Intracholecystic Papillary-Tubular Neoplasm Causing Hemobilia and Biliary Obstruction

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Background	An elderly male patient presented with epigastric pain and imaging showing a mass in the gallbladder and common bile duct.
Summary	An 89-year-old male patient presented with intermittent epigastric pain. Laboratory studies showed a cholestatic pattern, and imaging showed an enhancing irregular mass at the gallbladder neck extending to the cystic and common bile ducts. The presumed diagnosis was gallbladder carcinoma, and the patient underwent open radical cholecystectomy. Intraoperatively, the gallbladder was grossly distended, thin-walled, and purple, unlike a classic gallbladder cancer. The CBD was distended, but the wall appeared normal. A small tear was inadvertently made in the gallbladder wall, which yielded a stream of old dark blood, and an open exploration of the common bile duct revealed a blood clot cast of the biliary tree. A frozen section was obtained, and the gallbladder was resected with limited partial hepatectomy. Gross pathologic findings reported a large polyp measuring 7.9 cm in greatest dimension with patchy mucosal thickening of the background gallbladder wall. On histology, the polyp was classified as an intracholecystic papillary-tubular neoplasm (ICPN) with extensive high-grade dysplasia and intramucosal adenocarcinoma involving the adjacent gallbladder mucosa. This final diagnosis was favorable for our patient, as even ICPNs associated with invasion have a better prognosis than conventional pancreaticobiliary-type gallbladder carcinoma.
Conclusion	This is a case of an ICPN with focally invasive adenocarcinoma that caused hemobilia and secondary biliary obstruction. This final diagnosis had a much better prognosis than the presumed diagnosis of conventional gallbladder carcinoma, which was suspected preoperatively based on imaging and laboratory studies. The authors suggest that an enhancing gallbladder lesion on imaging with a cholestatic lab pattern should raise suspicion not only for carcinoma but also for ICPN with hemobilia. Surgical intervention is indicated in either scenario, given the premalignant potential of ICPNs.

Keywords	ICPN; gallbladder adenoma; hemobilia; biliary obstruction

DISCLOSURE STATEMENT:
The authors have no conflicts of interest to disclose.

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Case Description

An 89-year-old male with an unremarkable medical history presented to the hospital with four days of intermittent chest and epigastric pain. Physical exam was normal. An electrocardiogram and chest radiograph did not reveal cardiopulmonary pathology. Laboratory studies showed a cholestatic pattern (total bilirubin 5.4, alkaline phosphatase 134, ALT/AST 296/293). Ultrasound and abdominal CT imaging revealed an enhancing irregular mass at the gallbladder neck extending into the cystic duct, measuring 3.0 cm x 3.3 cm x 6.5 cm with distention of the gallbladder and layering sludge. Magnetic resonance cholangiopancreatography (MRCP) showed the mass extended into the mid-distal common bile duct (CBD), causing mild intrahepatic ductal dilatation. There were no focal hepatic or pancreatic lesions, pancreatic ductal dilatation, or lymphadenopathy (Figure 1).

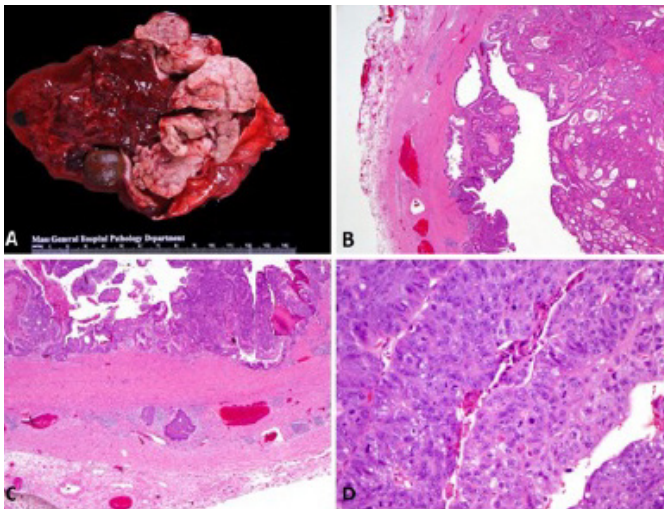
Figures 1. CT scan of the abdomen, revealing a 3.0 cm x 3.3 cm x 6.5 cm enhancing irregular mass at the gallbladder neck with distention of the gallbladder and layering sludge; there is also mild intra- and extra-hepatic biliary ductal dilation

The presumed diagnosis was gallbladder carcinoma. After discussing the risks and benefits of surgical intervention, the patient underwent open radical cholecystectomy. Intraoperatively, the gallbladder was grossly distended, thin-walled, and purple.

There did not appear to be a classic gallbladder cancer. A small tear was inadvertently made in the gallbladder wall, which yielded a stream of old dark blood. The CBD was distended, but the wall appeared normal. Once again, there was no evidence of cancer. The gallbladder was resected with a limited partial hepatectomy of segments 4b and 5. The decision was made to divide the cystic duct, which also appeared normal, and obtain a frozen section. When the cystic duct was divided, the clot under pressure extruded from the orifice. We proceeded with open CBD exploration and extracted a blood clot cast of the biliary tree (Figure 2). The afferent and effer-ent ducts were cleared with heparinized saline and a Fog-arty embolectomy catheter, resulting in bile drainage. The choledochotomy was repaired over a T-tube, and a Jackson-Pratt drain was placed.

Figures 2. Blood clot cast of the biliary tree

Postoperative laboratory studies showed resolution of the biliary obstruction, and his course was uncomplicated. He was discharged home on postoperative day number 3. Gross pathologic findings reported a large polyp measuring 7.9 cm in greatest dimension with patchy mucosal thickening of the background gallbladder wall and a single large cholelith. On histology, the polyp was classified as an intracholecystic papillary-tubular neoplasm (ICPN) with extensive high-grade dysplasia and intramucosal adenocarcinoma involving the adjacent gallbladder mucosa, with focal invasion through the muscularis layer into the perimuscular connective tissue (Figure 3).



Figures 3. Pathology of the specimen. A) Gross pathological findings included a large polyp measuring 7.9 cm in greatest dimension with patchy mucosal thickening of the background gallbladder wall. A single large cholelith was identified; on histology. B) The polyp was classified as an intracholecystic papillary-tubular neoplasm (IPCN) with extensive high-grade dysplasia. C) The gallbladder wall was extensively involved by highly atypical cribriform glands consistent with adenocarcinoma, which focally extended through the muscularis to involve the perimuscular connective tissue. D) On high power, the carcinoma was composed of enlarged cells with irregular nuclei, coarse chromatin, readily identifiable nucleoli, and moderately abundant eosinophilic cytoplasm; necrosis and mitotic activity were also present

Discussion

The term intracholecystic papillary-tubular neoplasm (ICPN) was defined in 2012 and refers to any preinvasive, intramucosal gallbladder neoplasm larger than 1 cm, encompassing a range of previously described gallbladder lesions including papillary adenomas, tubulopapillary adenomas, intestinal adenomas, biliary adenomas, transitional adenomas, papillary neoplasms, papillary carcinomas, and intracystic papillary neoplasm. ICPNs may display a spectrum of dysplastic changes, ranging from low-grade to high-grade dysplasia, and roughly one-half of ICPNs are associated with invasive carcinoma. ICPNs without associated invasion have the best prognosis, but even ICPNs associated with invasion have a better prognosis than conventional pancreaticobiliary-type gallbladder carcinoma.[1]

The recent adoption of specific diagnostic criteria for ICPNs makes their retrospective study difficult. Therefore, we understand the significance of our case through retrospective comparison with gallbladder adenomas, which encompass the majority of ICPNs. Although typically asymptomatic and detected incidentally on imaging or in cholecystectomy specimens, gallbladder adenomas rarely present with symptoms of cystic duct obstruction or hemobilia, as was the case for our patient. To date, there has been a single case reported of gallbladder adenoma causing hemobilia. This case report hypothesized that the long, slender stalk of the gallbladder polyp rendered it susceptible to torsion and subsequent hemorrhage.[2] The length of the ICPN, in this case, may have induced hemobilia by a similar mechanism. However, this mechanism may not fully explain the significant hemobilia caused by the ICPN in this report.

To further investigate this causal mechanism, it may be helpful to explore the relationship between adenomas elsewhere in the extrahepatic biliary tree and hemobilia. For example, a review in 1995 found that 7.7 percent of biliary cystadenomas to date presented with hemobilia.[3] Biliary papillomatosis, a condition characterized by multiple papillary adenomas in the biliary tree, also rarely presents with hemobilia. However, the condition most often presents with biliary obstruction attributed to direct mass obstruction, tumor emboli, and mucous plugs.

Conclusion

This is a case of an ICPN with focally invasive adenocarcinoma that caused hemobilia and secondary biliary obstruction. The final diagnosis had a much better prognosis than the presumed diagnosis of conventional gallbladder carcinoma, which was suspected preoperatively based on imaging and laboratory studies. The authors suggest that an enhancing gallbladder lesion on imaging with a cholestatic lab pattern should raise suspicion for carcinoma and ICPN with hemobilia. Surgical intervention is indicated in either scenario, given the premalignant potential of ICPNs.

Lessons Learned

Gallbladder adenomas and carcinomas are difficult to diagnose and distinguish. Both are typically asymptomatic, although either may present with symptoms of abdominal pain, cystic duct obstruction, or hemobilia. Surgical intervention is indicated in either scenario, given the premalignant potential of gallbladder adenomas.

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