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Intra Cholecystic Papillary Tubular Neoplasm – A Case Report Of A Rare Differential Diagnosis Of Carcinoma Gall Bladder

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ABSTRACT

We present a case report of a 57year old lady who presented with complaints of right sided upper abdominal pain. The patient was initially diagnosed with carcinoma gall bladder(CAGB) by CECT Abdomen and PET CT imaging studies. Intra cholecystic papillary tubular neoplasm of the gall bladder(ICPN) was diagnosed after histopathological examination of the radical cholecystectomy specimen. ICPN can be managed with a cholecystectomy if the diagnosis is known pre operatively as the prognosis for ICPN is much better as compared with that for gallbladder adenocarcinoma.

Keywords: Intra Cholecystic Papillary Tubular Neoplasm Gall bladder; Carcinoma Gall Bladder; Radical Cholecystectomy; Case Report

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Introduction

Intraepithelial neoplasia is a preinvasive neoplastic lesions found throughout in the digestive system. Such lesions when found in the gallbladder, are referred as intra cholecystic papillary neoplasm (ICPN). ICPN are rare tumours which show intraluminal papillary growth that can be associated with invasive carcinoma. Their natural history remains poorly understood. ICPN rarely infiltrates and metastasizes, and hence has better outcomes.

CASE REPORT

57 years old lady presented to the surgery OPD at Saveetha Medical College, Chennai with complaints of pain in the upper abdomen (right hypochondrium and epigastric region) for the past three days associated with vomiting. The pain was colicky in nature and the pain radiated to the back. There was no significant weight loss and she had no loss of appetite. Ultrasound study revealed a 12x6mm echogenic focus adherent to the wall of the gall bladder suspicious of neoplastic growth with dilated CBD and IHBR. A CT abdomen study showed a fairly defined dense lobulated lesion measuring approximately 2.8x1.1 cm in body of the gall bladder, which on contrast administration showed moderate enhancement in arterial and venous phase (Fig 1).

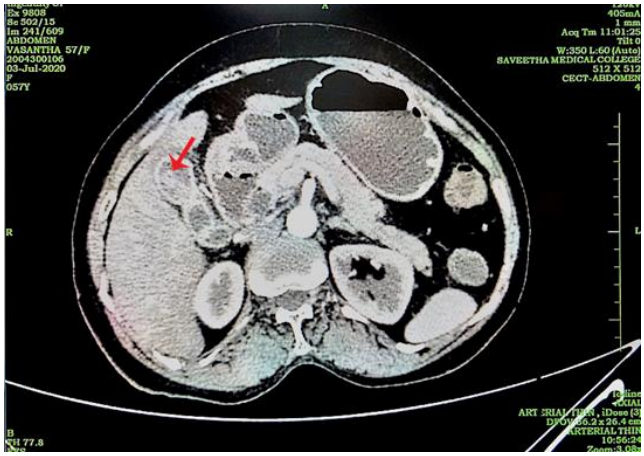

Fig1: Red arrow shows a fairly defined soft tissue dense lobulated lesion measuring 2.8x1.1cm in the body of the gall bladder.

UGI scopy was normal. Tumor markers CA19.9 was 27.1U/ml and CEA 1.11 ng/ml (showed no significant elevation). Patient underwent a PET CT scan which showed hyper metabolic mass with SUV max of 8.7 in the gall bladder suggestive of carcinoma (Fig 2), the lesion being adherent to the gall bladder fossa of liver suggestive of early invasion, 8mm calculus was also noted in the gall bladder.

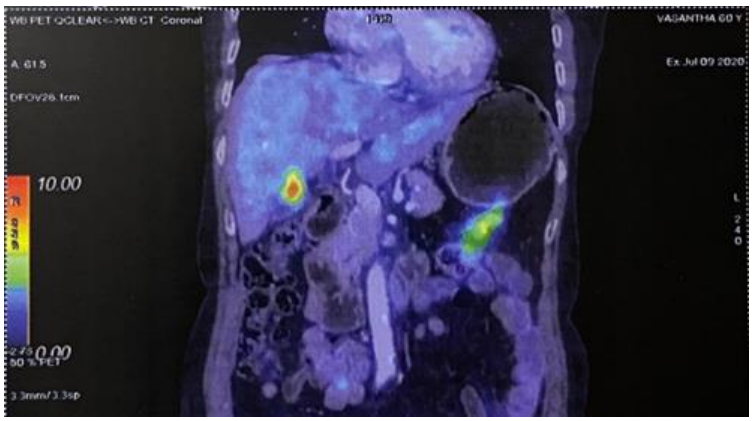

Fig 2: Hyper metabolic mass in the gall bladder suggestive of carcinoma on PET CT. SUV max 8.7. lesion appears adherent to the gall bladder fossa of liver suggestive of an early invasion.

Bulging ampulla was noted and there was no evidence of mass in the ampulla, periampullary region or pancreas. An 8mm cyst was noted in segment 4b of liver. Patient underwent a radical cholecystectomy procedure. The findings were a subhepatic appendix with pulled up caecum, liver and peritoneal surface free of metastasis and a pedunculated growth of size 1.8x1.5 x 1cm in the post wall of the gall bladder with a 1cm gall bladder calculi. Adjacent 5.5 x 3.5 cms of liver segment 4b and V was resected. Histopathological examination of the specimen revealed a polypoidal structure with tubular and papillary structures. The tubules are lined by columnar epithelium with focal areas showing goblet cells and pyloric type mucosa. Focal areas showed mild nuclear enlargement depicting low grade dysplasia. No invasion was noted. The features were consistent with intra cholecystic papillary tubular neoplasm of the gall bladder (Fig 4).

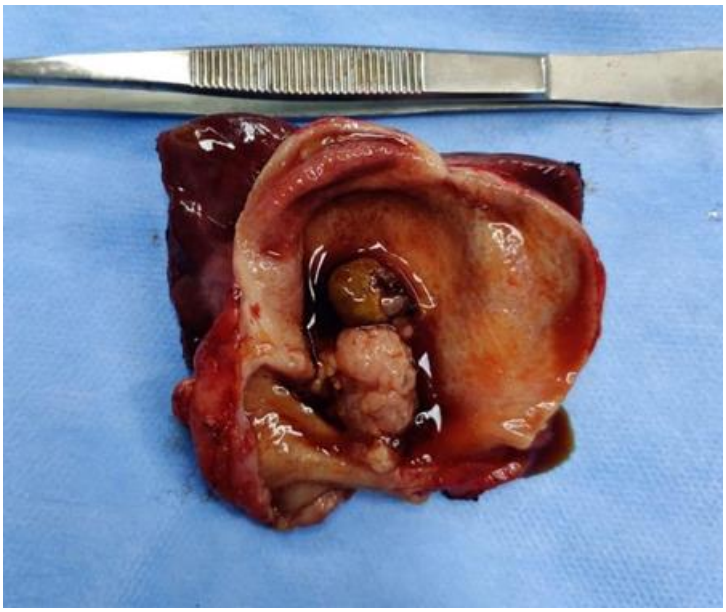

Fig 3: Gross specimen - pedunculated growth of size 1.8x1.5 x 1cm in the post wall of the gall bladder with a 1cm gall bladder calculi with the adjacent 5.5 x 3.5 cms of liver attached to the gall bladder.

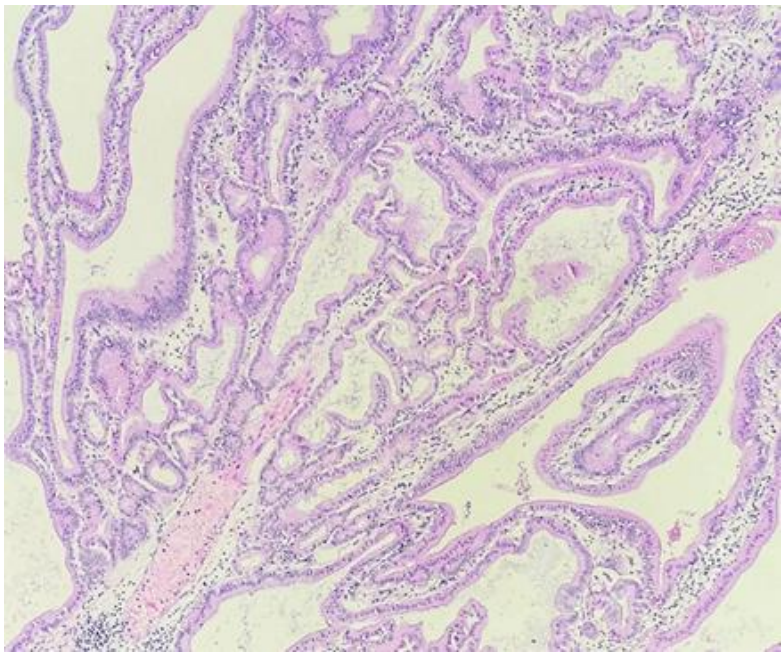

Fig 4: Microscopic features of ICPN - Tumor cells are arranged in a papillary architecture along thin fibro vascular stalks.

Discussion

Benign lesions of the gall bladder include inflammatory, cholesterol and adenomatous polyps, fibromas, leiomyomas, lipomas, hemangiomas, granular cell tumors, and heterotopic tissue, including gastric, pancreatic, and intestinal epithelium. Carcinoma of the gall bladder occurs in 50.0% of the gall bladders examined microscopically. Of these 90.0% are adenocarcinomas, 2% are squamous cell carcinomas and approximately 5% represent papillary adenocarcinomas. Intra cholecystic papillary–tubular neoplasm (ICPN) is a relatively new entity which includes neoplastic polyps, adenomas, and papillary neoplasms that are ≥1.0 cm.

ICPN was first described as gallbladder lesions of IPNB in the 2010 WHO classification and was classified as premalignant lesions of biliary system in the same category as adenoma, biliary intraepithelial neoplasia, and mucinous cystic neoplasm. They are more common in women and in the age group 26-65 years. They follow an adenoma carcinoma progression and have 5 different lineages of differentiation. ICPN has a histological pattern from stomach to colon. Five different patterns such as biliary, gastric pyloric, gastric foveolar, intestinal, and oncocytic types are recognized till now. The ICPN has tubular and papillary elements, with the latter more likely to be invasive. High grade dysplasia is a precursor for invasive cancer.

A simple cholecystectomy is sufficient for the treatment of non invasive ICPN as it rarely infiltrates or metastasizes. The 5-year survival rate for ICPN is 60% if including invasive carcinoma and 78% if excluding the invasive region. In contrast, the 5-year survival rate for gallbladder adenocarcinoma is 30%. However, it is difficult to preoperatively differentiate whether a growth in the Gall bladder is an ICPN or an adenocarcinoma.

Gallbladder polyps can be incidentally found on ultrasound or other imaging modalities. Preoperative imaging using CT or MRI is unable to differentiate ICPN from Carcinoma of gall bladder. The features described in view of ICPN are: [1] intramucosal, [2] preinvasive neoplastic (dysplastic), [3] mass forming: exophytic (papillary or polypoid), [4] size more than 1.0 cm, [5] compact, and [6] distinct from the neighboring mucosa. However, ICPN is a novel concept, and the diagnostic features remain uncertain [27]. In a study by Sakamoto et al. a novel scoring system using CEA and tumor diameter is used to predict the tumor depth of CAGB. CEA values are important for preoperative evaluation of CAGB [28]. Many studies show an increase in CA19.9 in the later stages of CAGB, however both CEA and CA19.9 have low specificity (CA 19-9 92.7% versus 79.20% CEA) and sensitivity (CA 19-9 50% vs 79.4% CEA) and baseline tests are only useful in monitoring response to therapy.

CAGB has a one-year mortality of 85% and a 5 years survival of 5%. The poor prognosis is attributed to late presentations with advanced stage of disease. In the present day, there is no physical exam findings, blood test or imaging findings that is highly suggestive of gallbladder cancer, which can be used as an early detection screening process worldwide [29, 30].

PET CT is not routinely recommended for staging in CAGB, although it may be useful for detection of regional nodal metastases and distant metastatic disease. Generally, a high FDG-uptake is associated with CAGB and a lower uptake is seen in benign etiologies such as focal adenomyomatosis, chronic cholecystitis or xanthogranulomatous cholecystitis. High uptake in the polyp compared to liver parenchyma has high sensitivity and specificity for malignancy in polyps larger than 1 cm. SUVmax is a semi-quantitative tool for assessing metabolic uptake. This is highly dependent on BMI, age, sex and injected FDG activity [31]. In our case PET CT showed and SUV max of 8.7 which is high and hence lead to higher suspicion of malignancy.

ICPNs account for only 6.5% of all surgically resected gallbladder neoplasms of which 16% are papillary tumors. Immunohistochemical studies of ICPN suggest that there is a higher expression of MUC5AC and MUC6, as compared to CAGB. ICPNs are genetically distinct from papillary and non-papillary gall bladder carcinomas. STK11, CTNNB1, and APC being identified as

major contributory genes for ICPNs [32].

Conclusions

ICPN account for 6.5% of resected gallbladder neoplasms. Given that they have a better prognosis as compared to adenocarcinoma, the surgeon must be aware of this pre invasive entity. While preoperative definitive diagnosis is difficult, frozen section can preclude a need for extensive radical dissection.

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