

# Acute Cholecystitis and Cholelithiasis Concurrence with Mucinous Adenocarcinoma

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Dear Editor,

Mucinous adenocarcinoma (MA) of the gallbladder (GB) is a less common histological type of carcinoma with an incidence of 2.5% in gallbladder tumors. It displays the presence of extracellular mucin that makes over 50% of the tumor volume. Tumors that have less than 50% of stromal mucin are classified as adenocarcinoma that have focal mucinous differentiation. When the mucinous content is greater than 90%, the tumor is classified as pure mucinous/colloid carcinoma. Patients with mucin that is limited to the lumina of the infiltrating glandular units, but not present in the stroma, are not diagnosed with MA. Cholelithiasis, choledochal cysts, porcelain GB, polyps, etc. are common risk factors for the advancement of GB carcinoma (1-3). We report a case with primary MA of GB as an unexpected histopathological finding and coexistent cholelithiasis in an elective cholecystectomy material.

A 67-years-old woman showed the symptoms of acute cholecystitis and cholelithiasis. Laparoscopic cholecystectomy was performed in the general surgery clinic. She had a history of poorly controlled type 2 diabetes mellitus and was diagnosed with hypercholesterolemia. A complete blood count revealed a total leukocyte count of 9000/mm<sup>3</sup> with 61% of polymorphs. The level of serum alkaline phosphatase (913 IU/L), gamma-glutamyl transpeptidase (1109 U/L), aspartate transaminase (178 U/L), alanine transaminase (280 U/L), and C-reactive protein (2.2 mg/dL) were markedly elevated. The total bilirubin (1.3 mg/dL) and direct bilirubin (0.41 mg/dL) were mildly elevated. The viral markers for hepatitis B and C were negative (HBsAg, AntiHBs, AntiHCV). An abdominal ultrasound showed that the gallbladder was fully filled with stone and mud. During the surgical procedure, the gallbladder was excised easily. The gallbladder material was sent to a pathology laboratory with preliminary diagnosis of acute cholecystitis and cholelithiasis. The macroscopic examination showed that the GB was distended, and it measured 10×9 cm. Inside the lumen, multiple stones (max. diameter, 1.5 cm) were discovered. A nodular mass that was 4×4×2.5 cm in size was found in the corpus. The cut surface of the mass was friable, shiny, and soft (Figure 1). The slides of the mass showed a tumor consisting of tumor cells in the extracellular mucin pools, and cells similar to a signet ring are observed in clusters or individually in mucin (Figure 2). The tumor infiltrated the muscle. There was no perineural or vascular invasion. Surgical margins were free of the tumor. Dysplasia, intestinal metaplasia, calcification, and chronic active inflammation were also found (Figure 3). The tumor cells were immunoreactive for CK7, CK19, CEA, and EMA but were nonimmunoreactive for CK20 and CDX2. A diagnosis of MA of the GB was made.

According to the literature, MA exhibits a different clinicopathologic behavior and prognosis than the usual adenocarcinoma. Although ordinary GB adenocarcinomas typically present with chronic cholecystitis, MA presents with an acute cholecystitis type picture. Calcification may be observed in the GB MAs. MAs are typically large and present at a very advanced stage at the time of diagnosis, and they therefore show a more aggressive behavior compared to usual GB carcinoma. MA can be distinguished from conventional GB adenocarcinomas by the MUC2 positivity. MA has a poor prognosis compared to that of conventional adenocarcinomas because of its tendency toward invasive growth (1).

This study was presented at the International Congress of the International Academy of Pathology and 28<sup>th</sup> Congress of European Society of Pathology, September 25-29, 2016, Köln, Germany.

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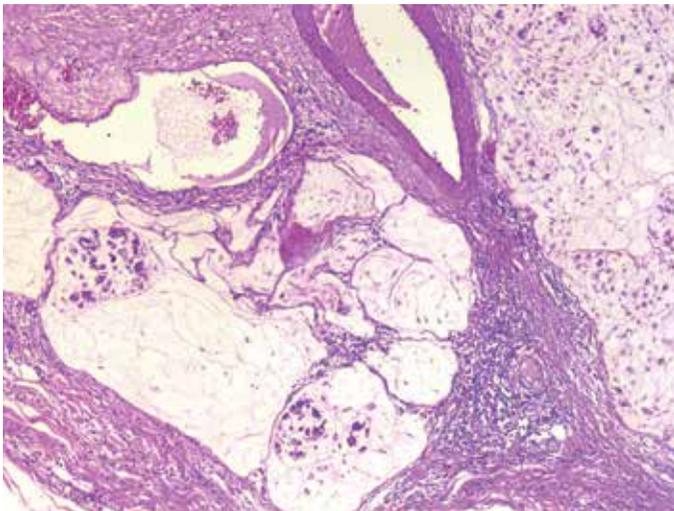
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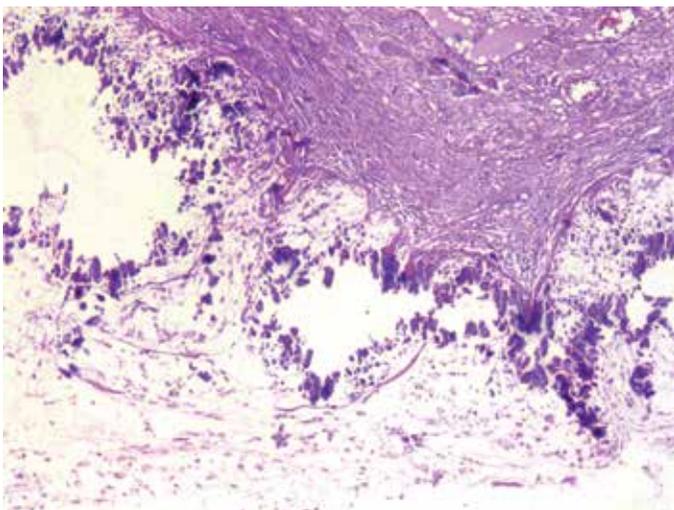
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**FIGURE 1.** The cut surface of the mass was friable, shiny, and soft.



**FIGURE 2.** Mucinous adenocarcinoma is composed of atypical tumor cells floating in the stromal mucin pools (hematoxylin and eosin stain, X50).



**FIGURE 3.** Calcifications in tumoral areas were detected (hematoxylin and eosin stain, X50).

Mucinous adenocarcinoma shows the CK7 positivity and CK20 negativity, opposed to intestinal adenocarcinomas. It can be diagnostically challenging to recognize a primary MA of the GB vs. pseudomyxoma peritonei disseminated to gallbladder, particularly in cases in which only the gallbladder is removed (1, 4).

Primary MA of the GB is a rare variant and unexpected histopathological finding in a cholecystectomy specimen examined for cholecystitis or cholelithiasis. Despite a growing awareness and improved diagnostic modalities, correct pre-operative diagnosis of gallbladder carcinoma is uncommon. Therefore, careful attention to any evidence of mural thickening and exact sampling of gallbladder specimens, particularly in older patients, are required so that any invasive malignancy would not be missed.

**Informed Consent:** Written informed consent was obtained from patient who participated in this study.

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