

## Gallbladder adenosquamous cell carcinoma: Report of two Cases

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### Abstract

Adenocarcinoma is the usual histological presentation of the very rare gallbladder carcinoma. Adenosquamous cell carcinoma accounts for less than 3.5% of gallbladder carcinomas, and is characterised by invasive growth, a reduced tendency for lymph node metastasis, an increased tendency for hepatic infiltration or liver metastasis, and a poorer prognosis than adenocarcinoma. We present two cases. The first patient presented to our institution with increased bilirubin levels and dilated intra- and extrahepatic bile ducts. Adenosquamous carcinoma of the gallbladder was diagnosed on the post-operative pathological specimen. After surgery, bilirubin levels decreased, but hepatic metastases occurred that did not respond to conventional chemotherapy. The second patient was admitted to our hospital with jaundice and abdominal pain. Abdominal computed tomography (CT) imaging showed marked thickening of the gallbladder with direct extension of a mass into the left liver lobe. Cytology specimens obtained with an endoscopic retrograde cholangiopancreatography (ERCP) procedure revealed a malignant epithelial tumour. The patient underwent surgery but the tumour was incompletely resected. A regimen of oral UFT (Tegafur + uracil) chemotherapy was begun. Serum bilirubin levels increased due to occlusion in the surgical area 15 weeks after the start of chemotherapy (*Acta gastroenterol. belg.*, 2005, 68, 440-442).

**Key words :** Gallbladder neoplasms, adenosquamous carcinoma.

### Introduction

Primary carcinoma of the gallbladder, first described by Stoll of Vienna 1777 (1), is an uncommon gastrointestinal malignancy that has a very poor prognosis with a mortality rate approaching 100% and a median survival of 6 months (2,3). These tumours represent the fifth or sixth most-frequent malignancies of the gastrointestinal tract. Despite dramatic advances in radiological imaging techniques of the abdomen, primary malignant tumours of the gallbladder are generally diagnosed late and often only during surgical exploration. About 5% are squamous cell carcinoma or have adenosquamous differentiation (4-5). We present 2 cases of adenosquamous cell carcinoma of the gallbladder.

### Case 1

A 60-year-old man presented to our institution with new-onset fatigue and painless jaundice. Physical examination revealed no hepatomegaly or ascites. Medical history revealed that 25 years ago, he had been treated for a duodenal ulcer with Billroth-I antrectomy and gastrojejunostomy. Abdominal ultrasonography (USG) showed dilated intra- and extrahepatic biliary ducts. His

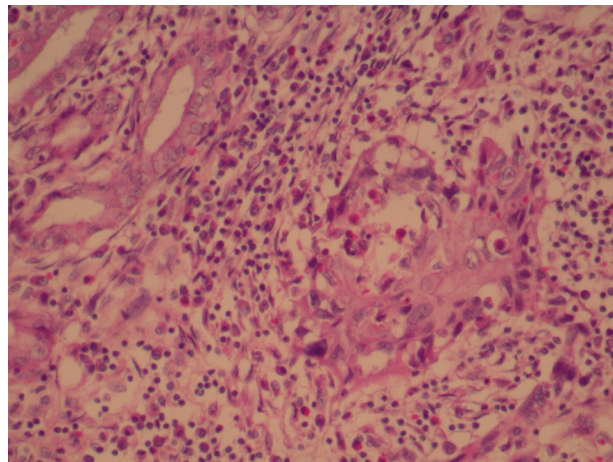


Fig. 1. — The tumour composed of a mixture of atypical glandular and squamous components (H&E  $\times$  200).

serum transaminase levels were increased, total and direct bilirubin levels were 8.8 and 7.6 mg/dl. An endoscopic retrograde cholangiopancreatography (ERCP) procedure could not be successfully performed owing to the prior gastric operation. Surgical intervention was performed, and a 1-cm mass in the gallbladder, invading the ductus cysticus and ductus choledochus, was seen. The gallbladder and main bile ducts were resected, and a Roux-Y hepaticojejunostomy procedure was performed. Pathologic evaluation showed moderately differentiated adenosquamous carcinoma of the gallbladder that extended into the ductus choledochus (Fig. 1). Serosal involvement and multiple gallstones were present. Total bilirubin level increased to 20 mg/dl just before surgery and decreased to 1.6 mg/dl after surgery. Systemic chemotherapy consisting of 5-fluorouracil (425 mg/m<sup>2</sup>) plus folinic acid (20 mg/m<sup>2</sup>) for 5 days every 28 days was started. Abdominal USG before the chemotherapy revealed a 2.5-  $\times$  3-cm single liver metastasis; however, there were multiple metastatic lesions after 3 courses of chemotherapy. The patient's disease was considered unresponsive to chemotherapy and palliative treatment was planned.

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## Case 2

A 50-year-old man was admitted to our institution with complaints of jaundice, fatigue, and right upper-quadrant and epigastric pain of 2 weeks' duration. On physical examination, the patient had right upper-quadrant pain and his scleras were icteric. The patient had type 2 diabetes mellitus and hypertension. His serum total and direct bilirubin levels were 10.1 and 8.0 mg/dl, and his serum transaminase levels were increased. Abdominal USG showed dilated intrahepatic bile ducts. CT imaging revealed marked thickening of the gallbladder with direct extension into the left liver lobe (Fig. 2). An ERCP procedure was performed, and cytological

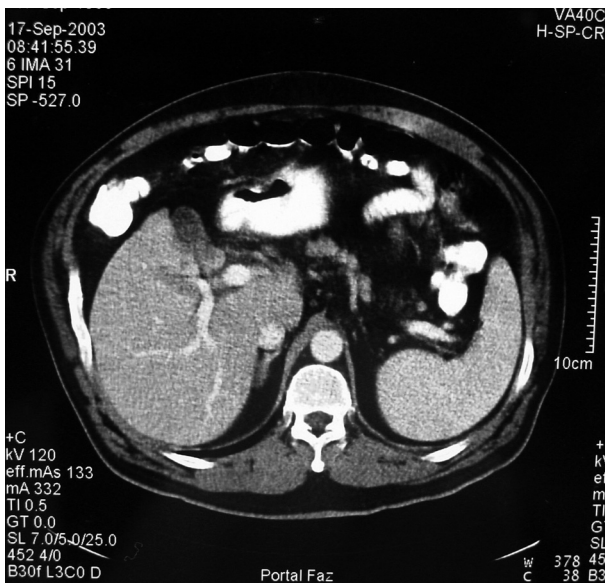


Fig. 2. — Abdominal CT scan : Marked thickening of the gallbladder with direct extension into the left liver lobe.

specimens were obtained from ductus choledochus. Histological diagnosis was a malignant epithelial tumour. The patient underwent cholecystectomy and wedge resection of left liver lobe. Histopathological diagnosis was a moderately differentiated adenosquamous carcinoma of the gallbladder (Fig. 3). Residual tumours were present in resected liver and ductus choledochus specimens. A percutaneous external drainage catheter was placed into main bile duct. A chemotherapy protocol of UFT (Tegafur plus uracil) 300 mg/m<sup>2</sup> for 5 days every week was initiated 4 weeks after surgery. Total serum bilirubin level was 2.82 before chemotherapy. Serum bilirubin levels and tumour markers (CEA and CA 19-9) were increased 15 weeks later, and chemotherapy was stopped due to tumour progression. CT scan showed no residual mass, but cholangiography showed occlusions and leakage in the bile ducts that had been operated on.

## Discussion

Gallbladder cancer is up to three times more common among women than it is in men in all populations. There

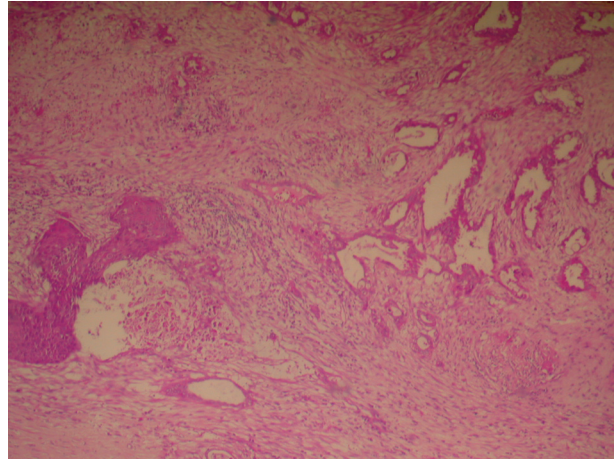


Fig. 3. — Microphotograph showing both glandular and squamous components of adenosquamous carcinoma of the gallbladder (H&E × 100).

is a prominent geographic variability in the incidence of gallbladder cancer, which correlates with the prevalence of gallstones. Populations with the highest incidences are Chileans, Bolivians, North American Indians, Mexican-Americans, and Central Europeans, all of who also have a high prevalence of cholelithiasis. The rates are highest in people from La Paz, Bolivia (11.5 per 100,000 persons) and lowest in the United States and the United Kingdom (approximately 1.2 cases per 100,000 persons). Incidence peaks in the seventh decade of life (5). Patients with gallbladder carcinoma may present with abdominal pain, jaundice, weight loss, anorexia, nausea, and vomiting, or they may be asymptomatic. Both of our patients were men who presented with jaundice.

The aetiologies of gallbladder cancer remain unknown. However, several factors associated with the disease deserve comment. Gallstones frequently accompany gallbladder cancer. Three fourths of all patients with a diagnosis of cancer of the gallbladder have cholelithiasis, suggesting that gallstones may play a causal role (2,3,6). One of our patients had gallstones.

Most carcinomas of the gallbladder are adenocarcinomas. The incidence of adenosquamous cell carcinoma of the gallbladder is extremely low. In a series by Yamaguchi and colleagues (7), 2 of 31 (6%) patients had adenosquamous carcinoma. Henson and co-workers reported 95 (3.5%) cases of adenosquamous carcinoma in a review of 3038 gallbladder carcinoma cases during a 10-year period (4).

Adenosquamous cell carcinoma of the gallbladder, although rare, is characterised by invasive growth, a reduced tendency for lymph node metastasis, an increased tendency for hepatic infiltration or liver metastasis, and a poorer prognosis than adenocarcinoma (4-7). Survival of patients with surgically resected adenosquamous carcinoma was shorter than those with papillary and well differentiated adenocarcinomas (mean : 10 months versus 99 and 86 months respectively)(8). In general, the

results of surgery, radiation therapy, and chemotherapy were disappointing and the treatment of choice remains palliation (2,3,6). Patients' outcome might only be improved by radical R0 surgical resection if possible (9).

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