A Case of Intracholecystic Papillary-Tubular Neoplasm

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Abstract

The World Health Organization (WHO) defines intracholecystic papillary neoplasms (ICPNs) as gallbladder lesions of intraductal papillary neoplasms of the bile duct (IPNB). We present a case of ICPN that was incidentally diagnosed following a cholecystectomy for cholecystitis and cholelithiasis. Abdominal ultrasonography and computed tomography showed thickening of the gallbladder wall and cholelithiasis but were not specific for a gallbladder tumor. Histopathological examination revealed an intracholecystic papillary-tubular neoplasm associated with a moderately differentiated adenocarcinoma.

Keywords: Intracholecystic papillary-tubular neoplasm; ICPN; Cholecystitis; Cholelithiasis cholecystectomy

Introduction

Intracystic papillary neoplasm is a form of intraluminal papillary neoplasms of the extrahepatic biliary tree that occurs in the gallbladder. The World Health Organization (WHO) defines intracholecystic papillary neoplasms (ICPNs) as gallbladder lesions of intraductal papillary neoplasm of the bile duct. ICPN is a preinvasive lesion that can have a pancreatobiliary or intestinal phenotype and may be associated with invasive adenocarcinoma which should be staged separately [1]. Here we discuss a case that presented with symptoms of acute cholecystitis and a ventral incisional hernia, and was incidentally found to have an ICPN associated with an intramucosal adenocarcinoma.

Case Report

Investigations

This patient is a 64-year-old male admitted to the hospital with right upper quadrant pain associated with nausea and vomiting. The patient had a past history of a ventral incisional hernia that was repaired with an underlay biologic mesh 6 years prior to presentation. He had undergone distal pancreatectomy and splenectomy for a pancreatic neuroendocrine tumor 8 years prior to presentation. Blood tests on admission showed white blood cell (WBC) 8.7 (normal range: 3.8 - 10.6 × 10^3/µL), red blood cell (RBC) 3.03 (normal range: 4.5 - 5.9 × 10^6/µL), hemoglobin (Hb) 7.8 (normal range: 13.5 - 17.5 g/dL), hematocrit (HCT) 25.6% (normal range: 40.2-50.2%), mean corpuscular volume (MCV) 84.5 (normal range: 80 - 100 fL), mean corpuscular hemoglobin (MCH) 25.7 (normal range: 26 - 34 pg), mean corpuscular hemoglobin concentration (MCHC) 30.5 (normal range: 31.1 - 36.6 g/dL), blood cell distribution width (RDW)-coefficient of variation (CV) 15.4 (normal range: 11.5-14.5%), platelets 155 (normal range: 130 - 400 × 10^3/µL). Abdominal computed tomography (CT) scan showed recurrent ventral hernia and cholelithiasis with no other acute findings (Fig. 1). Abdominal ultrasonography showed chole-
lithiasis with thickening of the gallbladder wall (Fig. 2). A hepato-iminodiacetic acid (HIDA) scan revealed non-visualization of the gallbladder consistent with cholecystitis.

**Diagnosis and treatment**

A diagnosis of acute cholecystitis and cholelithiasis was made and the patient was scheduled for surgery. He underwent open cholecystectomy due to prior extensive surgeries and the need to repair the ventral hernia. Resection and anastomosis of a segment of small bowel was performed due to extensive adhesions. The gallbladder was distended with surrounding adhesions consistent with the diagnosis of chronic cholecystitis.

The macroscopic findings of the resected specimen showed an intact saccular gallbladder measuring 14.0 × 7.5 × 6.0 cm in size with a lilac serosa. The gallbladder wall measured 0.2 cm and the mucosa was bile stained velvety with yellow stippling. There was a 4.5 × 2.5 × 0.8 cm exophytic soft mass, 1.0 cm from the cystic duct margin. The lumen contained a green thick sludge and yellow calculi measuring 3.5 × 3.0 × 2.0 cm in aggregate. Microscopic findings showed an intracholecystic papillary-tubular neoplasm (Figs. 3, 4) involving the lamina propria associated with a moderately differentiated biliary type intramucosal adenocarcinoma (Fig. 5). Cholelithiasis and cholesterolosis were present. The ICPN does not invade into the muscularis and had no lymphovascular or perineural invasion. The cystic duct margin was uninvolved, and no lymph nodes were dissected. Pathology stage was pT1aNXM0.

**Outcome and follow-up**

The post-operative period was complicated by respiratory failure, but the patient made a full recovery and was discharged home. The patient was seen 3 months after the surgery in the clinic and was completely asymptomatic and doing well.

**Discussion**

This case is presented as a rare diagnosis of ICPN presenting as an incidental finding in the gallbladder. The lack of specific symptoms and the incidental nature of the diagnosis are unfortunately common in ICPN cases. This case illustrates such diagnostic challenge which can lead to a later diagnosis.
patients with cholelithiasis develop carcinoma of the gallbladder [1]. It is estimated that 20% of all ICPN cases present with associated cholelithiasis [3].

Around half of all ICPN and gallbladder carcinomas are diagnosed incidentally with other half usually presenting with non-specific symptoms such as right upper quadrant pain resembling chronic cholecystitis [1, 3]. Imaging studies such as CT and ultrasonography may aid in the detection of gallbladder neoplasms [1]. This patient’s abdominal ultrasound and CT showed cholelithiasis and gallbladder wall thickening but was not particularly specific for a mass. Imaging may not be able to distinguish between a gallbladder stone and a tumor which highlights the difficulty of detecting ICPNs radio-graphically as has been shown in other studies. Some studies estimate that up to half of ICPN cases are detected incidentally and up to 10% are missed on imaging studies [3].

The 2010 WHO classification introduced the definition of intracystic papillary neoplasm as gallbladder lesions of intraductal papillary neoplasm of the bile duct (IPNB). Intracystic papillary neoplasm is classified as a premalignant lesion of the biliary system. The classification does not provide specific diagnostic criteria but rather classifies intracystic papillary neoplasm into intraluminal papillary neoplasms as opposed to adenomas [1]. These two categories were unified to form “intracholecystic papillary neoplasms” in 2012 by Adsay et al [3]. In their study, Adsay et al defined ICPNs as gallbladder neoplasms that are intramucosal, preinvasive neoplastic (dysplastic), mass forming and exophytic, compact, ≥ 1.0 cm in size, and distinct from the neighboring mucosa [3].

ICPN is a form of intraluminal papillary neoplasms of the extrahepatic biliary tree that occurs in the gallbladder. Low-grade lesions were previously referred to as “papillary adenomas” whereas high-grade lesions were referred to as “non-invasive papillary carcinomas”. Invasive adenocarcinoma may arise with intracystic papillary neoplasms. Such lesions usually have high-grade intraepithelial neoplasia characterized by complex papillary structures and should be reported and staged separately [1].

ICPN and IPNB are histologically similar [1]. IPNB shares features with intraductal papillary mucinous neoplasm (IPMN) of the pancreas including intraluminal growth [5]. The main difference between ICPN and IPNB is the anatomical location of the neoplasm. Other key distinguishing features include greater architectural complexity, cytological atypia, and increased mitotic figures seen in high-grade intracycystic papillary neoplasms. The majority of ICPNs have a biliary phenotype as opposed to the intestinal phenotype of papillary adenomas but they may overlap and can be difficult to distinguish from each other [1].

Prognosis for patients presenting with gallbladder cancer generally depends on the histological type and extent of the disease. Adenocarcinomas of the gallbladder confined to the lamina propria appear to be cured with a simple cholecystectomy as they do not metastasize. However, invasive adenocarcinomas extending through the entire thickness of the gallbladder wall have a 10-year survival rate of 30%. The best prognosis is associated with non-invasive intracycystic papillary neoplasms as they rarely metastasize regardless of size, cell phenotype, and degree of differentiation with a 5-year survival
rate of 78% [1, 3]. This patient had an early stage lesion and should be cured with a simple cholecystectomy. He was felt to not require further surgery due to the early T-stage.

Conclusions

ICPN is an uncommon tumor of the gallbladder that can be challenging to identify and diagnose both clinically and radiographically especially when accompanied by a different pathological process. This case report demonstrates the diagnostic challenge in a case presenting with acute symptoms obscuring an underlying ICPN.

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Conflict of Interest

None to declare.

Informed Consent

Subject consent has been waived under the IRB-approved study protocol and the identity of the subject has been protected.

Author Contributions

Each named author has substantially contributed to conducting the underlying research and drafting this manuscript.

Data Availability

Data supporting the findings of this study are available within the article.

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