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Case Report

Pathology Section

Hepatoid Adenocarcinoma of the Gall Bladder-A Rare Variant

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ABSTRACT

Hepatoid adenocarcinoma is a rare variant of extra hepatic adenocarcinoma, consisting of foci of both adenomatous and hepatocellular differentiation with morphological and functional resemblance to hepatocellular carcinoma and hence correct diagnosis is a challenge. The most frequent site is stomach. We present this case of hepatoid carcinoma of the gallbladder for its rarity and difficulty in diagnosis which on histology showed papillae, sheets and trabaculae of polygonal cells with eosinophilic cytoplasm and vesicular nuclei with prominent nucleoli with adjacent foci showing high grade dysplasia.

Keywords: Alpha feto protein, Hep Par1, High grade dysplasia

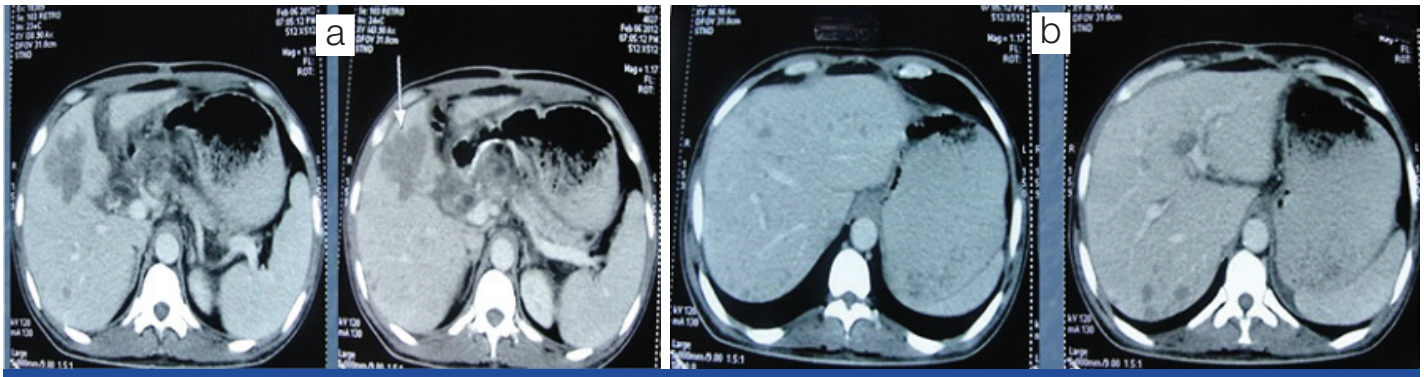
CASE REPORT

A 43-year-old male patient presented with abdominal pain for the past 7 months. Serum alpha feto protein level was markedly elevated to 23500 ng/ml (normal 7.0 ng/ml). Ultrasound showed a distended gall bladder with isoechoeic structure with increased vascularity. CECT abdomen showed a pseudocyst with peri-pancreatic fat stranding. Liver showed irregular and ill-defined lesion in the gall bladder bed with high signal intensity in the periphery of gall bladder suggesting carcinoma of the gallbladder [Table/Fig-1a]. Segment 6/7 of the liver showed ill-defined lesions suggesting metastatic deposits [Table/Fig-1b].

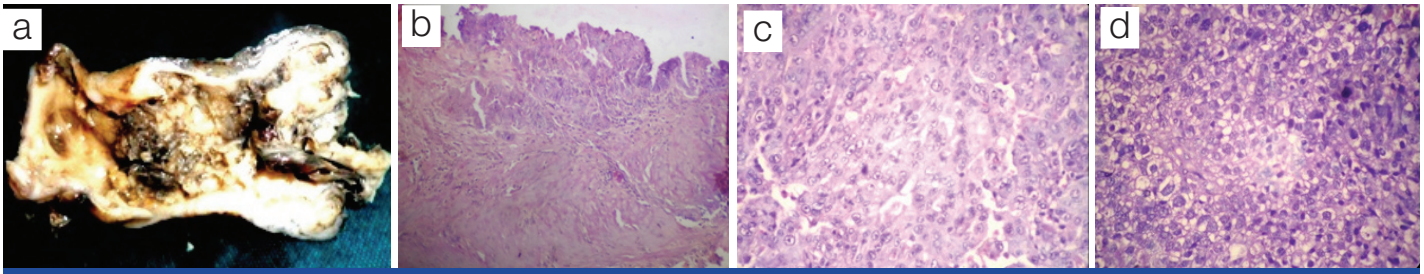
Cystogastrostomy with extended cholecystectomy was done and the intraoperative finding was a mildly distended gall bladder with a papillary mass completely occluding the lumen and extending upto the cystic duct. The involved liver segments and lymph nodes were not resected. The gross specimen of gallbladder measured 12x5x2 cm. Cut section revealed a greyish white, friable and papillary mass occupying the entire lumen which was found to extending upto the cystic duct [Table/Fig-2a]. Histomorphology revealed gall bladder parenchyma with high grade dysplasia of the lining epithelium and an adjacent infiltrating neoplasm composed of polygonal cells arranged in papillae, sheets and trabecular pattern [Table/Fig-2b-d], extending upto serosa. These neoplastic cells consisted of moderate amount of granular eosinophilic to clear cytoplasm with distinct cell borders and round vesicular nuclei with prominent nucleoli. Serosal blood vessels showed tumour emboli. Cystic duct and liver showed secondary carcinomatous deposit. Immunohistochemical profile revealed positivity for cytokeratin19, polyclonal CEA, Hep Par 1 and focal positivity for AFP [Table/Fig-3a-c]. CK 7 and 20 were negative.

DISCUSSION

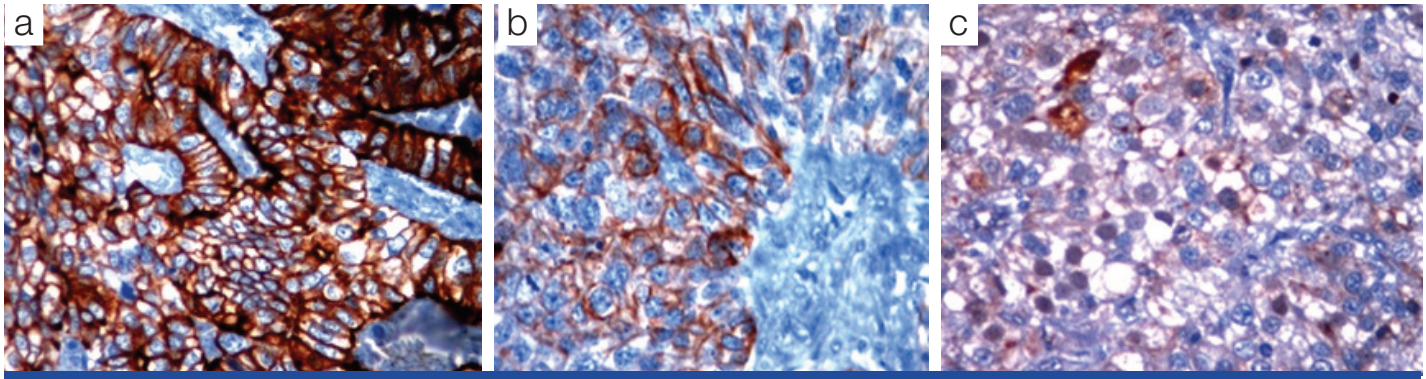
Hepatoid adenocarcinoma of the gall bladder, a rare variant was first described by Ishikura in 1985 [1]. So far only 8 cases have been reported in English literature and two cases were reported in Japan. This variant behaves morphologically and functionally as hepatocellular carcinoma [1,2]. The histogenesis of this tumour may be due to hepatoid differentiation in an adenocarcinoma as the tumour progresses or it may be from the bipotential cells that differentiate into cells with glandular and hepatoid features [2]. Most common sites are stomach, pancreas, kidney, urinary bladder, female genital tract and testicle [2,3]. The age group more commonly affected was found to be middle or old age. Gall-bladder tumours are rare and often diagnosed at a later stage because it is often



[Table/Fig-1a-b]: (a) Irregular ill-defined hypodense lesion in the gall bladder bed (b) Segment 6/7 of the liver showing ill-defined lesions suggesting metastatic deposits



[Table/Fig-2a-d]: (a) Gallbladder showing grayish white papillary mass (b) High grade dysplasia of the lining epithelium of the gallbladder (c) 40X Polygonal cells with eosinophilic granular cytoplasm and pleomorphic vesicular nuclei in trabecular pattern (d) 40X Sheets of polygonal cells with clear cytoplasm and pleomorphic vesicular nuclei



[Table/Fig-3a-c]: (a) 40X CK 19 POSITIVITY (b) 40X AFP POSITIVITY (c) 40X HepPar 1 positivity

asymptomatic as it is small and without biliary tract obstruction and patients commonly present with liver and lymph node metastasis. AFP is important for the diagnosis of hepatoid adenocarcinoma, since it is positive in the serum and in the tumour cells too. Though it is valuable in the diagnosis, hepatoid adenocarcinoma of the gall bladder does not always produce AFP [4-7] and hence it is mainly diagnosed on the basis of histomorphological features and immunohistochemical markers [5]. Primary AFP producing gall bladder tumours are undifferentiated carcinoma, papillary clear cell carcinoma and hepatoid carcinoma [4].

Histomorphologically the tumour is composed of hepatoid cells arranged in sheets and trabacular pattern. These neoplastic cells are polygonal with eosinophilic cytoplasm and vesicular nuclei with prominent nucleoli. Medullary proliferation, papillary, tubular and rosettoid patterns have also been reported in literature [8].

Hepatoid carcinoma can occur along with cholangiocarcinoma and in some cases occurs in a setting of well differentiated adenocarcinoma. In our case the adjacent lining epithelium exhibited high grade dysplasia with transition to hepatoid carcinoma.

The differentials for this tumour are hepatocellular carcinoma or combined hepatocellular carcinoma/cholangiocarcinoma invading the gall bladder.

Liver and lymph node metastases have been documented in few cases [1,2,5-7,9]. Liver showed multiple irregular ill defined metastatic deposits in our case. Immunohistochemistry plays an important role in differentiating hepatoid adenocarcinoma from hepatocellular carcinoma and cholangiocarcinoma. AFP positivity is considered an important marker for the diagnosis of this variant. Other markers which are positive and are in favour of this tumour are cytokeratin 8 and 19. Hep Par 1 is a specific marker for hepatoid differentiation and has been noted to be positive in many cases. Our case showed positivity for CK19, Hep Par 1 with focal AFP positivity. CK 7 was negative.

Hepatoid adenocarcinoma of the gallbladder whether producing AFP or not, is an aggressive tumour than the other AFP producing tumours and carries a bad prognosis [10,11]. In our case the patient was alive for only one month postoperatively and died due to wide spread metastasis. AFP levels were not done postoperatively.

CONCLUSION

Gallbladder origin of this tumour was confirmed by the presence of high grade dysplasia of the gall-bladder mucosa with transition to hepatoid carcinoma in our case. The tumour location, radiological features, high AFP, positivity for Hep Par 1 and cytokeratin 19 goes in favour of the diagnosis of hepatoid adenocarcinoma of the gall bladder. Thus we present this case of hepatoid adenocarcinoma of the gallbladder with secondary metastatic deposits in the liver for its rarity and poor prognostic significance.

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