Undifferentiated carcinoma of the gall bladder: a rare entity

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Abstract

Undifferentiated carcinoma of the gall bladder is an unusual tumor with a reported incidence of 0.38% of all gallbladder and extrahepatic bile duct cancers. We present a 65 year old female presenting with pain abdomen who was diagnosed with carcinoma gall bladder on ultrasound and CT abdomen. Histopathological examination revealed a 6.5x4x2 cm^3 growth extending from the body of the gall bladder upto the fundus. H & E stained sections from the growth revealed sheets and trabeculae of neoplastic cells which were round to polygonal with abundant eosinophilic cytoplasm, multinucleation at places and areas showing spindled tumor cells. A diagnosis of undifferentiated carcinoma of gall bladder with spindle and giant cell type was given. Tumor showed strong positivity for cytokeratin and vimentin. These tumors have a very poor prognosis and therefore early diagnosis is vital to the survival of the patient.

Keywords: Undifferentiated carcinoma, Gall bladder, Spindle and giant cell type

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Introduction

Although the majority of neoplasms occurring in the biliary tract are adenocarcinomas, the reported incidence of undifferentiated carcinoma is 0.38% of all gallbladder and extrahepatic bile duct cancers. [1] These are more common in the gallbladder than in the bile duct. There are four histological variants.[2] [3] [4] [5] Undifferentiated carcinoma, spindle and giant cell type is the most common type. We report a case of a 65 year old female presenting with carcinoma gall bladder which was categorised as undifferentiated carcinoma, spindle and giant cell type on the basis of histomorphology and immunohistochemical studies.

Case history

A 65 year old female presented to surgical OPD with complaints of pain abdomen of 1 month duration, aggravated on taking fatty meal along with episodes of vomiting. Routine examination of blood revealed a Hb of 6.7g/dl, total count of 6100/mm3 with normal differential count. Liver enzymes showed AST 85 U/L (N) , ALT-34 U/L (N) , GGT-91 U/L (HI) and PA view chest showed emphysematous changes with prominent bronchovascular markings. On Ultrasound abdomen an ill-defined soft tissue lesion measuring 3.6 x2.5 cm was noted arising from the fundus and body region of GB; the lesion shows vascularity on colour Doppler study. Fat plane of the GB with adjacent 2nd part of the duodenum was lost which showed irregular thickening of the wall with minimal vascularity on colour Doppler study, suggesting possibility of infiltration. A possibility of carcinoma of gall bladder with infiltration into 2nd part of duodenum was suggested. On CT abdomen, gall bladder was significantly distended in size with multiple areas of heterogeneously enhancing solid components intramurally. Intramural radiodense calculi were also noted. The 2nd part of duodenum was found to be compressed by the enlarged GB. CT features were suggestive of carcinoma gall bladder.

The patient underwent an open cholecystectomy and tissue was sent for histopathological examination. On gross examination, the gall bladder measured 9.5 cm x 4 cm. On cut section, a growth of size 6.5x4x2 cm^3 was seen extending from the body of the gall bladder upto the fundus. Growth was firmly adherent to the whole thickness of the body wall and some papillary projections noted adjacent to the growth in neck area. Cut section of the growth was firm, solid and whitish in colour. Two stones, larger one of size 0.8x0.8 cm^2 were noted in the lumen of the gall bladder, grossly resembling mixed cholesterol stones. H & E stained sections from the growth revealed sheets and trabeculae of neoplastic cells infiltrating into the fibromuscular tissue with large areas of haemorrhage and necrosis. Most of the neoplastic cells are round to polygonal with abundant eosinophilic cytoplasm, multinucleation at places and with irregular nuclear chromatin along with areas showing spindled tumor cells. A diagnosis of undifferentiated carcinoma of gall bladder with spindle and giant cell type was given. It was also noted in the report that hepatoid adenocarcinoma of the gall bladder, which is a rare neoplasm needed exclusion and patient was advised

immunohistochemical correlation with serum Alpha-fetoprotein estimation.

Subsequently, serum AFP came out to be normal, thereby excluding hepatoid adenocarcinoma. IHC was performed for cytokeratin and vimentin which showed strong positivity in the tumor cells. Desmin was negative.

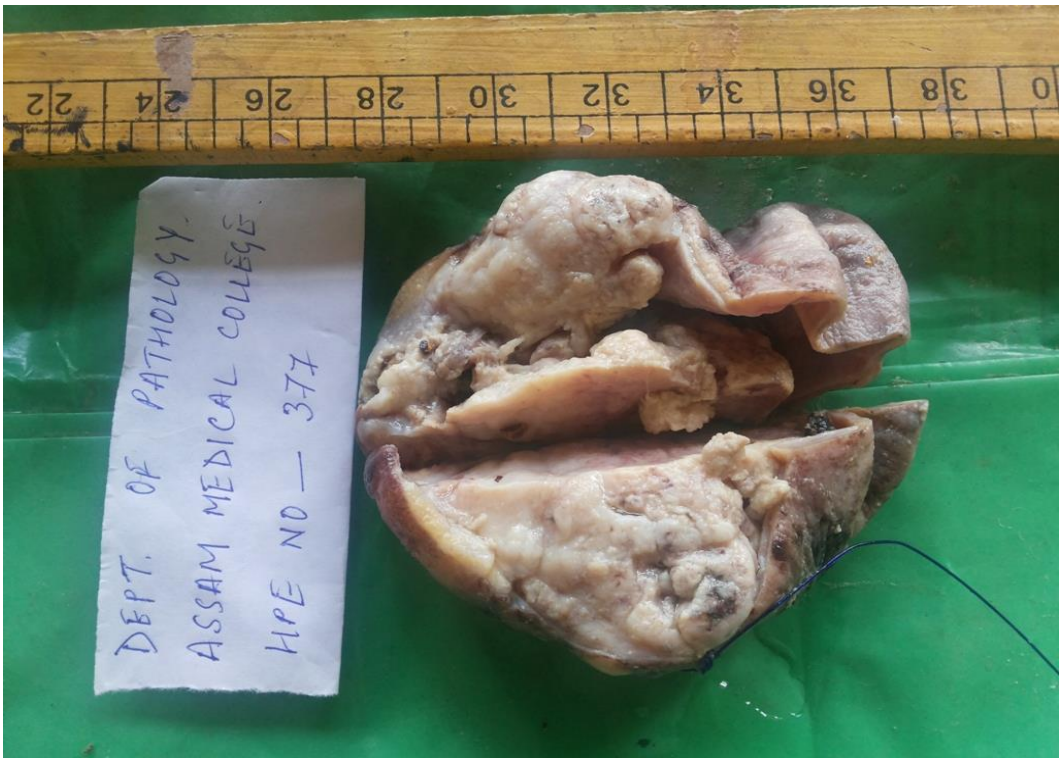

Fig. 1: Showing gross appearance of the tumor

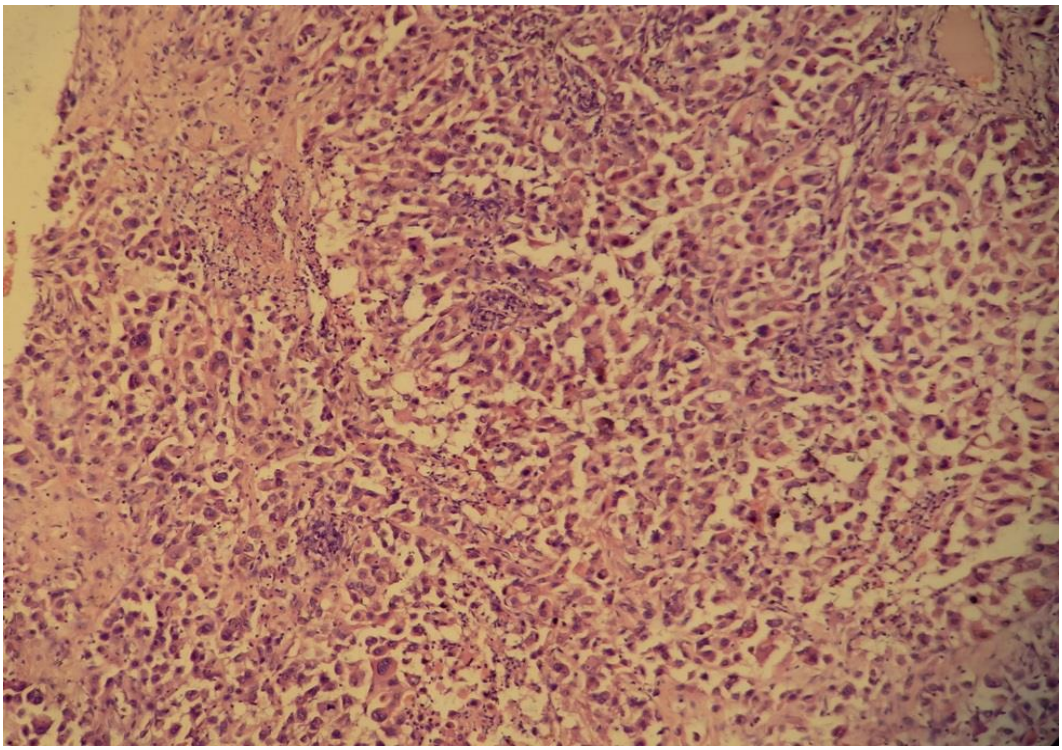

Fig. 2: Showing sheets of neoplastic polygonal to spindle cells (10X)

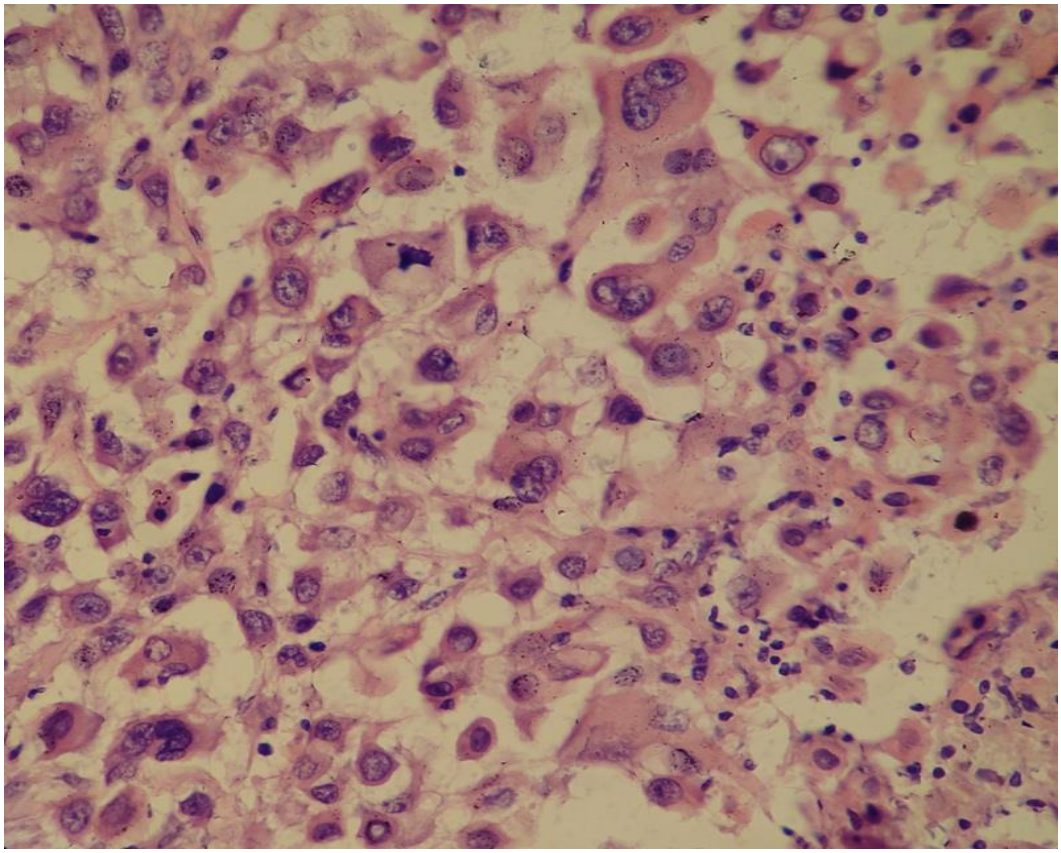

Fig. 3: Showing neoplastic cells under higher magnification. Multinucleation is seen at places(40X)

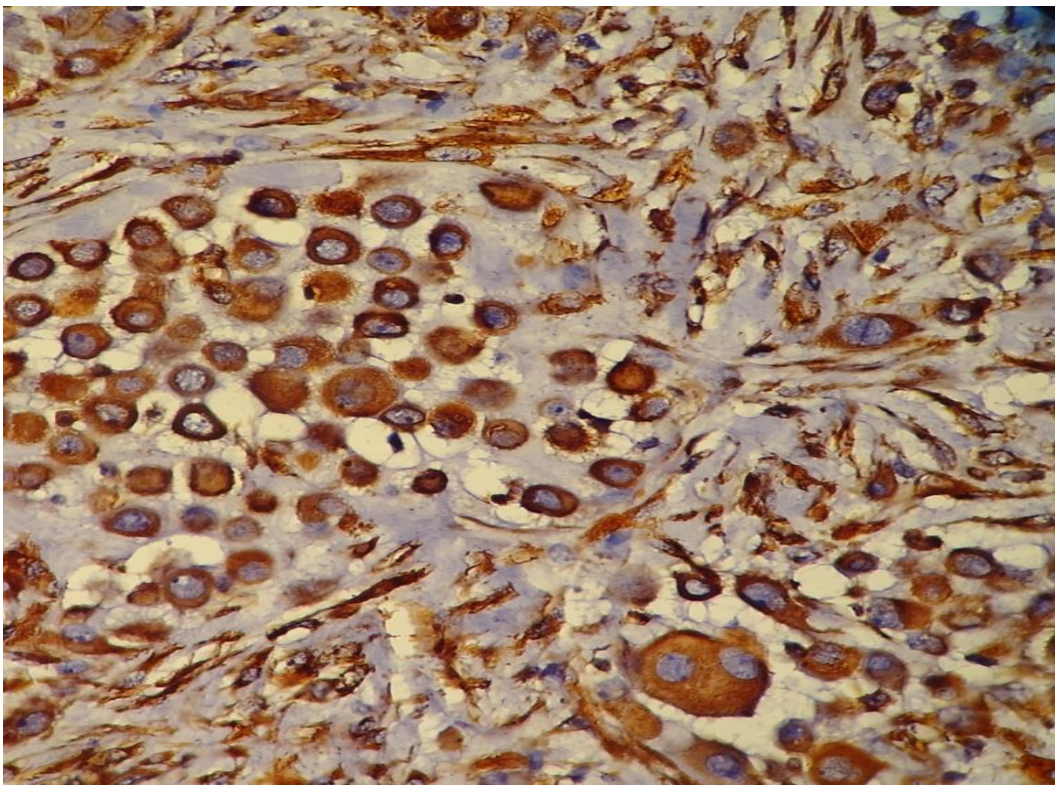

Fig. 4(a): showing positive staining for vimentin (40X)

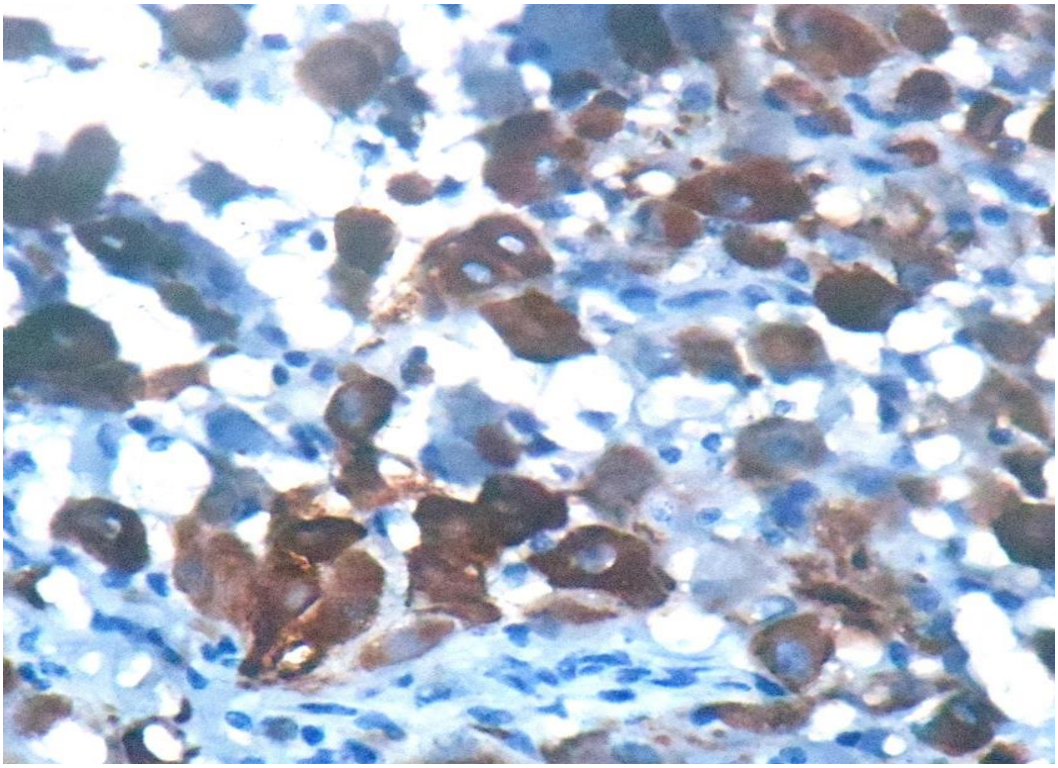

Fig. 4(b): showing positive staining for cytokeratin in the tumor cells (40X)

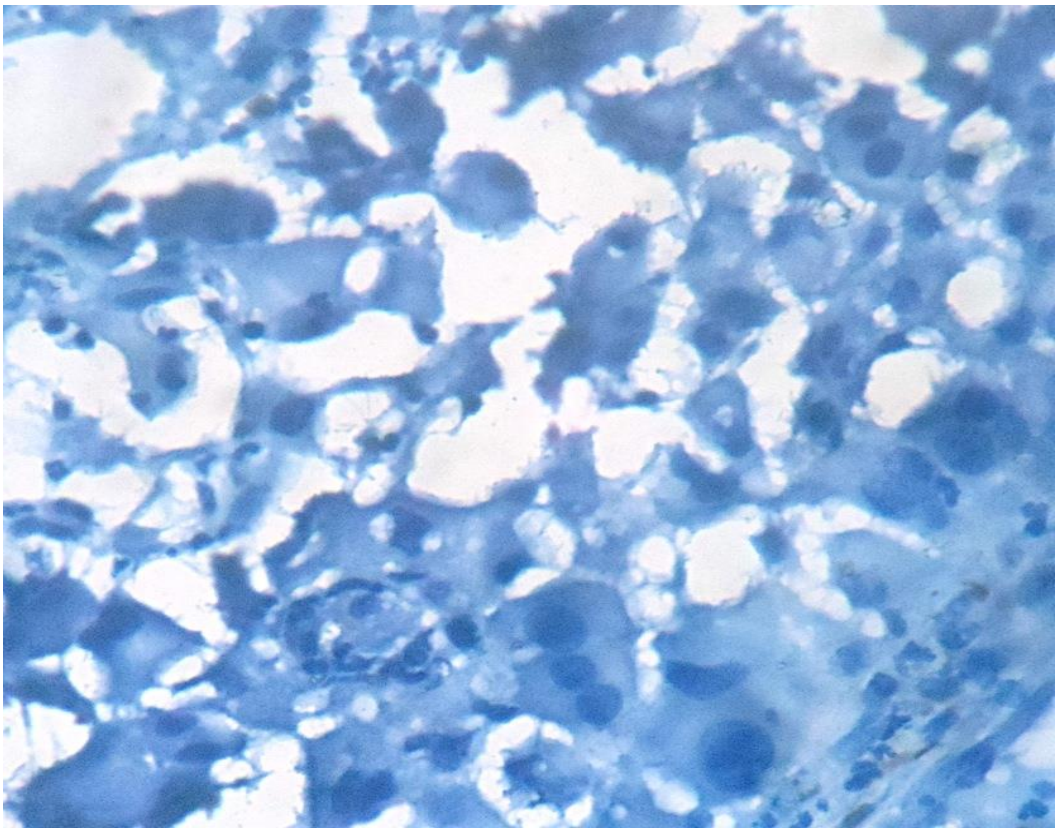

Fig. 4(c): showing negative staining for desmin (40X)

Discussion

The incidence of gallbladder carcinoma is 1.2 cases per 100 000 per year, increasing with age, particularly after the fifth decade of life. [4] [6] Risk factors include cholelithiasis, calcified gallbladder wall, adenomatous gallbladder polyps, obesity, oestrogen, choledochal cysts and chemical carcinogens. The majority of gallbladder carcinomas are adeno-carcinomas but less common histological types include clear cell, mucinous, squamous and adenosquamous cell, signet ring cell, small cell, spindle and giant cell, as well as undifferentiated carcinomas, the latter accounting for 10.4% to 10.9% of gallbladder carcinomas.[4]

Characteristically, glandular structures are absent in undifferentiated carcinomas, which is of four histologic types- undifferentiated carcinoma, spindle and giant cell type, undifferentiated carcinoma with osteoclast-like giant cells, undifferentiated carcinoma, small cell type and undifferentiated carcinoma, nodular or lobular type. In our case, glandular differentiation was absent, the tumor comprising mainly of polygonal to spindled cells with abundant eosinophilic cytoplasm, with irregular nuclear chromatin and multinucleation at places.

Undifferentiated carcinoma, spindle and giant cell type, have been referred to as pleomorphic spindle and giant cell adenocarcinomas or sarcomatoid carcinomas. They consist of variable proportions of spindle, giant and polygonal cells, but foci of well-differentiated neoplastic glands are usually found in some of these tumours after extensive sampling .The presence of cytokeratin in the spindle cells may help to distinguish this tumour from carcinosarcoma.[7] In our case however, no foci of neoplastic gland was seen but tumor showed positivity for cytokeratin.

Despite improvement in radioimaging techniques, most cases of gallbladder cancers are diagnosed at advanced tumour stage with consequent dismal outcome following treatment. In order to improve the prognosis of gallbladder carcinoma would early detection is therefore important. This would entail mass screening of population with high prevalence of gallbladder cancer using ultrasonography. [8] Regular screening with endoscopic ultrasonography in high-risk individuals such as those with congenital dilatation of common bile duct, abnormal pancreato-biliary duct connections, reflux of pancreatic juice into the bile duct, or gallstones, as well as individuals with family history of gallbladder cancer, holds the key to early detection of gallbladder cancer.

The presence of serosa invasion and/or involvement of other organs as well as advanced stage were two identified factors that portend poor postsurgical outcomes in these patients. Our case therefore fell into the poor prognostic category. As curative surgery is nearly impossible in most patients with gallbladder carcinoma due to advanced stage at presentation, patients and relatives should be thoroughly briefed about the biology of this tumour and prognosis following surgery. Newer chemotherapeutic regimen or targeted therapy need to be developed to prevent recurrences in these cases.

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