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Case report: Squamous cell carcinoma of the gallbladder

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Abstract

Squamous Cell Carcinoma (SCC) of the gallbladder, though rare, poses significant diagnostic and therapeutic challenges. We report the case of 51-year-old woman with no previous medical history; with a SCC discovered during complicated cholecystitis with cholangitis, treated by palliative chemotherapy underscoring the difficulty in early detection and the poor prognosis associated with advanced-stage diagnosis. Treatment options are limited, with palliative chemotherapy often being the primary recourse for unresectable tumors. Gallbladder cancers, including SCC, share risk factors with adenocarcinomas, but their distinct histopathological features and clinical presentations warrant careful consideration. Despite recent advancements in treatment modalities, including adjuvant therapy, optimal management strategies remain elusive, highlighting the need for further research to improve outcomes for patients with this aggressive malignancy.

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Introduction

Squamous cell carcinoma of the gallbladder accounts for only 1% of all gallstone-related cancers. Its rarity makes diagnosis very challenging, often at an advanced local stage, resulting in a very poor prognosis [1]. We present a case of squamous cell carcinoma of the gallbladder discovered during a complicated cholecystitis with cholangitis.

Case presentation

A 51-year-old woman with no previous medical history, presented with hepatic colic evolving over several months that has been worsening a month prior to admission, accompanied with a progressively developing jaundice, fever, dark urine, and pale stools with no signs of GI bleeding. She also reported a weight loss of 5 kg over two months.

Clinical examination revealed a right hypochondrial tenderness. Laboratory findings showed elevated CRP at 238, GGT levels, and Total Bilirubin at 240 mg/L, with a predominant direct bilirubin level of 167 mg/L. Liver function tests, lipase levels, and white blood cell count were within normal ranges. Additionally, there was evidence of hypochromic microcytic anemia with a hemoglobin level of 7.6 g/dL and hyperglycemia at 3.5 g/dL, indicating an incidental discovery of type II diabetes during hospitalization.

An abdominal CT was performed just before the cholangitis episode revealing a distended gallbladder with thick lithiasic content and thickened wall, as well as a normal-sized liver with regular contours, hosting a 5 cm collection in segment IV, suggestive of an abscess.

The Biliary MRI showed a regular tissue thickening of the gallbladder fundus, irregularly shaped, heterogeneous and budding, measuring 18 x 28 x 83 mm. It was identified as a locally advanced gallbladder cancer infiltrating the hepatic hilum and hepatic pedicle, contacting the patent portal vein, infiltrating the common bile duct with dilation of the upstream intrahepat-

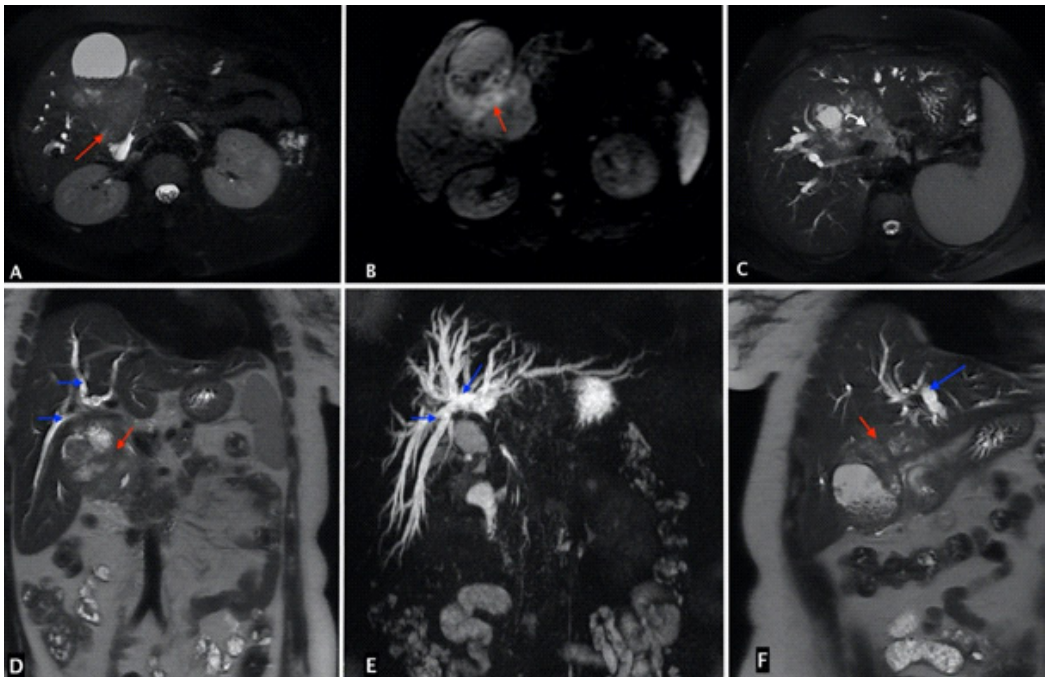

Figure 1: Biliary MRI: Sequences of an axial T2 FAT SAT liver MRI (**A** and **C**), axial diffusion b 800 **(B)**, coronal T2 without FAT SAT (**D** and **F**) and coronal 3D biliary sequence **(E)** showing a distended gallbladder site of a tissue thickening of the lower part, in T2 hyposignal, diffusion hypersignal (red arrows), encompassing the hepatic hilum and the VBP (white arrow) and responsible for a dilation of the VBIH (blue arrows). Note the gallbladder microlithiasis on the image **(F)**.

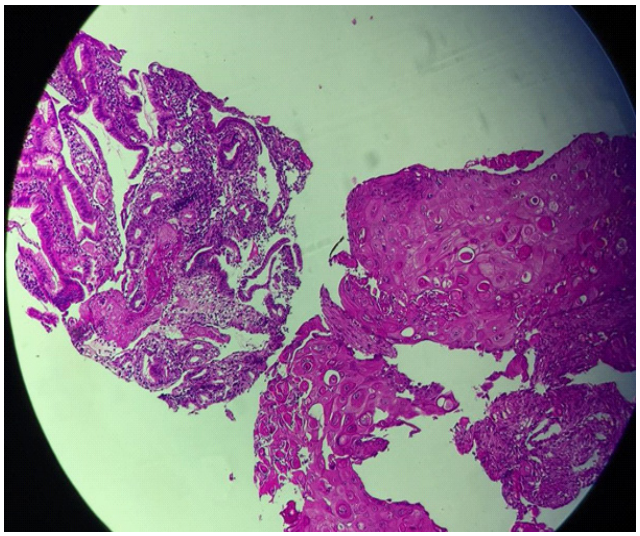

Figure 2: The vesicular mucosa is extensively infiltrated by a well-differentiated squamous cell carcinoma. The tumor cells are polygonal with well-defined cytoplasmic boundaries. Keratin pearls are also observed.

ic bile ducts, contacting the pancreas and duodenum without signs of invasion. They found no signs of metastatic localizations in the extension study (Figure 1).

Endoscopic Retrograde Cholangiopancreatography (ERCP) with stent placement was successfully performed, resulting in clinical and biochemical improvement of cholestasis. Histopathological examination of the biopsy taken from the posterior aspect of the superior duodenal flexure revealed a well-differentiated, infiltrating, and keratinizing squamous cell carcinoma (Figure 2).

After a multidisciplinary team discussion, palliative chemotherapy, made of gemcitabine and cisplatin protocol over three sessions, followed by reassessment was proposed due to the tumor being deemed unresectable.

Discussion

Gallbladder cancers are predominantly adenocarcinomas, with adenosquamous and squamous cell carcinomas accounting for only 0-12% of cases [1,2]. They are commonly found in patients aged between 40 and 60 years, with a male-to-female ratio of 3 to 1 [3]. Risk factors implicated are similar to those of other gallbladder cancers, including Salmonella typhi infections, chronic cholecystitis, gallbladder polyps, and gallstones. Large cholesterol gallstones are more associated with squamous cell carcinomas than adenocarcinomas [4].

Clinical signs are often absent in early stages and nonspecific, leading to diagnosis at an advanced local stage following episodes of cholecystitis or cholangitis [2-4].

Definitive diagnosis relies on biopsy findings, which typically resemble other squamous tumors, exhibiting large nuclei and eosinophilic cytoplasm. Keratin and desmosomes are often present [4,5].

The histopathology, still not entirely understood, may be attributed to local irritation (such as lithiasis, infections...) or metaplastic evolution from a preexisting adenocarcinoma, leading to the emergence of adenosquamous cells transforming into purely squamous cells through increased epithelial component. This hypothesis is supported by studies finding the association of adenocarcinomas and squamous cell carcinomas [5].

Tumor spread occurs locally and rarely through the lymphatic route. The tumor is characterized by rapid growth and local invasion facilitated by the absence of the mucosal muscle layer in the gallbladder wall and the serosa at the gallbladder bed. Involvement of the liver, duodenum, transverse colon, and left colonic angle is common [6].

Curative treatment depends on local-regional extension and is based on extended R0 surgical resection involving the gallbladder bed, associated with lymph node dissection, which is

recommended despite the limited lymphatic extension [6,7].

Adjuvant therapy can associate radiation therapy and chemotherapy, their respective place in a curative treatment scheme remains to be evaluated. Increased survival has not yet been shown after radiation therapy, chemotherapy, or both although recently, encouraging results have been reported [7]. On the other hand, adjuvant treatment has only a palliative effect [6].

Postoperative adjuvant chemotherapy and radiotherapy have been tried in few cases. Bourmeche, et al. reported the use of 45 Gy, combined with 5 fluorouracil and cisplatin chemotherapy, with complete remission. Based on the current literature and review of few cases of pure SCC of GB, postoperative chemotherapy and radiotherapy could be the best therapeutic option [7].

One limitation of this case report is the lack of long-term follow-up data, further follow-up would be necessary to fully understand the long-term outcomes and efficacy of the treatment provided.

Conclusion

In conclusion, gallbladder cancers present complex challenges in both diagnosis and treatment. Despite their rarity, they can have devastating effects, particularly due to late detection and limited treatment options. Advancements in understanding the disease's pathogenesis and refining treatment strategies offer hope for improved outcomes, but further research is needed to enhance survival rates and quality of life for affected individuals.

Declarations

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Ethics statement: All Authors declare no conflict of interest.

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