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Case Report

A rare case report of Intracholecystic papillary-tubular neoplasm of the gall bladder

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ABSTRACT

The understanding of Intracholecystic Papillary Neoplasm (ICPN) in the gallbladder is a recent development, hypothesized to have similarities in clinical and pathological traits with Intraductal Papillary Mucinous Neoplasm (IPMN) of the pancreas and Intraductal Papillary Neoplasm of the Bile Duct (IPNB). In this report, we present an uncommon instance of Intracholecystic Papillary-Tubular Neoplasms in a 38-year-old male. Although Intracholecystic Papillary Neoplasm (ICPN) is uncommon in the gallbladder lining, it typically presents a more favorable prognosis in contrast to gallbladder adenocarcinoma. Nonetheless, it still possesses the potential for metastatic spread to other organs. Our discussion delves into this patient's case within the context of current literature on ICPN, while also delineating future avenues for enhancing clinical comprehension. Moreover, we emphasize the importance of implementing screening protocols, taking into account identified risk factors, to elucidate the natural course of the disease and deter its progression into invasive gallbladder carcinoma.

1. Introduction

In 2010, the World Health Organization classification first identified Intracholecystic Papillary Neoplasms (ICPN) as a type of gallbladder tumor characterized by dysplastic cells. Previously, this condition was known by various terms including papillary adenoma, papillary in situ carcinoma, and papillary adenocarcinoma of the gallbladder. ICPN is more prevalent in women aged over 60 and has been reported in less than 0.5% of gallbladders removed due to cholelithiasis or chronic cholecystitis, though the imaging features remain unclear.[1–5] This report highlights a rare case of ICPN.

2. Case Report

A 38-year-old male arrived at our hospital reporting dull, aching pain in the right hypochondriac region. Physical examination indicated tenderness in the same area. Laboratory tests conducted upon admission showed elevated levels of aspartate aminotransferase (126 IU/L), alanine aminotransferase (213 IU/L), and gamma-glutamyl transpeptidase (196 IU/L). Abdominal ultrasound revealed calculi in the gallbladder lumen, with the largest measuring 8 mm, as well as a solid nodular hypoechoic mass measuring 10mmX11mm on the lateral wall of the gallbladder, exhibiting focal surface calcification speck with no vascularity. Abdominal CT scan indicated enhancing wall adherent lesions confined within the gallbladder wall, suggestive of a possible inflammatory polyp, with malignancy not conclusively ruled out. Additionally, gallbladder sludge and grade I fatty liver were noted. The patient underwent laparoscopic cholecystectomy,

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during which the gallbladder was found to be distended and adhered to the liver (Figure 1). We received a cholecystectomy specimen that was cut open, presenting in fragmented pieces measuring 6×3×1 cm. Within it, there was a grey-white nodule on the gall bladder wall measuring 50X20mm, accompanied by several crushable stones ranging in color from grey-brown to grey-black. The cut surface revealed papillary excrescence (Fig.2). Microscopic analysis revealed a neoplastic lesion arranged in a tubular papillary pattern, lined by cuboidal to columnar epithelium, with a high nuclear-cytoplasmic ratio, condensed chromatin, slightly irregular nuclear border, and moderate eosinophilic cytoplasm. Tumor infiltration into the gallbladder wall was also observed (Figures 3, 4 and 5). These findings were consistent with Intracholecystic Tubular-Papillary Neoplasms (ICPN). The patient experienced an uncomplicated recovery and was discharged on the third postoperative day. Subsequent follow-up examinations over the past year have not shown any signs of postoperative recurrence.

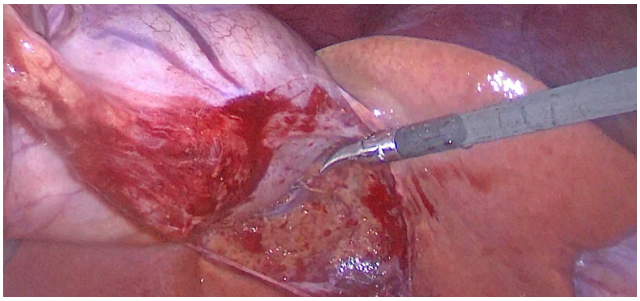

Figure 1: Intra-operative findings: distended gall bladder with adhesions to liver.

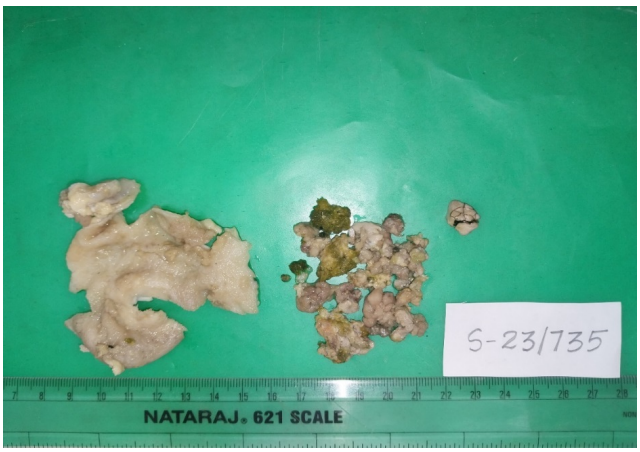

Figure 2: Grossly Cut opened specimen of the gall bladder shows papillary excrescence (red arrow) with multiple grey-brown to grey-black crushable stones.

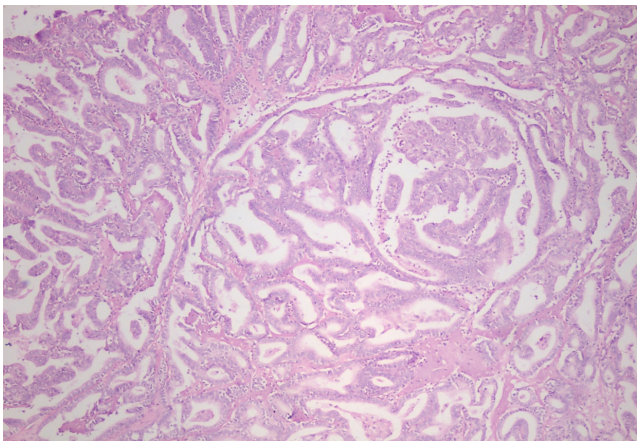

Figure 3: Neoplastic lesion arranged in tubular-papillary pattern.

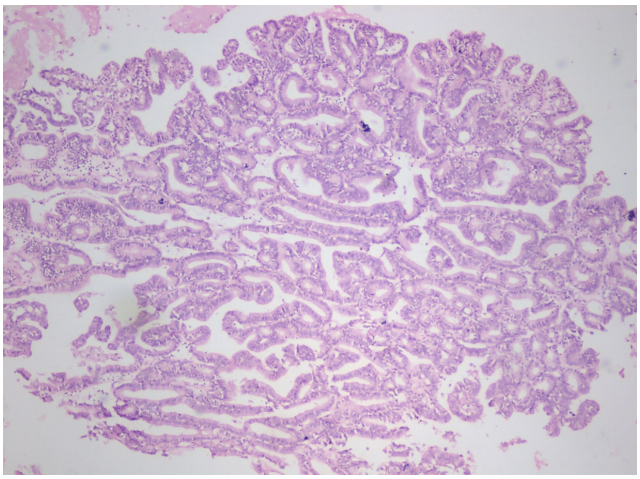

Figure 4: Focal area shows neoplastic lesion arranged in a tubular-papillary pattern, lined by cuboidal to columnar epithelium.

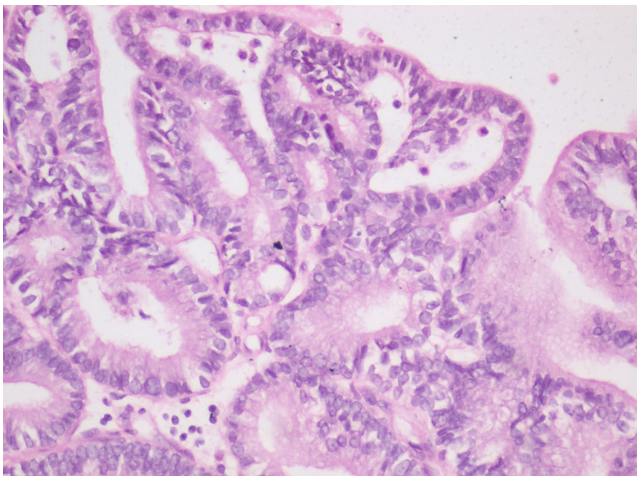

Figure 5: lining by cuboidal to columnar epithelium, with a high nuclear-cytoplasmic ratio, condensed chromatin, slightly irregular nuclear border, and moderateeosinophilic cytoplasm

3. Discussion

In the pancreatobiliary tract, mass-forming tumors consisting of preinvasive neoplastic cells and presenting as clinically detectable masses (≥1.0 cm) are collectively classified as follows:

1. Intraductal Papillary Neoplasms (IPNs) in the bile ducts.
2. Intracholecystic Papillary-Tubular Neoplasms (ICPNs) in the gallbladder.
3. Intra-Ampullary Papillary-Tubular Neoplasms (IAPNs) in the ampulla.
4. Intraductal Papillary Mucinous Neoplasms (IPMNs) or Intraductal Tubulopapillary Neoplasms (ITPNs) in the pancreas.

These tumoral intraepithelial neoplasms follow an adenoma-carcinoma sequence and display distinct clinicopathologic, immunophenotypic, molecular characteristics, and biological behavior compared to the non-tumoral (flat)-type preinvasive neoplasms of the respective organs. They share common features such as an exophytic nature, expression of various cellular lineages (biliary, gastric, intestinal, oncocytic), and a spectrum of dysplastic changes (adenoma-carcinoma sequence), often occurring in varying degrees. While distinct from the conventional invasive cancers of these sites, their mass-forming nature can sometimes lead to misdiagnosis.[2]

ICPNs are more commonly diagnosed in women, with a prevalence twice as high as in men. However, our case involved a male patient. The age range of affected individuals spans from 20 to 94 years. Approximately 50% of patients with ICPN present with right upper outer quadrant pain; however, in the remaining 50%, it is incidentally detected.[6,7] In our case, the patient presented with complaints of right hypochondriac region.

Macroscopically, Intracholecystic Papillary Neoplasms (ICPN) are identifiable by prominent exophytic growths within the gallbladder or soft, friable soft-tan excrescences, often associated with mucin overproduction. These growths may or may not exhibit a stalk. Microscopically, ICPN displays architectural features such as papillary, tubular, or a combination of patterns, the proportions of which can vary depending on the percentage of each pattern present. Lesions primarily exhibiting a papillary pattern, constituting over 75% of the total lesional area, are categorized as papillary, while those with less than 25% are categorized as tubular, and the remainder are classified as tubular-papillary lesions. The papillary pattern accounts for the majority of cases, encompassing around 43% of ICPN cases. Additionally, ICPN can display both low-grade dysplasia and areas with coexistent high-grade dysplasia.[8]

Cytologically, Intracholecystic Papillary Neoplasms (ICPN) are classified based on the predominant cell type present. ICPN can be categorized into the following types: pancreaticobiliary, gastric, intestinal, and oncocytic types.[2]

Immunohistochemical analysis is conducted using cell lineage markers, which have also been utilized for the subclassification of gastrointestinal tract tumors. These markers include:

1. MUC1: a marker of pancreaticobiliary differentiation.
2. MUC2: indicative of intestinal (goblet cell) differentiation.
3. CDX2: an intestinal transcription factor.
4. MUC5AC: a foveolar mucin marker.
5. MUC6: a pyloric marker.[9]

Differentiating between Intracholecystic Papillary Neoplasms (ICPN) and other gallbladder tumors using imaging studies poses challenges. CT scans and MRI findings are nonspecific and can be observed in other gallbladder tumors as well. Furthermore, Fluorodeoxyglucose (FDG) findings also lack discriminatory value. However, endoscopic ultrasound (EUS), incorporating techniques such as intraductal ultrasound (IDUS) or peroral cholangioscopy (POCS), has proven to be useful. Consequently, EUS and POCS may offer an improved definition of ICPN compared to other imaging modalities. Hence, clinicians should acquaint themselves with the characteristics of ICPN and strive for accurate diagnosis utilizing multiple imaging techniques.[10,11] Selecting the most appropriate surgical approach for ICPN can be challenging. Simple cholecystectomy suffices for cases where ICPN is confined to the gallbladder mucosa without invasion. However, approximately half of ICPN cases involve an invasive component. Choosing the optimal surgical procedure, which may include extended cholecystectomy, bile duct resection, or pancreaticoduodenectomy, is crucial to ensure complete oncological resection of the tumor. Additionally, close postoperative monitoring is essential, particularly for patients with advanced cancer originating from the tumor.[2,10–14]

Several studies have indicated that Intracholecystic Papillary Neoplasms (ICPN), whether with or without invasive carcinoma, generally demonstrate a favorable prognosis compared to other types of gallbladder carcinoma.[1]

4. Conclusion

ICPN represents a rare neoplasm that poses challenges in detection through conventional imaging modalities. Despite its rarity, a subset of cases can progress to invasive carcinoma. The absence of surveillance and diagnostic protocols may lead to delayed diagnoses, resulting in a poorer prognosis compared to cases diagnosed earlier and promptly treated with surgical removal. We anticipate that our contribution will aid in raising awareness among

clinicians regarding ICPN and related neoplasms, thereby facilitating timely screening and diagnosis in patients at risk of developing these conditions.

5. Source of Funding

None.

6. Conflicts of Interest

There is no conflict of interest.

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