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Intracholecystic papillary - Tubular neoplasm: A case report

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Abstract

Background: Intracholecystic Papillary-Tubular Neoplasm (ICPN) is defined as a rare pre-invasive lesion, with a characteristic papillary architecture on microscopy, similar to the intraductal papillary neoplasm of the bile duct, and the intraductal papillary mucinous neoplasm of the pancreas.

Case presentation: A 63 year old woman presented with a one-month history of abdominal discomfort. An abdomino-pelvic CT-scan was done and showed an over distended gallbladder harboring a 3 cm slightly hyperdense mass-like structure. Ultrasound revealed a well-defined echogenic polypoid mass with a large base and a vascularized pedicle. She underwent laparoscopic cholecystectomy. Pathological examination was diagnostic of an Intracholecystic Papillary-Tubular Neoplasm (ICPN).

Conclusion: ICPNs are rare, mass forming, neoplastic precursor lesions, measuring 1 cm or more. They have different types of histologic differentiation, and each type is associated with a different prognosis. They should be adequately sampled, in order to look for an invasive component.

Keywords

Intracholecystic papillary-tubular neoplasm; surgical pathology; gastrointestinal pathology; pre-invasive lesion; laparoscopic cholecystectomy.

Abbreviations

ICPN: Intracholecystic papillary-tubular neoplasm; BilIN: Biliary intraepithelial neoplasia; CT-scan: Computerized tomography-scan; PAS: Periodic acid schiff; MUC5AC: Mucin 5AC; MUC6: Mucin 6; CK20: Cytokeratin 20; CDX2: Caudal type homeobox 2; MUC2: Mucin 2; HepPar: Hepatocyte paraffin 1.

Introduction

Neoplastic precursors of the gallbladder are separated into two categories [1]. The first category consists of flat dysplastic lesions that undergo carcinogenesis following a metaplasia-dysplasia pathway.

These lesions are lumped under Biliary intraepithelial Neoplasia, and are histologically separated into BilIN1, BilIN2, and BilIN3 based on architectural and cytologic criteria. The second category consists of mass forming pre-invasive lesions, which the 2010 WHO classification divides into two groups: Intracystic papillary neoplasms and adenomas. Since no definite diagnostic criteria were provided to separate these two entities, Adsay et al. [2] proposed the use of the broad term "Intracholecystic papillary-tubular neoplasms", or ICPNs, to unify the lesions in this category. We hereby present the case of a 63-year-old Female patient who presented with an intracholecystic papillary-tubular neoplasm.

Case Presentation

A 63-year-old woman presented with a one-month history of diffuse abdominal discomfort. A gastroscopy and colonoscopy were performed and were negative for abnormal findings. An abdomino-pelvic CT-scan followed and showed an over distended gallbladder harboring a 3cm slightly hyperdense mass-like structure. The rest of the gallbladder wall was otherwise normal in thickness. No biliary ductal dilation or gross abnormalities were seen in the pancreatic bed. Specific etiologies such as an echogenic sludge ball could not be ruled out by the CT-scan, and an abdominal ultrasound was recommended. The latter showed a gallbladder of normal dimensions and wall thickness. A well-defined echogenic polypoid mass with a large base and a vascularized pedicle was once again noted in the anterior wall (Figure 1). The patient was thus scheduled for laparoscopic cholecystectomy.

Gross examination of the cholecystectomy specimen revealed a friable and fragmented exophytic polyp measuring 2 x 1.5 x 1.5 cm. There was no gross evidence of an infiltrative process. The rest of the gallbladder mucosa was within normal limits. Sections of the polyp and adjacent wall were submitted for histologic evaluation.

Microscopic examination showed an exophytic structure exhibiting a complex exuberant papillary proliferation associated with tubular formations (Figure 2A, B & C). The epithelial cells showed basally located mildly atypical nuclei compressed by large cytoplasmic clear vacuoles (Figure 2D). PAS and Alcian Blue special stains highlighted foci of both intracellular and extracellular mucinous secretions (Figure 3). The intervening fibrous stroma was punctuated by a mononuclear lymphoplasmacytic inflammatory infiltrate. No evidence of invasive malignancy was identified. The remaining cholecystic mucosa demonstrated a variably flat to focally hyperplastic epithelium with cystic glandular invaginations and pyloric gland metaplasia.

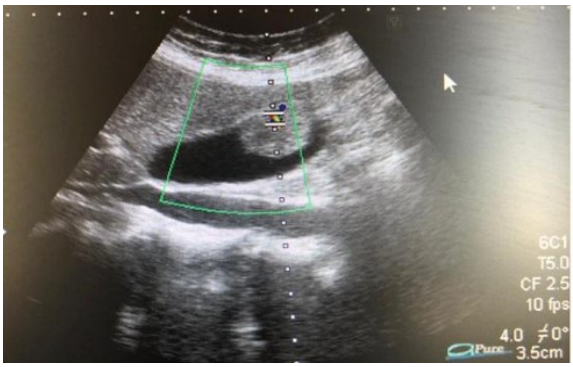

Figure 1: Gall-bladder that is normal in dimension, with thin wall. Evidence of anterior wall well-defined echogenic image.

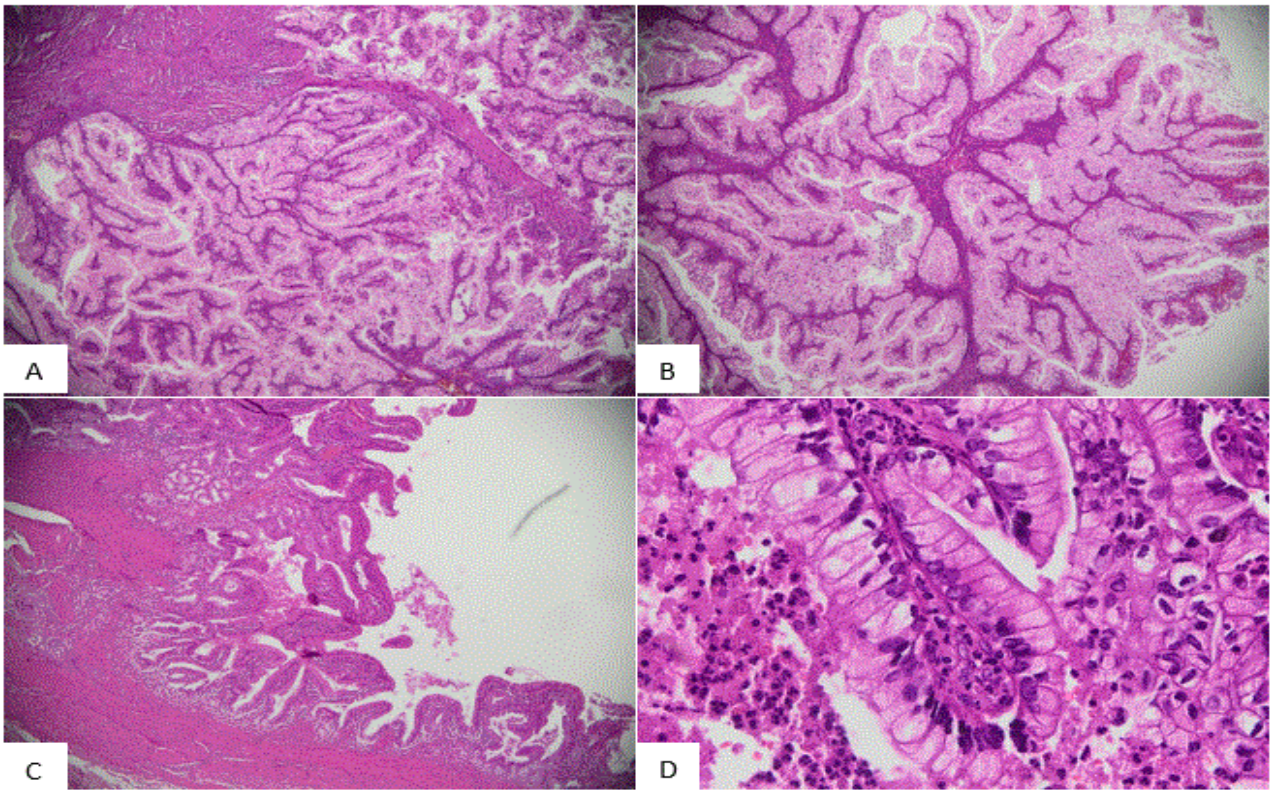

Figure 2: Hematoxylin and Eosin stain. A, B- 4x magnification showing papillary proliferation; C- 4x magnification showing tubular formation with adjacent normal mucosa; D- 40x magnification showing basally located mildly atypical nuclei compressed by large cytoplasmic clear vacuoles.

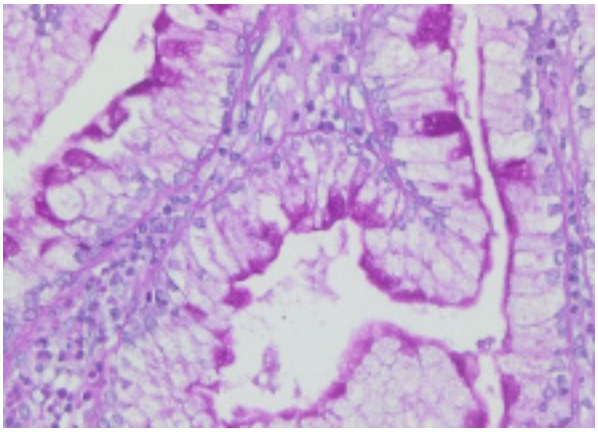

Figure 3: Periodic Acid Schiff (PAS), highlighting a focus of intracellular mucinous secretions.

Discussion

Epidemiology

ICPNs are rare lesions [1-5]; their incidence in cholecystectomy specimens varies between 0.4 and 0.61% [2,3]. Female patients are more commonly affected than men [1-5] with a 2/1 ratio [1-3]. According to a study by Argon et al [6], the mean age at presentation is 63 years (range 32 to 87 years). Clinical presentation is variable; while some patients are asymptomatic, most will present for non-specific right upper outer quadrant pain, mimicking other more common conditions such as cholelithiasis and cholecystitis [2,5].

Definition and gross finding

ICPNs consist of mass-forming, exophytic, intramucosal lesions that occur more commonly in the body or fundus of the gallbladder and are usually 1 cm or larger. They are compact, and should be distinct from the adjacent gallbladder mucosa. Grossly, they are soft and friable, sometimes presenting with a stalk.

Histopathologic appearance

Architecture

According to Adsay et al [2], ICPNs' growth patterns can be divided into three categories:

1. Papillary (43%), should the lesion have >75% papillary or villous growth;
2. Tubular (26%), should the lesion have >75% tubular growth;
3. Tubulopapillary (31%), should the lesion demonstrate an admixture of tubular and papillary structures.

Histologic differentiation and risk of invasive carcinoma:

Various cell lineages can be observed in the tumoral proliferation [7]:

1. Biliary-type epithelium is the most prevalent according to Adsay et al [2,7], with an incidence of 50%. It is characterized by an epithelial lining composed of cuboidal to columnar cells with non-mucinous eosinophilic cytoplasm. MUC1 is positive in 66% of cases. It is often associated with high grade dysplasia and invasive carcinoma [7];
2. Gastric foveolar-type epithelium (16%). The epithelial lining is composed of tall columnar cells with abundant, pale, mucinous cytoplasm showing MUC5AC positivity in all cases. Fifteen percent of this histologic tumor type progress to invasive carcinoma [7];
3. Gastric pyloric-type epithelium (20%). The epithelial lining is composed of glands lined by cuboidal cells without intracytoplasmic mucin formation, showing MUC6 positivity in 92% of cases. Very rarely associated with invasive carcinoma [7];
4. Intestinal-type epithelium (8%) characterized by pseudostratified columnar, cigar-shaped nuclei with conspicuous nucleoli. The lining shows CK20 positivity in all cases, CDX2 positivity in 75% of cases and MUC2 positivity in 50% of cases [7];
5. Oncocytic-type epithelium (6%) characterized by cells with a high eosinophilic cytoplasm, and a round central nuclei (5), which shows HepPar and MUC6 positivity in 17% of cases [7].

Grades of dysplasia

ICPNs exhibit a variable degree of dysplasia that ranges from low to high-grade depending on the degree of atypia. The presence of a papillary architectural pattern, the predominance of a non-pyloric cell lineage and high grade dysplasia are all associated with an increased risk of associated invasive carcinoma [7].

Prognosis

Compared to invasive carcinomas of the gallbladder with no ICPN component, ICPNs with an associated invasive malignancy have a better prognosis with a lower incidence of lymph node metastasis [2,3,7,8]. They are generally discovered early due to their exophytic nature causing early symptoms. Therefore, the invasive component is usually minimal at the time of diagnosis. As such, when invasive adenocarcinoma of the gallbladder is associated with ICPN, patients are proven to have a longer median survival of 35 months, versus 18 months for conventional adenocarcinomas of the gallbladder.

Non-invasive ICPNs have a 3 year survival rate of 90%, and a 5 year survival of 78%. Invasive lesions have a 60% survival rate at 3 and 5 years. Gallbladder carcinomas have a 5 year survival rate of less than 5 % [2,3].

Conclusion

We presented a case of an intracholecystic papillary tubular neoplasm. These tumors are rare, mass forming, neoplastic precursor lesions, measuring 1 cm or more. They have different types of histologic differentiation, and each type is associated with a different prognosis. The biliary-type ICPN is the most common form, and it is commonly associated with high-grade dysplasia and invasive carcinoma. ICPNs should be adequately sampled, in order to look for an invasive component. Even when these tumors are associated with an invasive component, they have a better prognosis, compared to the conventional adenocarcinomas of the gallbladder.

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