Small cell carcinoma of gall bladder: An uncommon histologic entity

Amit Gupta¹, Rohik T. Anjum Siddeek¹, Rishit Mani¹, Navin Kumar¹, Anoushika Mehan², Sweety Gupta³, Nilotpal Chowdhury², Utkarsh Kumar¹

¹Department of Surgery All India Institute Of Medical Sciences, Rishikesh Uttarakhand, India
²Department of Pathology All India Institute Of Medical Sciences, Rishikesh Uttarakhand, India
³Department of Radiation Oncology All India Institute Of Medical Sciences, Rishikesh Uttarakhand, India

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ABSTRACT:

Introduction: Gall bladder (GB) small cell carcinoma (SCC) comprises 0.5% of all gall bladder cancers. It carries a poor prognosis in view of its aggressive nature.

Case report: We here report a case of small cell carcinoma of GB in a female who presented with obstructive jaundice. Examination revealed a hard lump in the right upper abdomen. Tumour markers showed raised CA 19-9. Staging CECT of the thorax and abdomen reported polypoidal enhancing wall thickening of the gall bladder with multiple metastatic deposits close to the pancreatic head encasing the main portal vein and common bile duct. Histopathology report was suggestive of small cell carcinoma, which was confirmed by immunohistochemistry. Patient was referred to the Oncology Department for palliative chemotherapy.

KEYWORDS: metastatic, small cell, tumour markers

ABBREVIATIONS

CECT – Contrast-enhanced computed tomography
GB – Gall bladder
IHBRD – intrahepatic biliary radical dilatation
NETs – neuroendocrine tumors
PTBD – percutaneous transhepatic biliary drainage
SCC – small cell carcinoma

INTRODUCTION

Small cell carcinoma of the gall bladder is an uncommon pathological entity. It was first described by Albores-Saavedra in 1981 [1]. This pathology is characterized by extensive local invasion and metastases. It carries a poor prognosis because of its advanced stages at presentation and aggressive behaviour. Few cases have been reported on in literature. Here, we present a case of obstructive jaundice which was diagnosed as small cell carcinoma of the gallbladder on investigations.

CASE REPORT

A 55 year-old female presented with yellowish discolouration of eyes and urine for one month. It was associated with generalised itching, clay-coloured stools and weight loss. There was also a history of multiple episodes of vomiting after food intake, which increased over past week. There were no co-morbidities.

Physical examination revealed jaundice with extensive scratch marks all over the body. On per abdomen examination, a hard non-tender gall bladder was palpable and it moved with respiration. Other systemic examination was normal.

Routine blood investigations revealed elevated total leucocyte counts of 7,000/mL, raised bilirubin total/direct: 7.0 /6.57 mg/dL, and raised alkaline phosphatase 346 U/l. Tumour marker CA 19-9 was 86.53 U/mL. Ultrasound of the abdomen revealed gall bladder thickening with infiltration into the surrounding liver parenchyma with multiple metastatic deposits close to the pancreatic head encasing the main portal vein and common bile duct. Contrast-enhanced computed tomography (CECT) of the abdomen revealed polypoidal enhancing wall thickening of the gall bladder, indistinct fat planes with segment V of the liver, multiple calculi in the gall bladder lumen and moderate intrahepatic biliary radical dilatation (IHBRD). Metastatic nodal deposit of a 3.4 x 4.2 x 6.8-cm lesion close to the pancreatic head with mass effect over CBD with upstream IHBRD encasing and attenuating the main portal vein. Multiple enlarged retroperitoneal and aorto-caval lymph nodes were also noted (Fig. 1A, B.). In view of raised bilirubin and deranged coagulation parameters, the patient was started on vitamin K and given 4 units of fresh frozen plasma. Following this, percutaneous transhepatic biliary drainage (PTBD) with simultaneous stent placement (internal drainage) was carried out. Ultrasound-guided biopsy was taken from the gall bladder lesion.

Gall bladder biopsy showed a malignant small round cell tumour. Immunohistochemistry was done and tumour cells were found to be positive for chromogranin and synaptophysin with Ki-67 found to be 80% positive; suggestive of small cell carcinoma of the gall bladder (Fig. 2A.–E.). Diagnosis of gall bladder carcinoma cT3N2M1 (AJCC 8th edition), stage IVb was made. Due to metastatic nature of the disease, the patient was considered for cisplatin- and etoposide-based chemotherapy and she received four cycles of chemotherapy. After four cycles of chemotherapy her condition deteriorated and radiologically there was disease progression so she was considered for the best possible supportive care.
Fig. 1. (A) Right lateral wall thickening with indistinct fat planes in segment V of the liver; (B) Metastatic deposit close to the pancreatic head, causing mass effect over CBD with upstream IHBRD. A mass encasing and attenuating the main portal vein. No filling defects noted in the portal vein.

Fig. 2. (A) Section shows tumour cells arranged to form a solid pattern of large round to oval cells. Cells have finely granular and basophilic cytoplasm with round nuclei with prominent nucleoli (Hematoxylin and Eosin stain x 100). (B) Small cell carcinoma of the gall bladder: section shows cytoplasmic staining with chromogranin diffused in tumour cells (IHC x 100). (C) Small cell carcinoma of gall bladder: section shows cytoplasmic staining with chromogranin diffusely present in tumour cells (IHC x 100). (D) Small cell carcinoma of the gall bladder: section shows nuclear positivity with Ki-67 in 80% of tumour cells (IHC x 100). (E) Small cell carcinoma of the gall bladder: section shows cytoplasmic staining with cytokeratin focally positive in tumour cells (IHC x 100).
DISCUSSION

Round cell tumour of the gallbladder constitutes 0.5% of all gall bladder cancers according to the Surveillance Epidemiology and End Results (SEER) data, which makes it a rare type of cancer of the gall bladder [2]. A study conducted by Moskal et al. reported a higher incidence, of 3.5 [3] According to the available literature, median age of presentation was found to be 67 years, ranging from 25–86 years [4]. Round cell tumour of the gall bladder, similar to adenocarcinoma of the gall bladder, is more commonly found in females. Neuroendocrine cells usually are not seen in the GB mucosa [5]. Primary gallbladder neuroendocrine tumours are hypothesized to develop from (a) multipotent stem cell or neuroendocrine cells in intestinal or gastric metaplasia as a result of cholelithiasis and chronic cholecystitis (b) undifferentiated gallbladder stem cells that separate into neuroendocrine cells [6]. Neuroendocrine tumors (NETs) include well-differentiated NETs (classic carcinoid tumors), well-differentiated NECs (atypical carcinoids or malignant carcinoids), poorly differentiated NECs (high grade carcinoma: small-cell/large-cell types), and mixed exocrine-endocrine carcinomas [7]. Most of the cases present in advanced stages of the disease. Clinical symptoms are nonspecific, like abdominal pain, abdominal lump, weight loss and ascites. As many as 66% of patients have an evidence of metastases to regional, distant nodes, liver and lung [8]. Preoperative diagnosis of small cell carcinoma is difficult because of non-specific symptoms. Radiological diagnosis of gall bladder SCC is also problematic. It is mainly diagnosed at the time of radical surgery by histopathology. WHO (2019) classification defines small cell carcinomas as neuroendocrine tumours with >20 mitoses/2 mm² (mean 75/10 hpf) and small cell cytological features [9]. In Immunohistochemistry, cells express chromogranin A, synaptophysin and CD56, but NETs show diffuse positive staining while SCCs show focal staining [10]. Treatment options for gallbladder small cell carcinoma are highly variable including resection, radiation, and chemotherapy regimens. Surgery is the mainstay of treatment of a localized disease followed by adjuvant chemotherapy. Chemotherapy for a metastatic disease includes cisplatin- and etoposide-based regimen [11]. In a metastatic disease, chemotherapy is the only option. Median survival for metastatic gallbladder SCC is only 9 months [12]. Elm’hadi et al. suggested that maintenance chemotherapy may be an option in patients with a metastatic disease to prolong the response and decrease the progression of disease [13]. Fuzuii et al. utilized intra-arterial chemotherapy in this entity in one patient [14]. The prognosis of SCC of the gallbladder remains poor because a majority of patients usually present in advanced stages of the disease.

CONCLUSION

In small cell carcinoma, being a rare entity, the treatment options are variable. Also, due to paucity of data, it is clinically challenging to manage these patients, so all case studies should be analysed for better understanding and designing treatment strategies.

REFERENCES
