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CASE REPORT

Gallbladder Carcinosarcoma with Mirizzi Syndrome: a Rare Presentation

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Introduction

Gallbladder carcinosarcoma (GBCS) is characterized by both malignant epithelial and mesenchymal elements. It is very uncommon and less than 100 cases have been reported in the available literature [1]. Due to the low incidence and dismal prognosis of GBCS, it is necessary to share all the individual experience-based information.

As gallbladder carcinoma (GBC) has been linked with cholelithiasis and chronic inflammation, GBCS has also reported frequently in association with cholelithiasis. Hereby, we discuss a case of GBCS associated with Mirizzi syndrome managed with radical cholecystectomy with a short review of literature. The coexistence of Mirizzi syndrome and GBCS has never been reported before.

Case Presentation

A 50-year-old man presented with pain in the right upper abdomen for last 3 months, which was mild dull aching in nature, non-radiating, and not associated with vomiting. He also developed progressive jaundice over 1 month, associated with cholestatic features. He also had significant anorexia and weight loss. No history of abdominal distension and altered bowel or bladder habits noted. On examination, he was icteric and there was no supraclavicular lymph node palpable. On abdomen examination, gallbladder (GB) lump was palpable with mild hepatomegaly.

Biochemical investigation reported deranged liver function test (LFT): bilirubin-12.8 mg/dl, ALT-98 U/L, AST-158 U/L, and alkaline phosphatase-324 IU/L. Magnetic resonance imaging (MRI) of the abdomen was suggestive of heterogeneous lobulated mass with areas of necrosis in fundus and body of GB with impacted calculus at cystic duct and common hepatic duct (CHD) junction (Fig. 1a, b). He was resuscitated with intravenous fluids, parenteral antibiotics, and vitamin K. In view of high bilirubin with cholangitis, endoscopic biliary stenting was performed.

After 3 weeks, when his LFT normalized, contrast enhanced computed tomography (CECT) of the abdomen was done. CECT reported a heterogeneously enhancing intraluminal polypoidal lesion within the GB lumen with diffuse thickening of its wall and minimal pericholecystic fluid likely s/o malignant lesion. A calculus of size 13 × 11 mm is seen in distal cystic duct causing mild dilatation (11 mm) of upstream CHD with bilobar intra-hepatic biliary radicle dilatation (Fig. 1b–d). Biliary stent was seen in situ. CA 19–9 and CEA levels were normal.

With the provisional diagnosis of GB carcinoma with associated Mirizzi syndrome, he was planned for surgery. On staging laparoscopy, there was no evidence of liver, peritoneal, omental deposits. GB was distended with fundal mass with minimal liver infiltration, cystic duct forming a common cavity with common hepatic duct with proximal CHD dilated (~ 2 cm). After stone extraction, frozen section from GB wall margin over common bile duct (CBD) was sent which was negative for malignant cells. Further, radical cholecystectomy with standard lymphadenectomy was performed and CBD was primarily closed with interrupted 3–0 polyglactin (vicryl) sutures (Fig. 2a). He was allowed orally on first postoperative day (POD), his abdominal drain was removed on third POD and was discharged on fifth POD.

Cut section of the gallbladder showed solid, gray white sessile polyp in the lumen measuring 6.5 × 5.5 cm along with tiny yellow calculi (Fig. 2b). Histopathology examination

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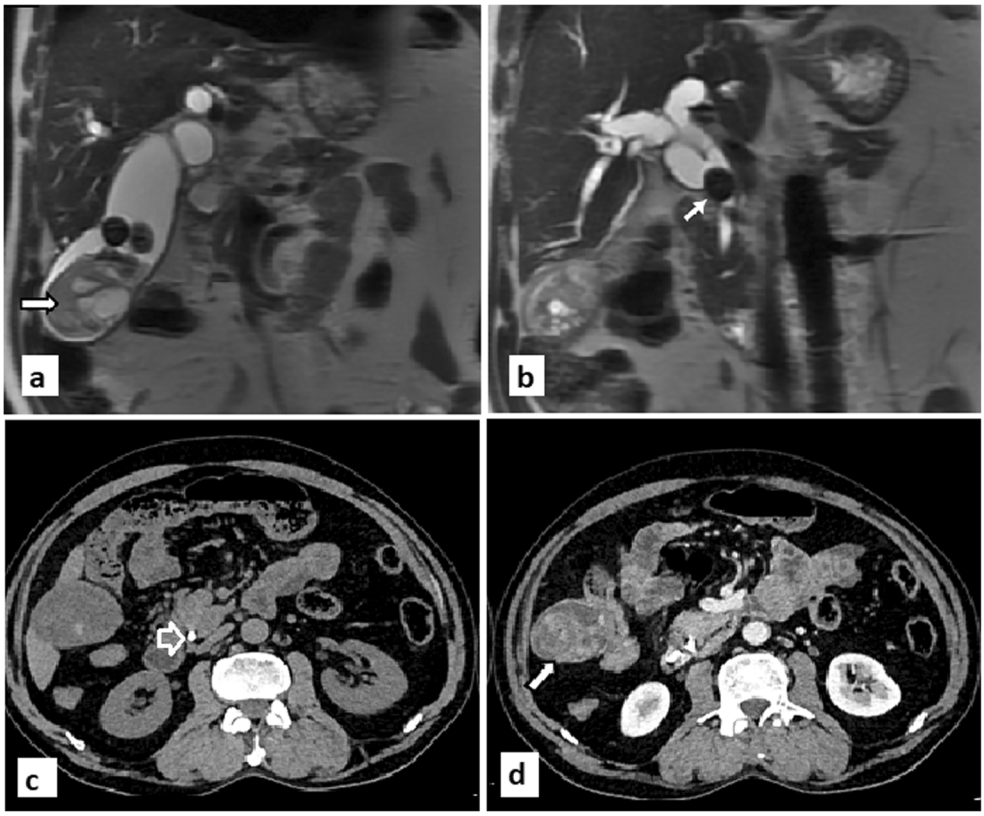

Fig. 1 **a** Coronal T2-weighted MR images showing moderately hyperintense polypoidal mass lesion (arrow) with cystic and necrotic changes within the gallbladder lumen. **b** A calculus (arrow) impacted at the cystic duct-CHD junction leading to Mirizzi syndrome. **c** Axial non-contrast CT image showing isodense mass lesion in gallbladder lumen with calcific foci and biliary stent in situ (arrowhead). **d** Axial contrast-enhanced CT image showing polypoidal (arrow) heterogeneous enhancement of the mass suggestive of gallbladder malignancy

reported variable sized atypical glands lined by neoplastic cells which had round nuclei and scant cytoplasm. The stroma of the polyp showed pleomorphic cells with high N/C ratio, moderate to scant cytoplasm, conspicuous nucleoli (Fig. 3a, b). The stroma also shows of atypical mitosis and presence of binucleate, multinucleate, and tumor giant cells. No heterologous elements identified. The wall of gallbladder showed presence of atypical glands reaching up to the muscularis propria. Large area of necrosis and vessel destruction was noted in the stroma of polypoidal mass. No lympho-vascular or perineural invasion was seen. The serosa, resected margin of gallbladder, liver, and all five lymph nodes resected were free from tumor infiltration. On immunohistochemistry, the stroma shows immune-expression for vimentin and atypical glands for cytokeratin (Fig. 3c, d). Hence, the final diagnosis was carcinosarcoma of the gallbladder was made.

He received 4 cycles of adjuvant chemotherapy in the form of gemcitabine and cisplatin. At the end of 6-month follow-up, he is doing well with no recurrence.

Discussion

Adenocarcinoma is the most common type of malignancy in the gallbladder. Gallbladder carcinosarcoma (GBCS) is encountered in less than 1% of cases [2]. It is more frequently diagnosed in women with female/male ratio of 3.2:1 and at the

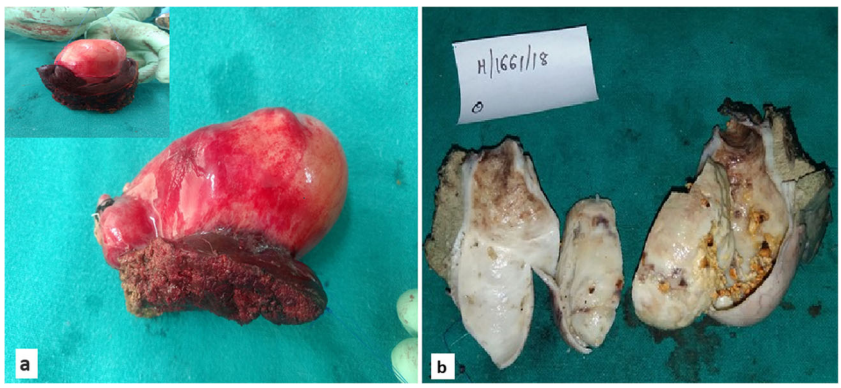

Fig. 2 **a** Resected specimen of radical cholecystectomy showing bulge in the fundus of GB (*inset*: end on view depicting fundus mass with wedge of liver). **b** Cut open formalin fixed specimen showing polypoidal mass in the fundus of GB with multiple calculi

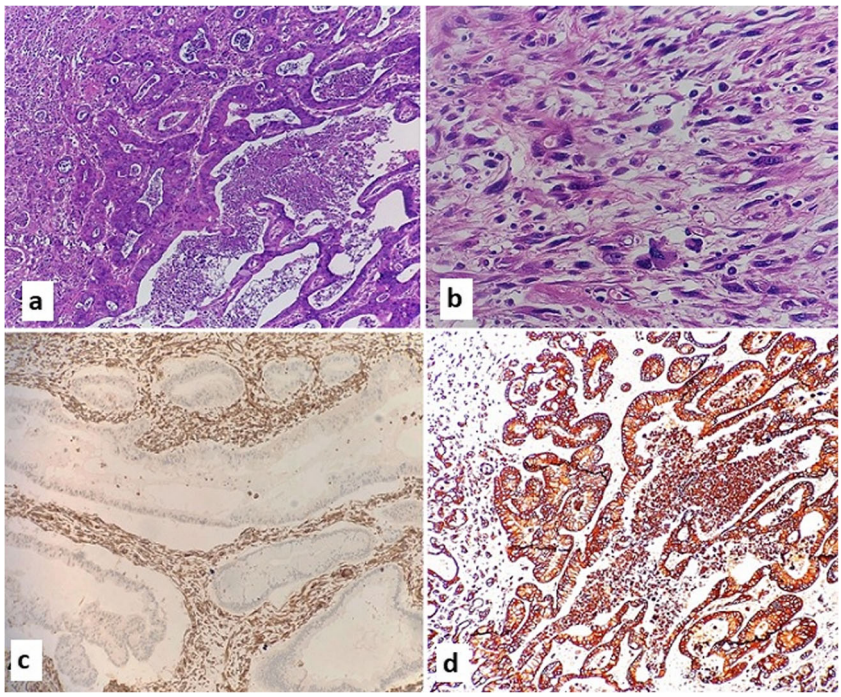

Fig. 3 Histopathology slides (× 40). **a** Atypical glands lined by neoplastic cells [H&E]. **b** Stroma showed pleomorphic cells, moderate to scant cytoplasm, and conspicuous nucleoli. **c** Vimentin immune-expression in stroma. **d** Cytokeratin immune-expression in atypical glands

median age of 68 years [3]. We encountered the disease in a middle-aged male patient.

Preoperative diagnosis of GBCS is difficult due to its non-specific clinical and imaging findings. Clinically, it can present as abdominal pain, fever, nausea, vomiting, jaundice, anorexia, weight loss, or palpable mass. The presentation of GBCS with jaundice is not very well reported as in our case. Similarly, there are no specific radiological features to differentiate GBCS from gallbladder carcinoma (GBC). GBCS tumor is relatively larger than GBC with mean size of 8.4 (2.5–16) cms [4]. Neovascularity, enhancing solid mass lesion, or calcification within the tumor are few features on CT scan that are particularly seen with GBCS [5]. On MRI, GBCS may show moderately high signal on T2-weighted images, with a heterogeneous septated appearance, resembling the appearance of visceral sarcomas due to presence of mesenchymal component within these tumors whereas GBCs show intermediate-to-low signal intensity on T2-weighted images [6].

As cholelithiasis and chronic inflammation have been linked with gallbladder carcinoma (GBC), similarly it has been associated with GBCS in up to second or third of cases, akin to our case with multiple calculi. Prasad et al. reported the incidence of Mirizzi syndrome in GBC to be 5.3% [7]; however, GBCS with Mirizzi syndrome has not been reported before. This is the first reported case of GBCS with Mirizzi syndrome. Its association with Mirizzi further reinforces chronic inflammatory process as an etiology for development of malignancy in GB.

Surgical treatment remains the only curative management option. Radical cholecystectomy with or without CBD resection, partial resection of the small intestine and/or colon, and pancreaticoduodenectomy are options available to get R0 resection. We performed radical cholecystectomy with CBD exploration and primary closure of CBD.

GBCS anatomically is most commonly located in the body (50%) and equally distributed in the fundus and neck (25%). It comprises of malignancy of both the epithelial and mesenchymal components with positivity for both cytokeratin and vimentin. Tumor invasion is noted up to muscularis propria in first or third of cases; however, in majority cases, it perforates the visceral peritoneum or invades other organs at presentation. The median survival of GBCS is 5 months (0–85 months) with overall 1-year and 5-year survival rates of $19 \pm 5\%$ and $16 \pm 5\%$ as reported by Zhang et al. [3]. The poor prognostic factors associated with GBCS are size > 5 cm, presence of serosal invasion, and/or involvement into other organs, i.e., advanced stage and non-Japanese race. Our case had one good prognostic factor, i.e., invasion up to muscularis propria and one poor prognostic factor size > 5 cm.

Overall, GBCS has greater malignant potential than GBC and median time to recurrence is less than 1 year. The recurrence occurs primarily in liver, lymph nodes, and peritoneal cavity. Adjuvant chemotherapy in the form of 5-fluorouracil with either cisplatin or oxaliplatin has been given in few cases. However, its role is not well defined due to lack of high volume of evidence [4, 8].

In conclusion, GBCS can present in middle-aged male patient with variable clinical and imaging findings. Cholelithiasis or chronic inflammation can be implicated as a risk factor for development of GBCS and radical cholecystectomy is treatment of choice despite overall poor prognosis, when operable.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Declaration of Patient Consent The authors certify that they have obtained all appropriate patient consent forms.

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