions and metastatic survey (11). At any of these imaging techniques, GBCA may appear as a mass completely occupying or replacing the gallbladder lumen (40-65%), a focal or diffuse asymmetric gallbladder thickening (20-30%), or an intraluminal polypoid lesion (15-25%) (12).

The mass appears on US as a heterogeneous, predominantly hypoechoic tumor. Anechoic foci of trapped bile or necrotic tumor can be present, as well as echogenic shadowing from gallstones, porcelain gallbladder, or tumor calcifications (13).

GBCA are usually hypodense on unenhanced CT, with up to 40% of lesions showing hypervascular foci of enhancement equal to or greater than that of liver after IV contrast administration (14).

On MRI, GBCA usually shows hypo- to isointense signal characteristics on T1-weighted and moderately hyperintense signal characteristics on T2-weighted sequences. On CT and MRI, intense irregular enhancement may occur at the periphery during early arterial phase. During portal venous and delayed phases, contrast enhancement may be retained in fibrous stromal components (12).

At ^{18}F-FDG PET, an intense tracer accumulation in the region of the gallbladder suggests malignancy, although this lacks specificity in distinguishing GBCA from other malignant lesions (15).

MDCT has an accuracy of up to 84% in determining the local extent (T staging) of GBCA (16) and 85% in predicting resectability (17). MRI with cholangiographic and contrast-enhanced arterial and portal phase 3D angiographic images may be up to 100% sensitive for bile duct and vascular invasion, but only only 67% sensitivity for hepatic invasion and 56% for lymph node metastases (18).

In patients with suspected GBC, depending on the disease stage, open surgical resection is appropriate. Adjuvant combination chemotherapy and molecular targeted therapy are emerging as therapeutic options in those with advanced GBC (19).

The poor prognosis associated with GBC is mainly related to advanced stage of disease at diagnosis, which is mainly due to the vague and non-specific clinical symptoms.

Conclusion

Gallbladder carcinoma is a relatively rare type of cancer, associated with a poor prognosis, related to the advanced tumor stage at diagnosis. Advances in radiological imaging have aided early detection and accurate staging of the tumor.

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