

Case Report

# Squamous Cell Carcinoma of the Gallbladder Masquerading as Complicated Cholecystitis: A Case Report and Review

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**Abstract:** In summary, squamous cell carcinoma (SCC) of the gallbladder, although rare, poses significant diagnostic and therapeutic challenges. We report the case of a 51-year-old woman with no previous medical history, with 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.

**Keywords:** gallbladder tumor; squamous cell carcinoma; case report; general surgery



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## 1. Introduction

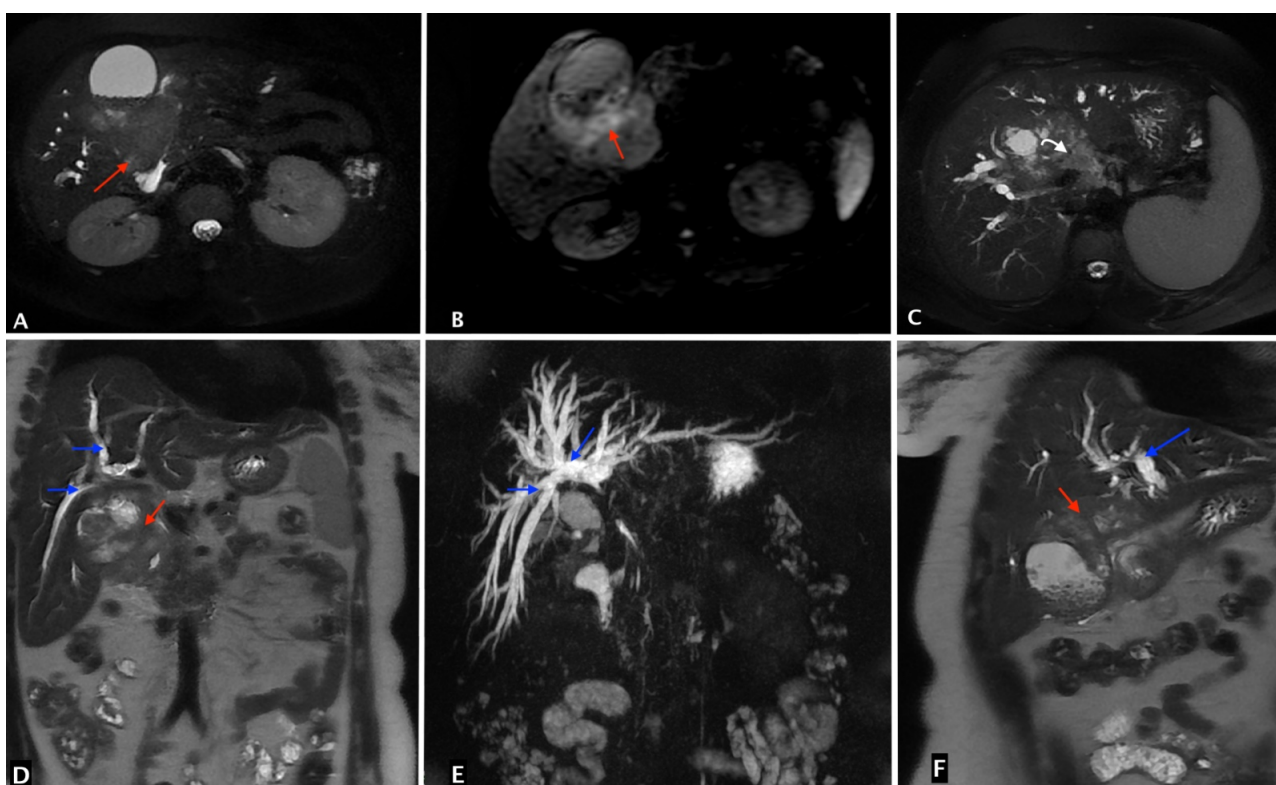
Gallbladder cancer is the most common type of biliary tract malignancy, comprising approximately 80–90% of biliary tract cancers worldwide [1], with an estimated incidence of 11,980 cases in the United States in 2020 [2]. While the vast majority of gallbladder cancers show adenocarcinoma on histology, squamous cell carcinoma of the gallbladder accounts for only 1% of all gallstone-related cancers. The existing literature on squamous cell carcinoma of the gallbladder primarily consists of case reports and case series [1,3,4]. Its rarity makes diagnosis very challenging, often at an advanced local stage, resulting in a very poor prognosis [5]. At present, radical surgery is the only chance to gain long-term survival for patients with early-stage gallbladder cancers. No therapy is defined for unresectable cancer of the gallbladder, especially for squamous cell carcinoma [6]. We report a case of squamous cell carcinoma of the gallbladder discovered during complicated cholecystitis with cholangitis and provide a review of the current data available regarding pathogenesis, diagnosis, imaging, and treatment.

## 2. Case Study

As shown in the table summarizing demographic and etiological information about the patient, a 51-year-old woman with no previous medical history, who presented with hepatic colic evolving over several months, had experienced worsening symptoms a month prior to admission. This was accompanied by progressively developing jaundice, a fever, dark urine, and pale stools, with no signs of GI bleeding.

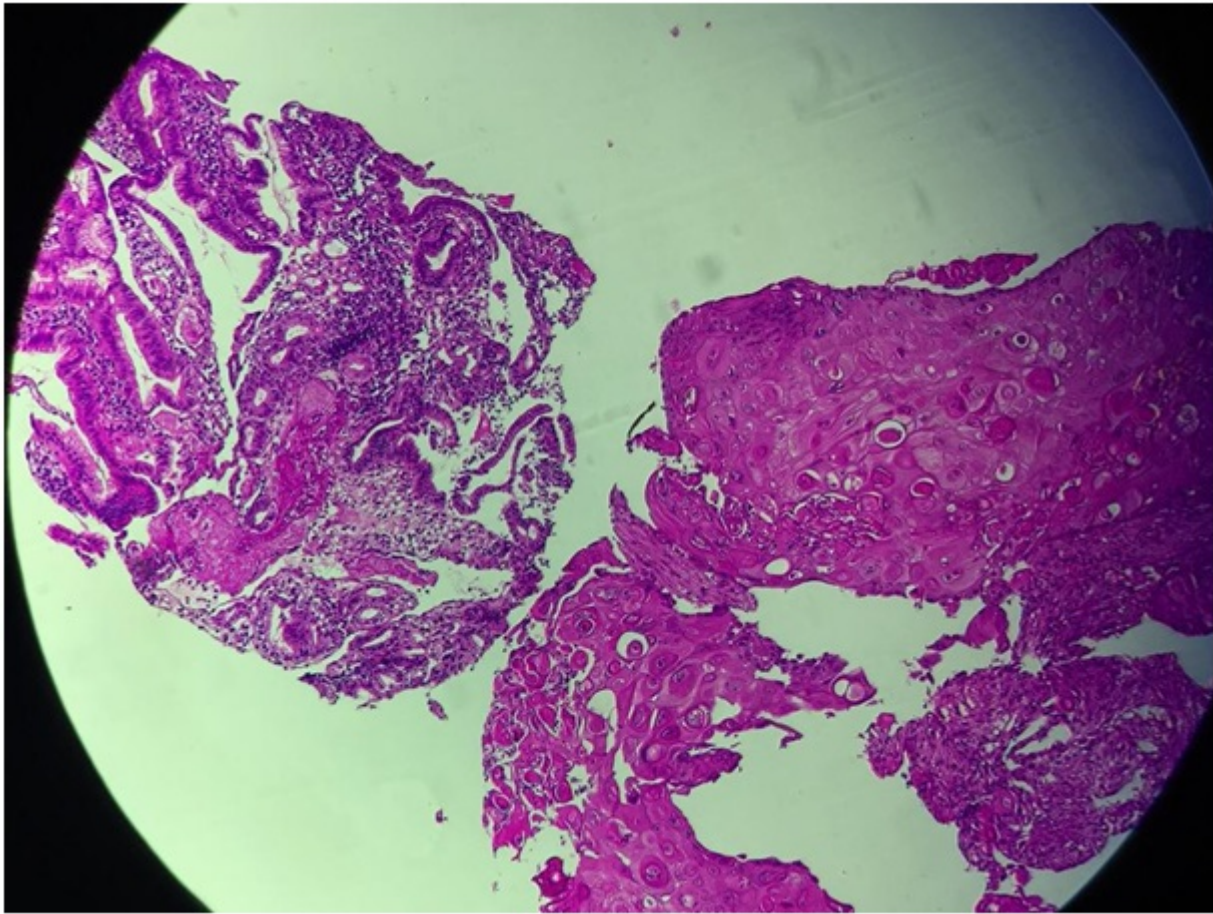
She also reported a weight loss of 5 kg over two months. Clinical examination revealed right hypochondrial tenderness. Laboratory findings showed elevated CRP at 238, elevated

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 the incidental discovery of type II diabetes during hospitalization. An abdominal sonography was performed just before the cholangitis episode, revealing a distended gallbladder with thick lithiasic content and thickened walls, as well as a normal-sized liver with regular contours, hosting a 5 cm collection in segment IV, suggestive of an abscess. As shown in Figure 1, the biliary magnetic resonance imaging (MRI) showed regular tissue thickening of the gallbladder fundus, irregularly shaped, heterogeneous, and budding, measuring  $18 \times 28 \times 83$  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 intrahepatic bile ducts, and contacting the pancreas and duodenum without signs of invasion. No signs of metastatic localizations were found in the extension study.



**Figure 1.** Biliary MRI: Sequences of an axial T2 FAT SAT liver MRI (A,C), axial diffusion b 800 (B), coronal T2 without FAT SAT (D,F), and coronal 3D biliary sequence (E) with 5 mm Scale Bar showing a distended gallbladder with tissue thickening in the lower part, with T2 hyposignal and diffusion hypersignal (red arrows), encompassing the hepatic hilum and the VBP (white arrow) and causing dilation of the VBIH (blue arrows). Note the gallbladder microlithiasis in the image (F).

Endoscopic retrograde cholangiopancreatography (ERCP) with stent placement was successfully performed, resulting in clinical and biochemical improvement of cholestasis. As shown in Figure 2, the 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.** The vesicular mucosa on lowpower (x40) 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.

After a multidisciplinary team discussion, palliative chemotherapy, consisting of gemcitabine 1000 mg/m<sup>2</sup> and cisplatin 25 mg/m<sup>2</sup> over three sessions, without radiotherapy (Table 1), followed by reassessment, was proposed due to the tumor being deemed unresectable. During the 6-month follow-up period, the patient passed away at home.

**Table 1.** Demographic and etiological information about the patient.

Category	Details
Age	51 years
Gender	Female
Medical History	No previous medical history
Diagnosis	Squamous cell carcinoma (SCC) of the gallbladder
Presentation	Complicated cholecystitis episode
Risk Factors	No specific risk factors identified
Diagnostic Method	Likely detected during imaging
Treatment Approach	Palliative chemotherapy without radiotherapy

### 3. Discussion

Gallbladder cancers are predominantly adenocarcinomas, with adenosquamous and squamous cell carcinomas accounting for only 0–12% of cases [5]. They are commonly found in patients aged between 40 and 60 years, with a male-to-female ratio of 3 to 1 [7]. Risk factors implicated are similar to those of other gallbladder cancers, including *Salmonella typhi* infections, chronic cholecystitis, gallbladder polyps, and repeated trauma to the gallbladder mucosa caused by the presence of gallstones, leading to a state of chronic



inflammation, which may represent a possible link between gallstones and the development of gallbladder cancer [8]. There are forms of cholecystopathies, such as porcelain gallbladder, that often hide a neoplasm and are subtle due to the complete absence of symptoms associated with the presence of stones surrounded by tissue that has completely lost the possibility of contracting. In such cases, the chemistry of inflammation induces neoplastic genesis [9]. Large cholesterol gallstones are more associated with squamous cell carcinomas than adenocarcinomas [10]. Clinical signs are often absent in the early stages and are nonspecific, leading to diagnosis at an advanced local stage following episodes of cholecystitis or cholangitis [7,10,11]. Ultrasound is usually the first diagnostic modality, but a definitive diagnosis is confirmed by histology). CT scan and MRI should be performed to rule out metastasis and aid in surgical planning [12]. Definitive diagnosis relies on biopsy findings, which typically resemble other squamous tumors, exhibiting large nuclei and eosinophilic cytoplasm. Keratin and desmosomes are often present [10,13]. The histopathology, still not entirely understood, may be attributed to local irritation (such as lithiasis, infections, etc.) or metaplastic evolution from a pre-existing adenocarcinoma, leading to the emergence of adenosquamous cells transforming into purely squamous cells through increased epithelial components. This hypothesis is supported by studies that have found an association between adenocarcinomas and squamous cell carcinomas [13]. 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 [14]. 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 [14,15]. Adjuvant therapy can include radiation therapy and chemotherapy, although their respective roles in a curative treatment scheme remain to be evaluated. Increased survival has not yet been shown after radiation therapy, chemotherapy, or both, although recently, encouraging results have been reported [15]. On the other hand, adjuvant treatment only has a palliative effect [14]. Postoperative adjuvant chemotherapy and radiotherapy have been tried in a 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 a review of a few cases of pure SCC of the GB, postoperative chemotherapy and radiotherapy could be the best therapeutic option [15]. The benefit of adjuvant therapy in patients with high-risk features, including positive nodes and incomplete resection, has been reported in many studies. Still, it remains unclear which treatment—chemotherapy or radiotherapy—is better. The National Comprehensive Cancer Network recommends chemoradiotherapy [16]. The prognosis for this type of tumor is generally poor. However, Ayabe et al., after analyzing 1048 cases from the National Cancer Database, found that incomplete tumor removal, larger tumor size, advanced AJCC stage, and higher histological grade were all independently linked to lower survival rates [3].

#### 4. Conclusions

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.

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