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PRIMARY POORLY DIFFERENTIATED SQUAMOUS CELL CARCINOMA OF THE GALLBLADDER: RARE CLINICAL PRESENTATION

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Abstract

Squamous cell carcinoma of the gallbladder (SCC) is a rare histological subtype, accounting for less than 2% of all gallbladder carcinomas. It is most often diagnosed in an advanced stage due to non-specific symptoms, infiltrative growth, and early locoregional invasion. Early recognition of infiltration and biliary obstruction is crucial for surgical planning.

We present a patient with right upper quadrant abdominal pain for a couple of months. Contrast-enhanced CT of the abdomen revealed an irregularly thickened gallbladder wall with a mass formation and pronounced pericholecystic infiltration. Loss of the boundary towards segment VI of the liver was noted, suggesting local invasion.

The patient underwent surgical treatment. Intraoperatively, extensive tumorous infiltration was identified, tumour mass within segment VI of the liver and compressing the extrahepatic bile ducts. A radical cholecystectomy with wedge hepatic excision and dissection of the hepatoduodenal ligament was performed. Due to the involvement of the choledochus, it was ligated, and a hepatojejunostomy T-L was performed with a smooth operative and postoperative course. Pathological examination is the gold standard for the diagnosis of squamous cell carcinoma. Tumor tissue showed specific microscopic features of squamous differentiation, which are distinct from the more common adenocarcinoma. Immunohistochemistry is the technique that uses specific markers to confirm the diagnosis and rule out other types of cancer. In our case, the tumor cells were positive for CKAE1/AE3 and p63.

Keywords: gallbladder carcinoma, CT diagnostics, squamous cell carcinoma, immunohistochemistry, biliary obstruction.

Introduction

Squamous cell carcinoma of the gallbladder (SCC) is a rare histological subtype, accounting for less than 2% of all gallbladder carcinomas. SCC is characterized by the presence of keratinizing malignant squamous cells and typically lacks glandular differentiation. The pathogenesis of gallbladder SCC remains unclear, but chronic inflammation, often associated with long-standing cholelithiasis, porcelain gallbladder, or recurrent infections, is believed to play a central role in promoting squamous metaplasia and subsequent malignant transformation. Gallbladder SCC is often aggressive and is mostly diagnosed in an advanced stage due to non-specific symptoms (right upper quadrant pain, weight loss, or jaundice), infiltrative growth, and early locoregional invasion. Early recognition of infiltration and biliary obstruction is crucial for surgical planning[1-3].

Due to its rarity, optimal diagnostic strategies and management approaches are not well established, and current treatment guidelines are largely extrapolated from those for gallbladder carcinomas. Reporting individual cases is therefore essential to improve understanding of their clinical behavior, radiologic characteristics, histopathologic features, and treatment outcomes[2-9].

Here, we present a very rare case of squamous cell carcinoma of the gallbladder in a 71-year-old male patient.

Case Presentation

The following text presents a rare case of squamous cell carcinoma of the gallbladder in a 71-year-old patient with infiltration into the liver and extrahepatic biliary ducts.

A 71-year-old male patient was admitted to our department for elective operative treatment with the following symptoms: pain under the right costal arch for a period of 3-4 months, intermittent and progressive.

On physical examination, there was mild painful sensitivity upon palpation under the right costal arch, a slightly enlarged liver, but no jaundice (icterus) at the initial examination. A series of investigations were performed: laboratory analyses, abdominal ultrasound (ECHO), and CT of the abdomen with intravenous contrast.

Laboratory Results: CRP 20mg/L - moderately elevated, LDH 267 U/L; other parameters were without significant deviation.

ECHO Finding: The gallbladder towards the fundus had an irregular, infiltrated wall. There was no clear boundary between this part of the gallbladder and the surrounding liver parenchyma.

Thick sludge was present in the lumen. There was no dilation of the biliary pathways.

Contrast-Enhanced Abdominal CT: The gallbladder wall was followed with irregular contours that attenuated on the post-contrast series. The changes are highly suspicious for neo-infiltration,

involving the surrounding hepatic parenchyma in the projection of the VI segment. Blurring of the perihepatic fatty tissue was observed, which somewhat affects the wall of the hepatic flexure, but without infiltration. Lymph nodes up to 7mm were followed paracolic.(Figure 1-4)

Following appropriate preoperative preparation, the patient underwent right subcostal laparotomy.

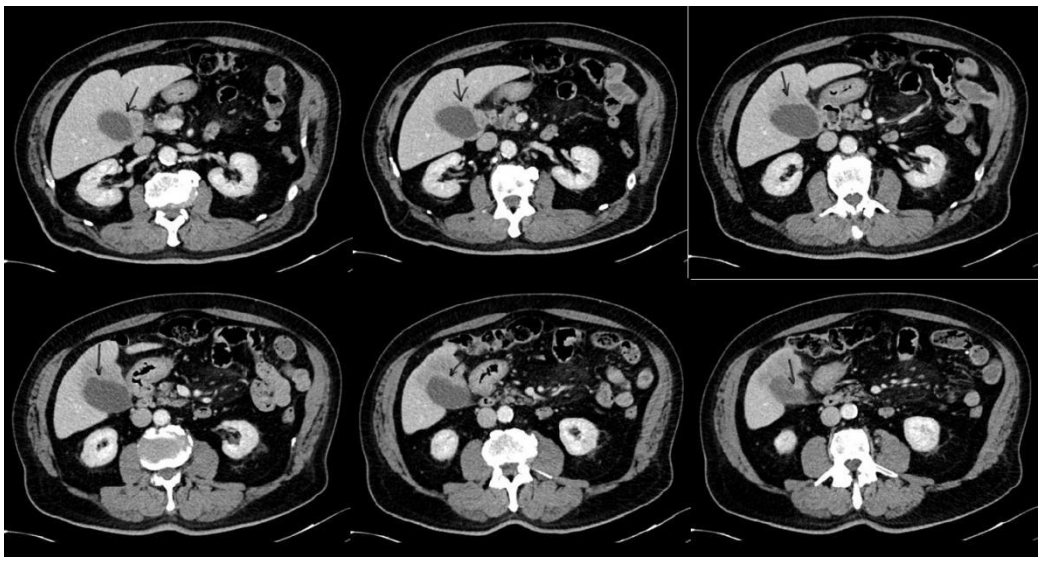

Figure 1-6. Display of the thickened wall of the gallbladder and tumor in the liver's VI segment

Operative Finding: Cholecystectomy with a wedge excision of the liver was performed. Due to the involvement of the choledochus, it was ligated, and a hepatojejunostomy T-L was performed. Systemic lymphadenectomy was performed. Two drains were placed, subhepatic and Douglas. The wound was closed in layers. The intraoperative course was uneventful, without complications. The patient was in good general condition post-surgery. The postoperative course was regular. The patient recovered well, without complications. He was discharged home in good health after a 7-day hospital stay.

The surgical specimen was a gallbladder measuring 10x6x3cm with a thickened wall up to 2,3cm. There was a whitish tumor in the fundus measuring 6x2.3x1 cm with wall infiltration and serosa penetration. The liver excision weighed 66.8g and measured 12x4x1,5 cm with tumor mass measuring 5,5x3,5x2 cm. The histology analysis revealed poorly differentiated squamous cell carcinoma with an infiltrative pattern

involving the whole wall thickness. (Figure 7A). Key features included large, polygonal malignant cells with abundant eosinophilic cytoplasm, large nuclei, keratin pearls, and visible intercellular bridges.

There was lymphovascular invasion, and the liver metastasis was confirmed. (Figure 7B) Resection margins were tumor-free. Immunohistochemical analysis showed that tumor cells revealed diffuse positivity for CKAE1/AE3 (Figure 7C) with diffuse and strong nuclear positivity for p63(Figure 7D), and they were negative for CK7, CEA, and MUC5AC. The postoperative stage was IVB.

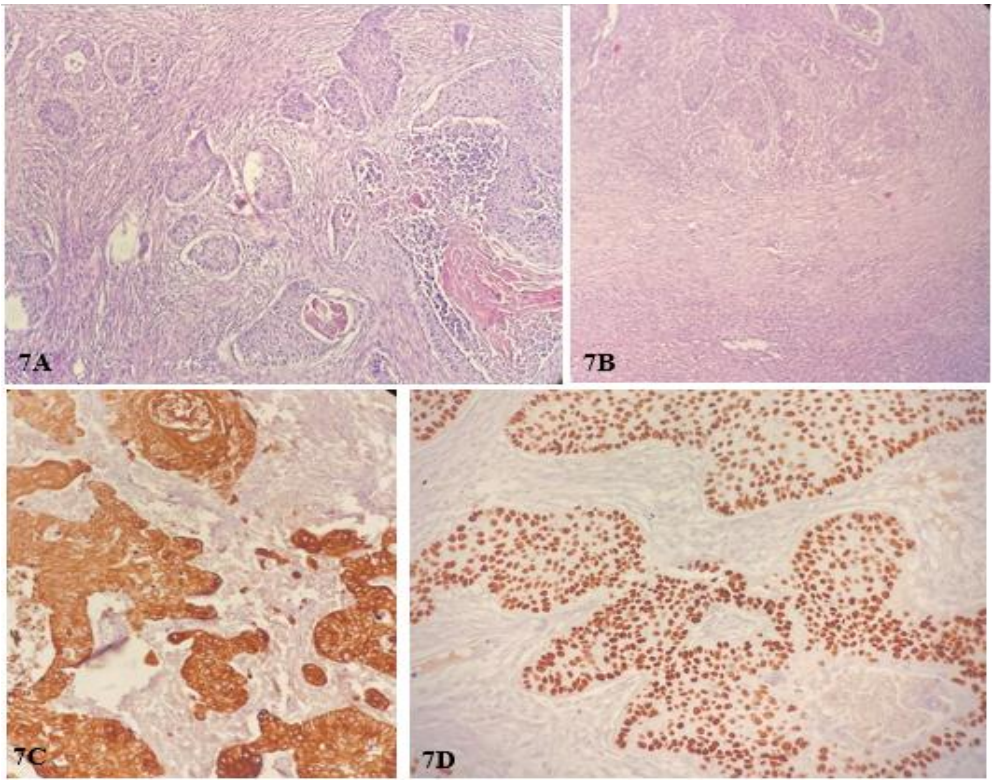

Figure 7.

Legend:
Figure 7A: Islands of atypical squamous cells (HEx100)
Figure 7B: Liver metastasis (HEx100)
Figure 7C: CKAE1/AE3 positivity (x200)
Figure 7D: p63 diffuse nuclear positivity (x200)

Discussion

Squamous cell carcinoma of the gallbladder is a rare and aggressive malignancy, constituting a small fraction of all gallbladder cancers, with pure SCC accounting for only approximately 3% [1,10]. This subtype is particularly aggressive, often diagnosed at advanced stages due to its nonspecific initial symptoms and rapid progression, leading to a significantly poorer prognosis compared to adenocarcinoma of the gallbladder [2.3]. Clinically, these tumors frequently present with larger dimensions and more advanced pathological stages at initial diagnosis, often accompanied by cholelithiasis in up to 80% of cases [4,11]. Histological examination is crucial for definitive diagnosis, revealing characteristics of squamous cell differentiation [5]. The presence of specific immunohistochemical markers further aids in confirming the diagnosis and differentiating it from other gallbladder pathologies [5]. Local invasion in the liver, duodenum, stomach and omentum is the feature of presentation in most cases [12-14]. Despite advancements in diagnostic techniques, the pathogenesis of primary gallbladder squamous cell carcinoma remains incompletely understood, although proposed mechanisms include squamous metaplasia within pre-existing adenocarcinoma or malignant transformation of heterotopic squamous epithelium [4]. The rarity

of this histological subtype, accounting for approximately 1-12% of all gallbladder malignancies, contributes to the limited available literature [6]. Adenocarcinoma is the predominant histological subtype of gallbladder carcinoma, while squamous cell carcinoma represents only 2–10% of all gallbladder cancers [1]. This rarity underscores the challenges in comprehensive clinicopathological studies and the development of standardized treatment protocols [6]. Some studies propose that systemic inflammatory biomarkers or jaundice may have predictive value for the prognosis of patients with gallbladder cancer [15].

Conclusion

We present a rare case of primary poorly differentiated squamous cell carcinoma of the gallbladder, diagnosed in an advanced stage. Operative treatment achieved tumor-free resection, but the high stage indicates the need for a multidisciplinary oncological approach and careful monitoring.

Primary poorly differentiated squamous cell carcinoma of the gallbladder is an exceptionally rare and highly aggressive malignancy that is usually diagnosed at an advanced stage due to its non specific clinical presentation and rapid local invasion. In the present case, despite the absence of jaundice at admission, imaging studies revealed extensive local disease with hepatic involvement and biliary compression, which was confirmed intraoperatively. Histopathological and immunohistochemical analysis established the definitive diagnosis, demonstrating characteristic squamous differentiation and confirming the metastatic spread to the liver.

Although radical surgical resection achieved tumor free margins, the advanced stage of disease (stage IVB) highlights the biologically aggressive nature of this tumor and its poor prognostic implications. This case underscores the importance of early radiological suspicion, prompt surgical intervention when feasible, and thorough pathological evaluation including immunohistochemistry for accurate diagnosis.

Given the rarity of primary squamous cell carcinoma of the gallbladder, there are no standardized treatment protocols, and management remains challenging. A multidisciplinary approach involving surgeons, pathologists, radiologists, and oncologists is essential to optimize outcomes. Furthermore, accumulation of such case reports is important for better understanding of disease behavior, refining diagnostic criteria, and improving future therapeutic strategies.

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