Intracholecystic Papillary Neoplasm of Gallbladder in a Middle-Aged Woman—A Rare Entity

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Abstract

Intracholecystic papillary neoplasm of the gallbladder is a rare and relatively new entity in the fifth edition of the World Health Organization classification of tumors of the digestive system. It mainly occurs in elderly women. It is an exophytic, granular, and friable mass seen in gallbladder mucosa, often mistaken clinically as sludge. We report a middle-aged female with abdominal pain and a vague mass in the right hypochondrium. A computed tomography scan of the abdomen and pelvis showed a heterogeneously enhancing lesion in the gallbladder lumen extending from the fundus to the neck, causing an irregular luminal obstruction. Histopathological examination of the cholecystectomy specimen showed features of intracholecystic papillary neoplasm of biliary and oncocytic type with low-grade dysplasia.

Keywords

- intracholecystic papillary neoplasm
- gallbladder
- histopathology

Introduction

Intracholecystic papillary neoplasm (ICPN) is a rare, noninvasive epithelial neoplasm of the gallbladder (GB).[1] It is found in 0.4% of GBs removed for cholelithiasis or chronic cholecystitis. ICPNs are more common in women, with the mean age of occurrence being 60 years. Patients present with right upper quadrant pain, or it may be an incidental finding. Almost two-thirds of the cases are suspected radiologically and are misdiagnosed as malignancy. Commonly used modalities include ultrasound sonography (USG), computed tomography (CT) scan, and magnetic resonance imaging (MRI).[2] Cholecystectomy should be considered for ICPNs that are symptomatic, sessile, multiple, or larger than 1 cm. Grossly, ICPNs appear as an exophytic, granular, friable mass in the GB mucosa, which can detach and be mistaken as sludge by surgeons.[1] Histopathology shows tumor cells in tubulopapillary pattern limited to the mucosa. If there is a component of invasive carcinoma, the lesion is called an ICPN with associated invasive carcinoma.[3] Herein, we present a case of ICPN in a 43-year-old female who came with pain abdomen on the right side, clinically and radiologically suspected as a malignant lesion of the GB. Histopathology of cholecystectomy specimen showed ICPN of biliary and oncocytic type with low-grade dysplasia.

Case Report

A 43-year-old female presented with a history of pain abdomen of 5 days duration. The pain was insidious in onset, gradually progressive, colicky type, in the right upper abdomen. The pain was associated with vomiting five to six times per day that was aggravated by food intake. She had a history of similar episodes of pain in the past. She is a known case of cerebrovascular accident with left hemiparesis, type 2 diabetes mellitus, and systemic hypertension for 5 years and has not been on any medications. On examination, a vague mass measuring 2cm x 2cm was felt in the right hypochondrium, which was firm and tender. Clinical diagnoses like cholelithiasis, GB polyp, and GB malignancies were considered. Laboratory investigations showed low hemoglobin level and erythrocyte sedimentation rate of 90mm at the end of 1 hour. Liver function test showed elevated direct bilirubin, serum glutamic-oxaloacetic transaminase, serum glutamic-pyruvic transaminase, and alkaline phosphatase. The rest of

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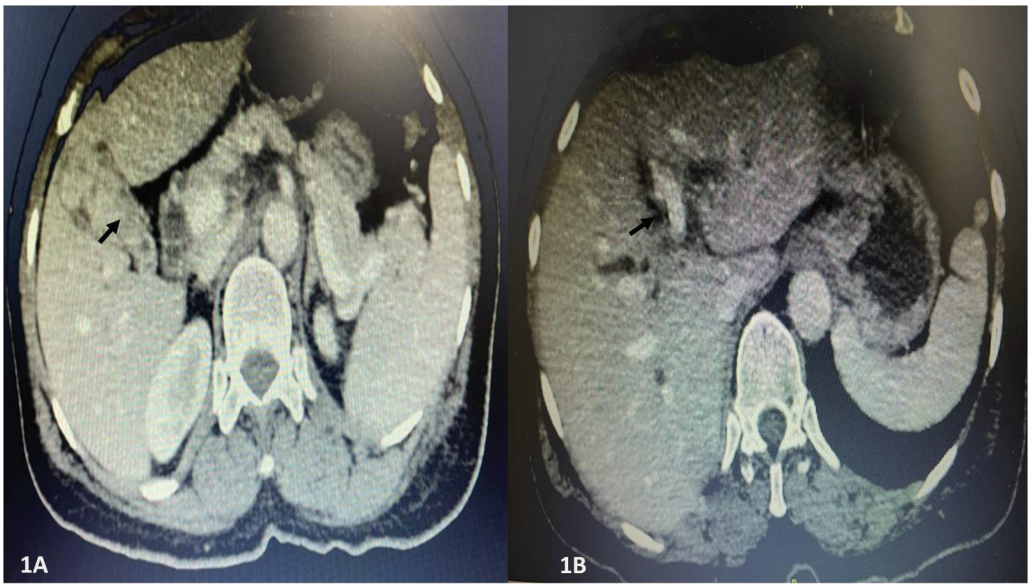

Fig. 1 (**A**) Computed tomography abdomen and pelvis showing a heterogeneously enhancing lesion in the gallbladder lumen, causing irregular luminal obstruction (black arrow). (**B**) Dilated bilobar intrahepatic biliary radicals (black arrow).

the laboratory investigations, including electrocardiogram, renal function test, coagulation profile, and urine analysis, were normal.

The USG abdomen showed a well-defined polypoidal hypoechoic lesion in GB, intrahepatic biliary radical (IHBR) dilatation, and dilated common bile duct (CBD) of 11 mm. The CT (plain and contrast) of the abdomen and pelvis showed a heterogeneously enhancing lesion measuring 21×44 mm in the GB lumen extending from the fundus to the neck, causing an irregular luminal obstruction (►**Fig. 1A**). The lesion extends to the GB wall without pericholecystic extension. There was reactive hyperemia of the liver parenchyma adjacent to the GB fossa. There was dilated bilobar IHBR and extrahepatic biliary radicals secondary to intramural extension of GB mass (►**Fig. 1B**). An enlarged lymph node was also noted in GB fossa. A probable diagnosis of a malignant lesion was made. Esophagogastroduodenoscopy showed features of pangastritis. Linear endoscopic ultrasound showed dilated IHBR, common hepatic duct (CHD), and proximal CBD with echogenic debris in the overdistended GB, spilling over into the cystic duct and the CHD. Guided fine-needle aspiration cytology of this lesion showed very sparse epithelial cells with mild nuclear enlargement and dense sheets of acute and chronic inflammatory cells. There was no evidence of malignancy. Hence, a diagnosis of over-distended GB and CHD with sludge was made. The patient underwent open cholecystectomy with choledochoduodenostomy. The lymph node at the GB fossa was not sampled. Intraoperatively, the GB was distended and adherent to the inferior surface of the liver. Proximal CBD was

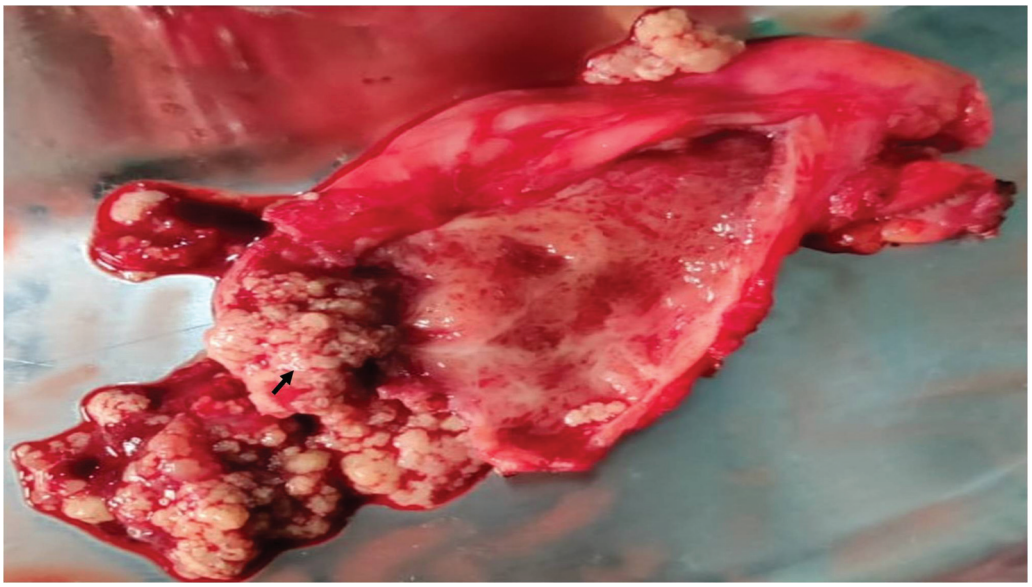

Fig. 2 Gross photograph of gallbladder showing an exophytic papillary mass in lumen at fundus (black arrow).

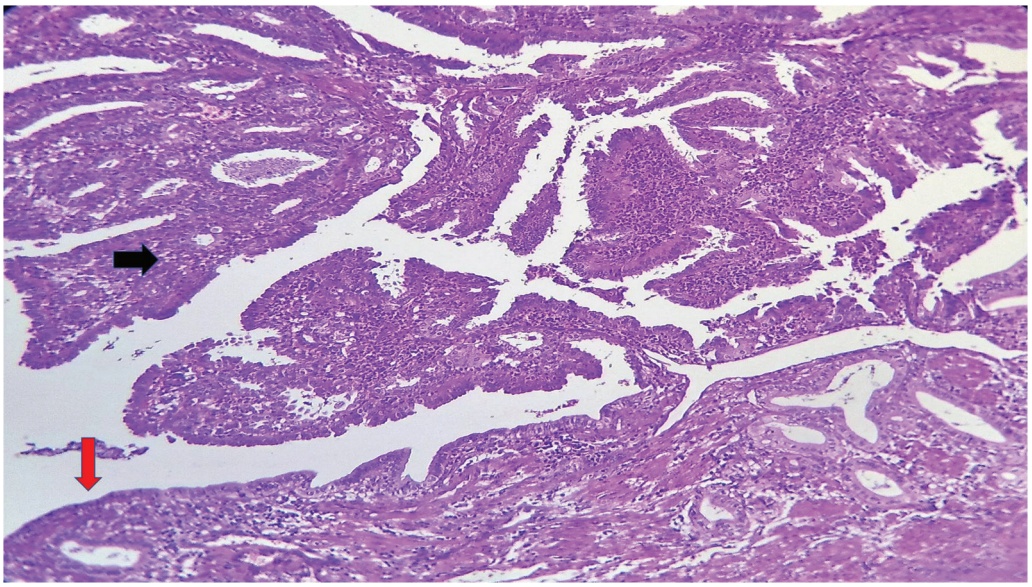

Fig. 3 Histopathology showing gallbladder mucosa (red arrow) with a proliferative, papillary-tubular tumor (black arrow), hematoxylin and eosin, 100x.

dilated, and putty-like material was noted in proximal CBD and GB.

Grossly, we received a cut-open cholecystectomy specimen measuring $5.5 \times 3 \times 2$cm. The cut surface showed a sessile mass with papillary excrescences measuring $1.5 \times 1.4 \times 1.8$ cm (depth) in the fundal area (►**Fig. 2**). Wall was thickened and appeared uninvolved by the tumor. Adjoining mucosa appeared unhealthy and eroded. The cystic duct was unremarkable. Another container with necrotic sludge was also received.

Microscopy showed GB mucosa with a proliferative tumor showing cells arranged in papillary and tubular patterns (►**Fig. 3**). The tumor cells lining the tubules and papillae were cuboidal, having clear-to -eosinophilic cytoplasm and enlarged nuclei with prominent nucleoli (►**Fig. 4**). Oncocytic epithelial cells displayed low-grade dysplasia showing a single-to-stratified layer of cells with enlarged round to oval hyperchromatic nucleus, apical snouting, and abundant eosinophilic granular cytoplasm (►**Fig. 5**). Foamy macrophages were seen in the core of the papillae (►**Fig. 6**). Adjoining mucosa showed flat dysplasia. Subepithelial stroma showed chronic inflammation, Rokitansky-Aschoff sinuses, thickened muscle wall, and subserosal fibrosis. Section from sludge showed tumor cells and purulent exudate. Features were suggestive of ICPN—biliary and oncocytic type with low-grade dysplasia with cholesterolosis and chronic cholecystitis. There was no evidence of invasive carcinoma.

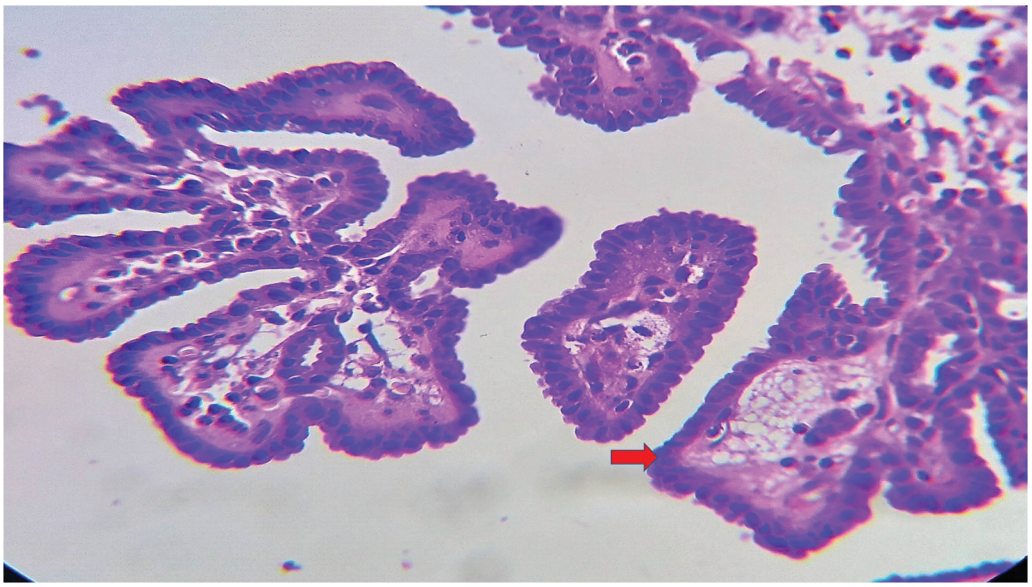

Fig. 4 Tumor cells lining the papillae are of biliary type composed of cuboidal cells (red arrow), hematoxylin and eosin, 100x.

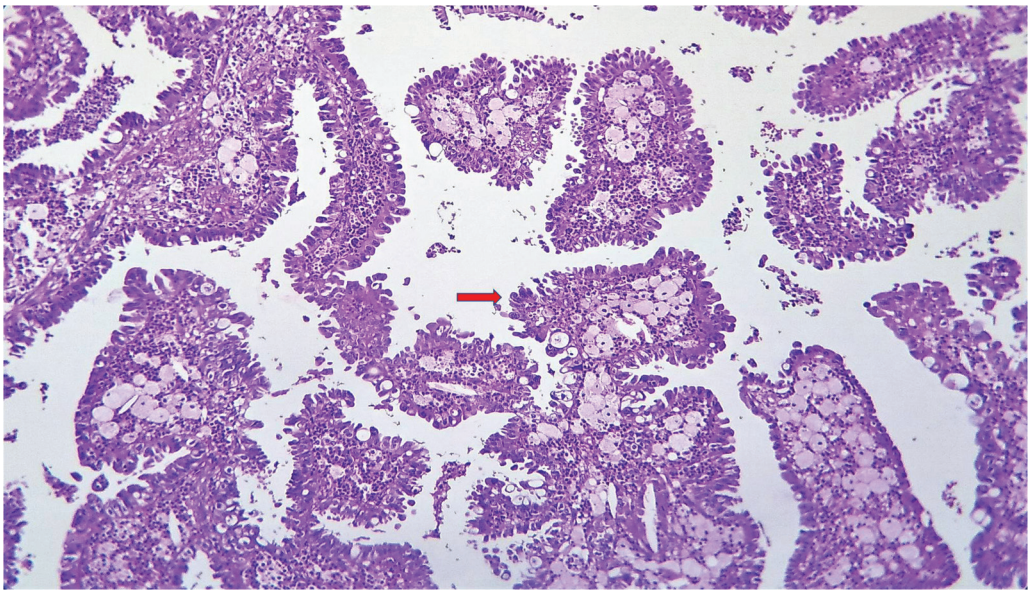

Fig. 5 Oncocytic epithelial cells with apical snouts and abundant eosinophilic cytoplasm with low grade dysplasia (red arrow), hematoxylin and eosin, 100x.

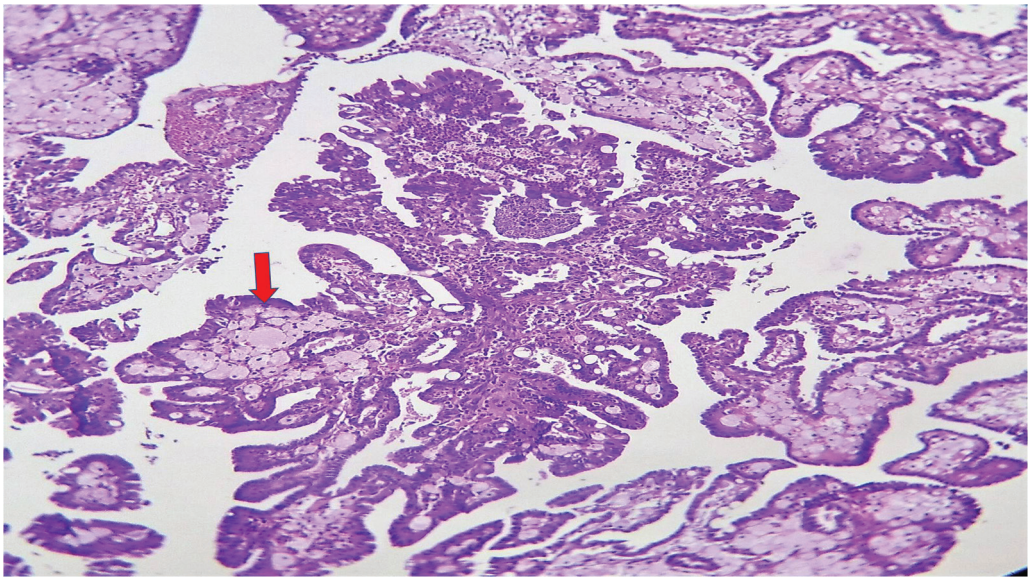

Fig. 6 Foamy macrophages in the core of papillae (red arrow), hematoxylin and eosin, 100x.

The postoperative period was uneventful, and the patient has been on regular follow-up for 7 months.

Discussion

In the 2019 World Health Organization classification of tumors of the digestive system, ICPN is proposed as a unique preinvasive neoplasm of the GB, and lesions with invasive carcinoma components are classified as ICPN with an associated carcinoma. ICPN is a rare entity and accounts for only about 0.5 to 0.6% of GB neoplasms and is often associated with the overproduction of mucin.[1] It is commonly detected incidentally with imaging studies, but in some cases, patients may present with abdominal pain. In USG, ICPN manifests as polypoid lesions. At CT, the mass is hypointense and appears as a filling defect. Strong enhancement is seen in the early phases of the contrast-enhanced study. A hypointense stalk may be identified on T2-weighted MRIs, and diffusion-weighted MRI usually shows restricted diffusion.[2] In our case, a CT scan showed a heterogeneously enhancing lesion extending from the fundus to the neck, causing an irregular luminal obstruction. Cholecystectomy is the mode of treatment for noninvasive ICPN.

Grossly, ICPNs have prominent exophytic growth within the GB or are granular, friable soft-tan excrescences.[3] The papillary (granular) growth usually appears sessile with a broad base, while the pedunculated growths have thin stalks and detach easily. Based on the highest degree of

cytoarchitectural atypia in the epithelium, ICPNs are graded into low grade and high grade. Four morphologically predominant patterns are biliary, gastric, intestinal, and oncocytic.[4] Biliary morphology is the most common pattern, with cuboidal cells having clear to eosinophilic cytoplasm, enlarged nuclei, and prominent nucleoli.[1,5] Gastric morphology is characterized by elongated glands lined by tall columnar cells with abundant pale cytoplasm and basal nuclei. Intestinal morphology is characterized by tall columnar cells with pseudo stratification, cigar-shaped nuclei, and basophilic cytoplasm.[1,6] Oncocytic morphology is characterized by arborizing papillae lined by multiple layers of cells with abundant acidophilic granular cytoplasm and single prominent nucleoli, and it is the least common. In our case, patient underwent cholecystectomy and was diagnosed as ICPN—biliary and oncocytic type with low-grade dysplasia.

The 5-year survival rate for ICPN is 78%.[7] ICPN has a better prognosis as compared to GB carcinoma.[8] Long-term follow-up is suggested after ICPN resection due to the field effect rendering a high incidence of biliary tract carcinoma.[1]

Conclusion

ICPN is a rare and relatively new entity. Thorough sampling is necessary predominantly in biliary morphology and extensive high-grade lesions. Histopathological evaluation is necessary for a definite diagnosis and grading of disease. ICPN has a good prognosis after cholecystectomy.

Conflict of Interest
None declared.

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