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Squamous Cell Carcinoma of Gallbladder – An Uncommon Presentation

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Authors' contributions

This work was carried out in collaboration between all authors. Author VG wrote the protocol. Authors PK and AKC prepared final manuscript. Author AK did literature searches. Author PP provided the histopathological photographs. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

A 51-year-old male patient presented with pain in the upper right quadrant of abdomen since two months, associated with weight loss and fever. Contrast enhanced computed tomography abdomen revealed gallbladder with wall thickening which was asymmetric and heterogeneous at junction of body. An initial diagnosis of cholecystitis with element of cholangitis and abnormal wall thickening with multiple tiny calculi was considered. Open radical cholecystectomy was done. Microscopic and immunohistochemical findings established the diagnosis of moderately differentiated squamous cell carcinoma of the gallbladder. Adjuvant chemotherapy regimen consisting of paclitaxel 175 mg/m^2 and carboplatin AUC 6 was given three weekly for six cycles in the present case. Six months after treatment completion, patient is on regular follow up and disease free on clinical and radiological examination.

Keywords: Cholecystitis; gallbladder; squamous cell carcinoma.

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1. INTRODUCTION

Gallbladder carcinomas are uncommon and constitute only 2 to 4% of all gastrointestinal malignancies. Most common histology encountered in gallbladder malignancies are adenocarcinoma. Incidence of Squamous cell carcinoma (SCC) may reach 12.7% of tumours of the gallbladder [1].

We report a single case of SCC of gallbladder that was initially diagnosed as cholecystitis with element of cholangitis and abnormal wall thickening with multiple tiny calculi.

2. CASE REPORT

A 51-year-old male, who belongs to Haryana, presented with complaints of intermittent pain in the upper right quadrant of abdomen and weight loss for two months with associated fever. Patient was known a case of diabetic and on regular medication.

On per abdominal examination, there was tenderness in right hypochondrium and there was no clinically palpable organomegaly. Vital signs were normal. Complete haemogram and renal function tests were within normal limits. Liver function tests showed elevated aspartate transaminase (184 U/L), alanine transaminase (208 U/L) and alkaline phosphatase levels (243 U/L) with normal serum bilirubin level.

Magnetic resonace imaging (MRI) of the upper abdomen with magnetic resonance cholangiopancreatography (MRCP) revealed gallbladder wall thickening, sludge, calculus, and no obvious biliary ductal dilatation or filling defects (Fig. 1). Contrast enhanced computed tomotherapy (CECT) of the abdomen revealed pathological gallbladder with wall thickening which was asymmetric and heterogeneous at the junction of the body region (Fig. 2) and there were mild thickening and enhancement of the proximal extrahepatic bile duct walls. On this basis, an initial diagnosis of cholecystitis with cholangitis considered. Keeping in view of abnormal wall thickening with multiple tiny calculi the patient underwent open radical cholecystectomy which included resection of gallbladder, IV B and V segments of liver, and lymph nodes from pericholedochal, hepatoduodenal tissue, hepatic artery, celiac and gastric regions. Operative findings included a hard mass in *fundus* and body of gallbladder invading into liver. There were no obvious metastasis in liver, peritoneum and *omentum*. The pericholedochal, periportal and hepatic artery nodes were not enlarged.

The macroscopic findings were polypoidal growth measuring 2x2 cm inside the gallbladder infiltrating the muscle layer, but underlying liver was grossly free of tumor. Multiple samples were obtained from representative areas and routinely processed. Histopathological examination revealed moderately differentiated squamous cell carcinoma of gallbladder with area of poor differentiation infiltrating the entire thickness of the wall (Figs. 3 and 4). Nineteen lymph nodes were identified and all were free of tumor. Immunohistochemical study showed that tumor cells were negative for cytokeratin 7, cytokeratin 20 and p63 antibodies, but showed equivocal result with high molecular weight cytokeratin. Postoperative period was uneventful.

The patient was planned for adjuvant chemotherapy with paclitaxel 175mg/m^2 and carboplatin AUC 6, both intravenously three weekly, into a total of six cycles. Six months after operation, the patient is disease free on clinical and radiological examinations.

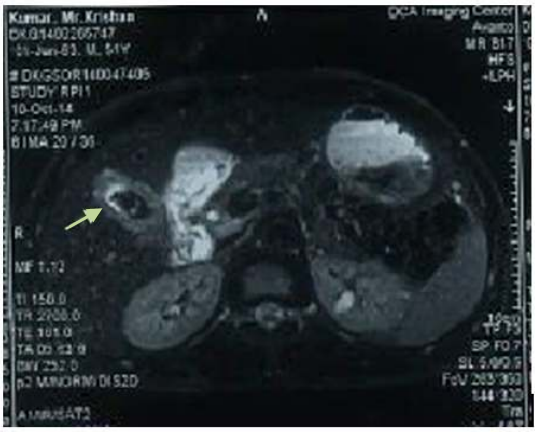

Fig. 1. MRI scan of the abdomen (transverse view) showing the gall bladder with asymmetric and hetereogenous wall thickening (arrow) and multiple tiny gallstones

3. DISCUSSION

Gallbladder cancer is the commonest biliary malignancy. The prevalence of this cancer shows geographical variations. It is reported to be rare in India. However, the incidence of gallbladder cancer in north and central India is very high. Gall stone disease is associated in over 80% of all GB cancer cases. Gall stone disease is

common in north India. Incidence of metaplasia and dysplasia increased with the age and the metaplastic alterations and dysplasia are taken as precancerous lesions [2].

Fig. 2. CT scan of the abdomen (transverse view) showing gall bladder with asymmetric wall thickening (arrow)

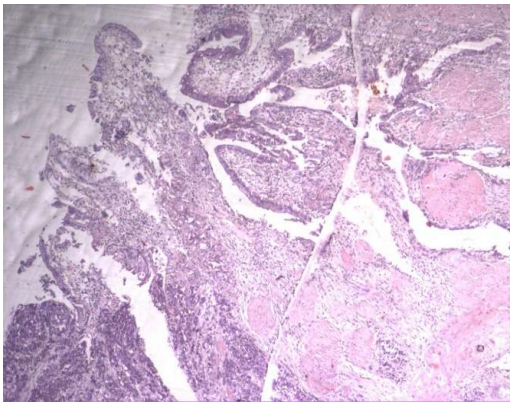

Fig. 3. Photomicrography showing the gall bladder wall with infiltration by carcinoma (H&E,100X)

Squamous cell carcinoma (SCC) of the gallbladder is a rare and aggressive form of gallbladder cancer. Long term prognosis for patients who have SCC of gallbladder is poorer than patients who have adenocarcinoma of gallbladder [3,4]. The most common type of gallbladder cancer is adenocarcinoma with female/male ratio 3:1. The commonly presenting age group for gallbladder cancer is 40 to 60 years [4].

Early stages of gallbladder cancers do not produce any symptoms. When symptoms are present, the presentation is similar to biliary colic or chronic cholecystitis [5]. SCC of gallbladder is characterized by rapid growth, diffusely local and regional infiltration and early metastatic dissemination. Despite of these characteristics, peritoneal seeding is rare while hepatic metastases are more frequent [4]. The time for duplication for adenocarcinoma is two times higher as that for SCC of gallbladder; thus, the SCC growth is faster than that of adenocarcinoma. Therefore, SCC is more aggressive with poor prognosis as compared to adenocarcinoma [3,4].

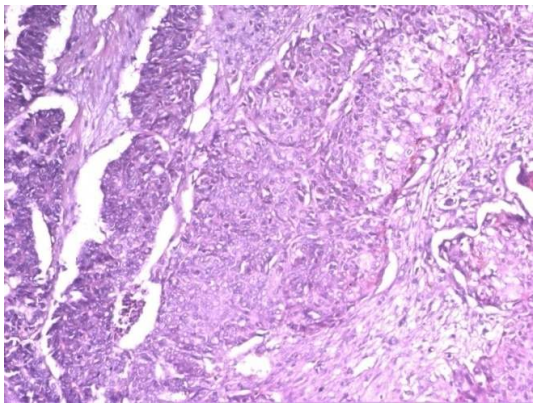

Fig. 4. Photomicrography showing the tumor cells with squamoid differentiation (H&E, 100X)

Roppongi et al. [6] mentioned that due to inclusion of heterogenous neoplasm such as adenosquamous carcinomas and some misdiagnoses, SCC of gallbladder comprise upto 12.7% of gallbladder cancers. According to the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute, out of 3038 patients with gallbladder cancer only 45 (1.7%) were SCC [4,6].

Due to foregut origin of gallbladder, most gallbladder carcinomas are heterogeneous during neoplastic transformation [7]. As a result, pure SCC of the gallbladder is a rare entity. SCC of the gallbladder is thought to arise from the basal cell layer of the epithelium either due to squamous metaplasia or squamous differentiation of a pre-existing adenocarcinoma. Others believe SCC originates from squamous differentiation of the adenocarcinoma via expression of mixed phenotypes within a single tumor [4].

Radical resection is the mainstay of treatment with curative intent for patients with locally invasive SCC. The most important parameter in determining survival is the extent of tumor invasion at the time of diagnosis. Death occurs

within six months of diagnosis without radical surgery [3,4]. Laparoscopy should not be done if gallbladder cancer is suspected [8]. Postoperative radiotherapy and chemotherapy may be used; however, results are inconsistent [9].

Oohashi et al. [10] compared radical resection and primary tumor resection alone in terms of survival in adenosquamous carcinoma of gallbladder. These authors found that 5- year survival of 48.6% with radical resection compared to a 3-year survival of 7.7% with primary tumor resection alone. Residual tumor *status* was the only significant independent prognostic factor. Patients with no residual tumor had a 5-year survival of 62.9% compared to patients with residual tumor whose the 5-year survival was nil.

4. CONCLUSION

SCC of gallbladder is a rare malignancy. Main treatment modality is surgery. Even though chemotherapy and radiation therapy has been used in the adjuvant setting, it does not provide additional benefits. Careful radiological examination may help to decrease the mortality associated with this disease enabling early detection at an earlier stage.

CONSENT

Informed consent has taken from patient. Privacy of the patient protected.

ETHICAL APPROVAL

All authors have obtained all necessary ethical approval from suitable Institution. This confirms either that, this study is not against the public interest, or that the release of information is allowed by legislation.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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