

A Rare Case of High-Grade Intracholecystic Papillary Neoplasm in the Gallbladder

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ABSTRACT:

Intracholecystic papillary neoplasm (ICPN) is a rare pre-cancerous lesion. We report a unique case of 52 years-old male who presented with chronic upper abdomen pain, the exact nature of pathology was found after cholecystectomy on histopathological examination that reveals non-invasive ICPN of the gallbladder, unfortunately involving the resection margin with high-grade dysplasia. Due to limited cases recorded globally, definitive guidelines on the management of ICPN are lacking. We suggest long-term surveillance in all cases of incidental ICPN.

Keywords: Intracholecystic papillary neoplasm of gallbladder (ICPN), Intraductal papillary mucinous neoplasm (IPMN), Intraductal papillary neoplasm of bile duct (IPNB).

How to cite this Article:

Ali A, Shahid M, Agha SN, Malik H, Farishta S, Hudaib M. A Rare Case of High-Grade Intracholecystic Papillary Neoplasm in the Gallbladder. *J Bahria Uni Med Dental Coll.* 2023;13(4):308-10 DOI: <https://doi.org/10.51985/JBUMDC2023210>

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BACKGROUND

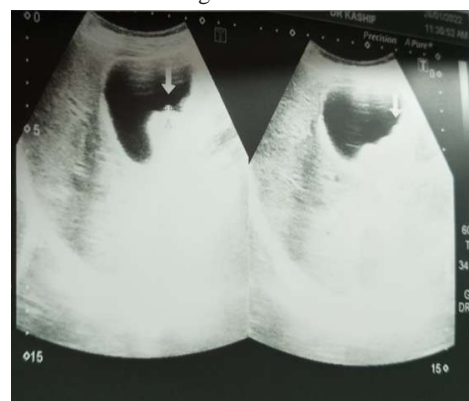
ICPN is described as a grossly apparent, intraluminal developing mass-forming tumour that is histologically lined by epithelia that exhibit papillary/villous lesions as well as tubular structures with fine fibrovascular stalks and little intervening stroma. In addition, the term "ICPN with stromal invasion" also refers to ICPNs that exhibit microscopically discernible stromal invasion without nodular sclerosing reaction in the wall. Rare precancerous lesions of gallbladder cancer include intracholecystic papillary-tubular neoplasms¹. It was found in only 0.4% of gallbladder specimen². The

radiological properties of ICPN have not yet been firmly standardized due to their rarity.^{3,4}

CASE PRESENTATION

A middle-aged male patient aged 52 years presented at the outpatient clinic complaining of frequent right upper quadrant pain and nausea after heavy meals, which had worsened in the past 6 months, with no history of significant weight loss or anorexia. He is known hypertensive for which he has been taking amlodipine for the last 5 years. He had no prior

Figure 1: Upper abdominal ultrasound showed Polyps on the fundus measuring about 0.5x0.3cm.



surgeries or hospitalizations. No history of any addiction. He used to take a mixed diet. On examination, general physical examination and abdominal examination were unremarkable.

His ultrasound abdomen was negative for cholelithiasis but revealed the gallbladder wall was slightly thickened approx. 0.4 cm. and irregular/polypoidal in appearance. A few polyps were seen largest one at the fundus measuring about 0.5 x 0.3cm (overall diameter of 1.5cm) and the proximal two-third common bile duct is dilated measuring about 0.7cm

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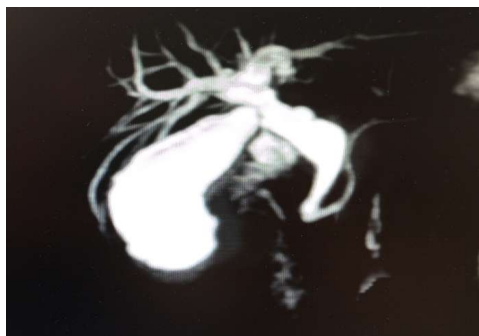
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Received: 19-06-2023
Accepted: 20-09-2023

Figure 2: Preoperative magnetic resonance cholangiopancreatography shows a Distended irregular thick-walled gallbladder and proximal CBD dilatation with distal tapering.



and distal CBD was narrowed. MRCP planned.

MRCP shows irregularly thickened wall gallbladder predominately region of body and fundus with tiny signal void foci. Mild dilatation of intrahepatic biliary channels, Common hepatic duct, and proximal CBD 7.8 mm with the abrupt reduction in caliber in distal CBD. Possibility of smooth stricture in the distal part of CBD. ERCP was not planned because there was no evidence of cholangitis or obstructive jaundice.

His liver function tests were normal, total bilirubin 16 $\mu\text{mol/L}$ (0-17 $\mu\text{mol/L}$), alkaline phosphatase 235 IU/l (65-270 IU/l), alanine aminotransferase 19 IU/l (0-42 IU/l).

His leukocyte count was also within the normal range.

He underwent laparoscopic cholecystectomy, which was difficult but done successfully. Cystic duct and artery clipped separately as shown in Figure 3.

Postoperatively patient develops acute hepatitis which was managed conservatively in the surgical ICU. The patient was discharged on the 9th postoperative day.

Incidentally, on histopathology, we found ICPN Type 1 biliary type with high-grade dysplasia extends to the margin of resection. Negative for invasive malignancy. Fig.5. Post-operative workup for the invasive disease was negative. Including, Ca19-9 was 33.38U/ml (<37U/ml), CEA was 1.13ng/ml (Smoker <5. Non-Smoker <3), AFP was 6.2 (<14.4 IU/ml). All results came out negative. CECT abdomen and pelvis demonstrate streaks of fluid around the liver. The small multi-septated intraperitoneal collection was noted. Intrahepatic ducts are mildly dilated. CBD is dilated (1.2cm) till its distal third where it abruptly reduces in caliber. Few enlarged necrotic lymph nodes are seen alongside the common iliac artery. A few prominent enhancing mesenteric lymph nodes were noted on the right hemi abdomen. See Figure 6.

We enrolled this patient into a surveillance program with 6 weekly Ca 19-9 levels and ultrasound abdomen, And after every three months, a Tri-phasic CT scan abdomen to evaluate gallbladder fossa mass.

Figure 3. Pre-operative image showing cystic duct and artery clipped separately

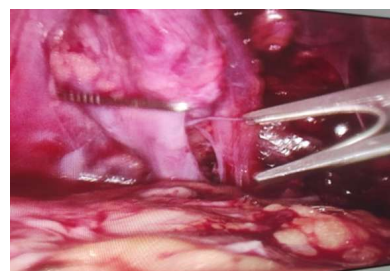


Figure 4: ICPN: Neoplastic growth with papillary pattern having fine fibrovascular stalks. Type 1 Biliary type with high-grade dysplasia.

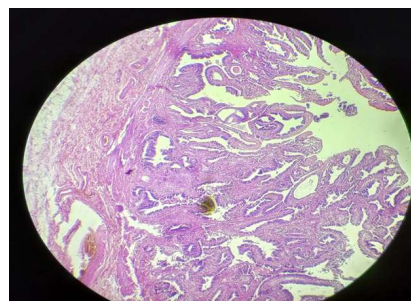


Figure 5: Contrast-enhanced CT abdomen (Sagittal image) showing Small intraperitoneal collection. Dilated proximal CBD. No gallbladder fossa mass



Recurrence was not reported at 14 months of follow-up.

DISCUSSION:

The World Health Organization initially provided a description of the relatively new entity ICPN in 2010³. For the characterization of several mass-forming precursor lesions, such as tubule-papillary adenomas, intestinal adenomas, papillary adenomas, and a few others, Adsay et al. suggested ICPN as a distinct pathologic entity in 2012¹. ICPN is known as “Preinvasive adenocarcinoma of the gallbladder”. It is characterized by an intracholecystic papillary growth that may be connected to invasiveness. Invasive carcinoma is noted in 68 ICPN patients out of 123 that is 55% of ICPN patients, with a frequency of ICPN of less than 0.5%.⁴ Furthermore, about 50% of patients have no symptoms at all, and the features of ICPN are incidental during abdominal radiological investigations⁴. It is exceedingly challenging to distinguish ICPN from gallbladder

polyps and cancer in imaging investigations since their imaging findings are identical.

ICPNs are twice common in women⁵ and approximately 0.5% of cholecystectomy specimens operated for symptomatic cholelithiasis or acute/chronic cholecystitis have them present. These lesions are all described as polypoid/papillary dysplastic neoplasms that manifest multifocal or diffuse growth on the mucosal surface of the gallbladder^{6,10} most commonly involve body and fundus of gallbladder⁹. The cystic duct is a part of the gallbladder in the biliary system, not the extrahepatic bile duct. Additionally, a gallbladder cystic duct ICPN is incredibly uncommon but it is present in our case.⁷

These lesions also have a high rate of invasive malignant transformation and often show at least focal areas of high-grade dysplasia, with > 50% having an associated invasive carcinoma⁶.

ICPN is divided into four morphological subgroups, including biliary, oncocytic, gastric, and intestinal morphologies^{8,9}. The most typical subtype is allegedly the biliary morphology⁸ as in our case. In around half of all resected ICPNs, invasive cancer is discovered, especially in lesions with a mostly biliary architecture may have significant high-grade dysplasia.

These uncommon tumours frequently exhibit an intramucosal papillary or polypoid mass and mucin overproduction. IPMN and IPNB are thought to have certain traits in common with ICPN, although there are some differences as well³.

The ICPN's natural history has not been thoroughly studied. After cholecystectomy, ICPN without aggressive cancer has a favourable prognosis. Those with pre-invasive ICPN have a 5-year survival rate of 78%, compared to those with invasive cancer, who have a 5-year survival rate of approximately 60%¹¹. The overall survival outcome of ICPN is significantly better than that of ordinary-type gallbladder adenocarcinoma which is not associated with ICPN and has a 5-year survival rate of 18 to 30%¹¹. Following the resection of both the ICPN and the IPMN, surveillance is required.

CONCLUSION:

A rare case of high-grade ICPN was incidentally discovered in 52-year-old male after laparoscopic cholecystectomy with a positive resection margin. A distinct pre-invasive neoplasm known as ICPN manifests as intraluminal mass lesions. As we previously noted, some patients will progress more aggressively metaplasia-dysplasia-carcinoma pathway, whereas some may do so via the more passive adenoma-carcinoma pathway¹. Therefore, ongoing surveillance is advised.

Authors Contribution:

Aun Ali: Design, writing the final draft, data collection and analysis
Madeeha Shahid: Research conception, data collection and analysis

Shazadi Neelum Agha: Research conception
Hurais Malik: Data collection and analysis
Sidra Farishta: Data collection and analysis
Muhammad Hudaib: Data collection and analysis

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