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Intracholecystic Papillary-Tubular Neoplasms (ICPN) of the Gallbladder

Intracholecystic Papillary-Tubular Neoplasm (ICPN) is a rare tumor characterized by intraluminal papillary growth which may be associated with invasive carcinoma. In this study, we aimed to present the patient with the final pathologic diagnosis of end-stage ICPN presenting with the preliminary diagnosis of Gallbladder cancer.

KEY WORDS: Cholecystectomy, Intracholecystic papillary neoplasm, Gallbladder cancer

Introduction

Intracholecystic tubulopapillary neoplasms are defined as preinvasive neoplasms, which form a distinct mass in the gallbladder mucosa. Since these lesions may include severe epithelial dysplasia and an invasive carcinoma component, detailed evaluation is important. The World Health Organization 2010 classification distinguishes two categories, the "adenomas" and the "intracystic papillary neoplasms"1 but without providing specific diagnostic criteria and thus allowing significant overlapping.
In 2012, Adsay et al. [2] proposed unification of those lesions under the category of "intracholecystic papillary-tubular neoplasm" (ICPN) identifying common morphological, immunohistochemical and clinical characteristics. Intracystic papillary neoplasm (ICPN) of the gallbladder is a preinvasive neoplastic lesion and is considered to share similar characteristics with intraductal papillary mucinous neoplasm (IPMN) and intraductal tubulo papillary neoplasm of the pancreas and intraductal papillary neoplasm of the extrahepatic bile duct [3].
In the literature, adenomas are generally considered to be benign (especially if <1 cm), intracholecystic papillary neoplasms have been reported to be generally associated with invasive tumors [2].
We present a case of an unusual premalignant gallbladder neoplasm.

Case Presentation

A female patient aged 52 years came to our hospital complaining of chronic right upper quadrant pain. Physical examination was normal. She was investigated with upper abdominal ultrasound that was negative for chololithiasis and showed polipoid lesions in the gallbladder wall.
Her laboratory values were within normal limits, with total bilirubin of 0.63 mg/dl, alkaline phosphatase (ALP) at 63 U/l, and γ- GT 15 U/l. The blood cell count tests were normal. Serum tumor markers were within normal limits.
The patient was further studied with magnetic resonance imaging, and magnetic resonance cholangiopancreatography that proved simple hepatic csyt and the number of polypoid lesions of the gallbladder wall.

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Fig. 1: Magnetic resonance cholangiopancreatography that proved simple hepatic csyt and the number of polypoid lesions of the gallbladder.

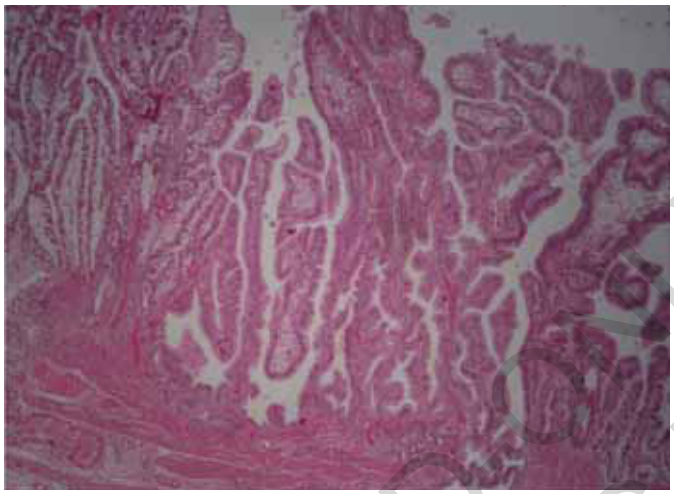

Fig. 2: H&E X40 the polypoid lesion was composed of the cells had abundant eosinophilic cytoplasm, hyperchromatic oval-round nuclei, mild to moderate atypia.

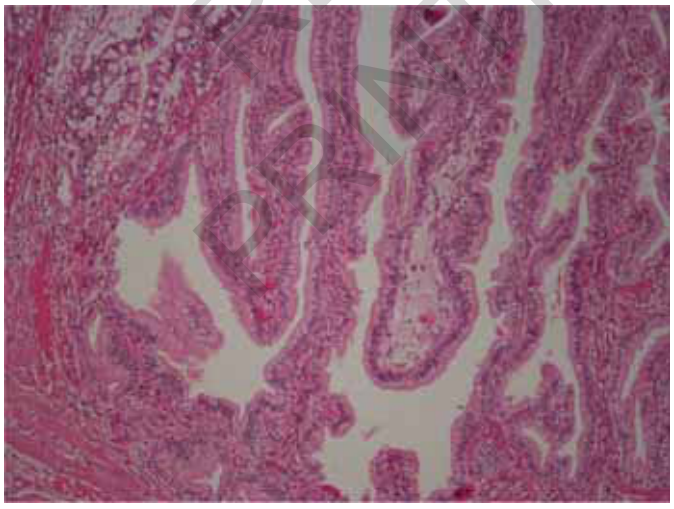

Fig. 3: H&E X100 the polypoid lesion was composed of the cells had abundant eosinophilic cytoplasm, hyperchromatic oval-round nuclei, mild to moderate atypia.

Intrapancreatic portion was normal (Fig. 1). The investigation was negative for cholelithiasis and was otherwise unremarkable. Pancreaticobiliary junction was normal. Cholecystectomy was performed with a preoperative suspicion of gallbladder tumor. The macroscopic examination of the resected specimen showed multiple polypoid lesions of 0.5 cm in size in the mucosa.

The gallbladder was sent frozen section and a tumor was not detected in the frozen section. Histologically, polypoid lesions showed a tubulopapillary configuration consistent with Intracholecystic Papillary-Tubular Neoplasms (ICPN) of the Gallbladder (Figgs. 2, 3).

The patient had an uneventful recovery and left the hospital on the fifth postoperative day.

Discussion

Intraepithelial neoplasias are preinvasive neoplastic lesions found throughout in the digestive system, and when such lesions are discovered in the gallbladder, they are referred to as ICPN [2,4].

Intracholecystic papillary-tubular neoplasms (ICPNs) are uncommon lesions that occur in the gallbladder and are categorized under an umbrella of related neoplasms. These clinically detectable dysplastic lesions (1.0 cm) are similar to intraductal papillary neoplasms (IPNs) in the bile ducts as well as intraductal papillarymucinous neoplasms (IPMNs) and intraductal tubulopapillaryneoplasms (ITPNs) that develop in the pancreas [2,5].

ICPNs are incidentally found at only 0.4% of cholecystectomies. Approximately 6.4% of gallbladder cancers carry an ICPN component, indicating that ICPNs can progress to gallbladder cancer. Patients with ICPNs are typically clinically similar to those presenting with cholelithiasis, cholangiocarcinoma or gallbladder cancer.

In a study by P. Paliogiannis et al., a preneoplastic/neoplastic lesion was detected incidentally in 8.6% of cases after elective cholecystectomy [6]. The diagnosis of ICPN is most commonly made only after surgery and pathologic evaluation of surgical specimen. As discussed, the clinical presentation will vary and the preoperative indications for cholecystectomy are often for common symptoms such as biliary colic related to cholelithiasis. According to Adsay et al [2].

ICPNs can be of papillary (43 %), tubular (23%), or mixed (31%) configuration and of biliary (50%), gastric (36%), intestinal (11%), or oncocytic (9%) cellular lineage. Biliary type ICPNs commonly express MUC1, a marker of biliary differentiation; gastric type ICPNs express MUC5AC; intestinal type ICPNs express CK20; and oncocytic type ICPNs express HepPar. Mixed forms are common. Biliary phenotype and MUC1 expression are bad prognostic factors, correlated to progression to carcinoma and worse prognosis. ICPN component at invasive cancer usually is of papillary configuration and

has a more extensive component of high-grade dysplasia, indicating a stepwise progression, to carcinoma [2].
The overall prognosis for ICPNs is significantly better than thatof invasive carcinomas of the gallbladder, but also depend on thedegree of invasion within the ICPN. The 3- and 5-year survival for noninvasive ICPN lesions is 90% and 78% versus 60% and 60% for invasive lesions [2,5].
As stated in the study conducted by Panebianco A. et al., because of the possibility of incidental gallbladder cancer, surgery should be performed carefully in cases of cholecystitis or when gallbladder neoplasm and/or cancer is suspected preoperatively, due to risk of tumor spread during surgery
(In summary, this report presented a rare case of ICPN. Surgeons and surgical pathologist should be familiar with the disease which requires meticulous clinicopathological evaluation and careful patient management.

Riassunto

La neoplasia papillare-tubulare intracholecistica (ICPN) è un tumore raro caratterizzato da crescita papillare intraluminale che può essere associata a carcinoma invasivo. In questo studio, abbiamo mirato a presentare al paziente la diagnosi patologica finale dell'ICPN allo stadio terminale presentando la diagnosi preliminare del carcinoma della cistifellea.

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