

Mucin-Producing Carcinoma of the Gallbladder: Evaluation by Magnetic Resonance Cholangiopancreatography in Three Cases

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We report three cases of mucin-producing carcinoma of the gallbladder, along with the magnetic resonance (MR) findings, especially the findings on a MR cholangiopancreatography. In our cases, linear or curvilinear streaks were detected running along the long axis of an enlarged gallbladder (mucus thread sign). When such findings were seen, a mucin-producing carcinoma of the gallbladder should be included as a differential diagnosis. Thus, gadolinium-enhanced MR imaging is mandatory for the precise diagnosis of the mucin-producing carcinoma of the gallbladder.

Index terms: Gallbladder, neoplasms; Bile ducts, neoplasms; Magnetic resonance; Cholangiopancreatography; Gadolinium; Ultrasound

INTRODUCTION

Most gallbladder carcinomas show histological evidence of the capacity to produce mucin, but the tumors which secrete clinically detectable amounts of mucin are extremely rare (1, 2); these tumors have been labeled as "mucin-producing carcinoma of the gallbladder (MPGBC)" (3, 4).

There have been several reports describing the imaging findings of MPGBC on ultrasonography (US), computed tomography (CT) and endoscopic retrograde

cholangiopancreatography (3-5). However, to the best of our knowledge, there has been only one case report until now that contains at least a short description of the findings on magnetic resonance cholangiopancreatography (MRCP) (6).

The purpose of this report is to characterize the magnetic resonance (MR) findings of MPGBC, especially the findings on MRCP and to correlate their appearance with the histopathologic features. We also discuss the usefulness of MRCP in the diagnosis of this tumor in comparison with that of US and CT.

CASE REPORTS

Case 1

A 59-year-old man was referred to our hospital for a gallbladder tumor detected by abdominal US during a health check-up. Laboratory results showed some abnormalities, including elevated levels of aspartate and alanine aminotransferase, as well as gamma-glutamyl transpeptidase, but the levels of tumor markers such as carcinoembryonic antigen (CEA) and carbohydrate antigen

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(CA) 19-9 were within normal limits.

Ultrasonography revealed a 17-mm protruding mass and hyperechoic streaks with spontaneous wave-like movements in the enlarged gallbladder (Fig. 1A). CT showed a mild

increase in attenuation of the gallbladder content and a localized thickened wall with enhancement; however, tumors were not visualized even on contrast-enhanced CT.

Using a 1.5-T MR system with a torso phased-array

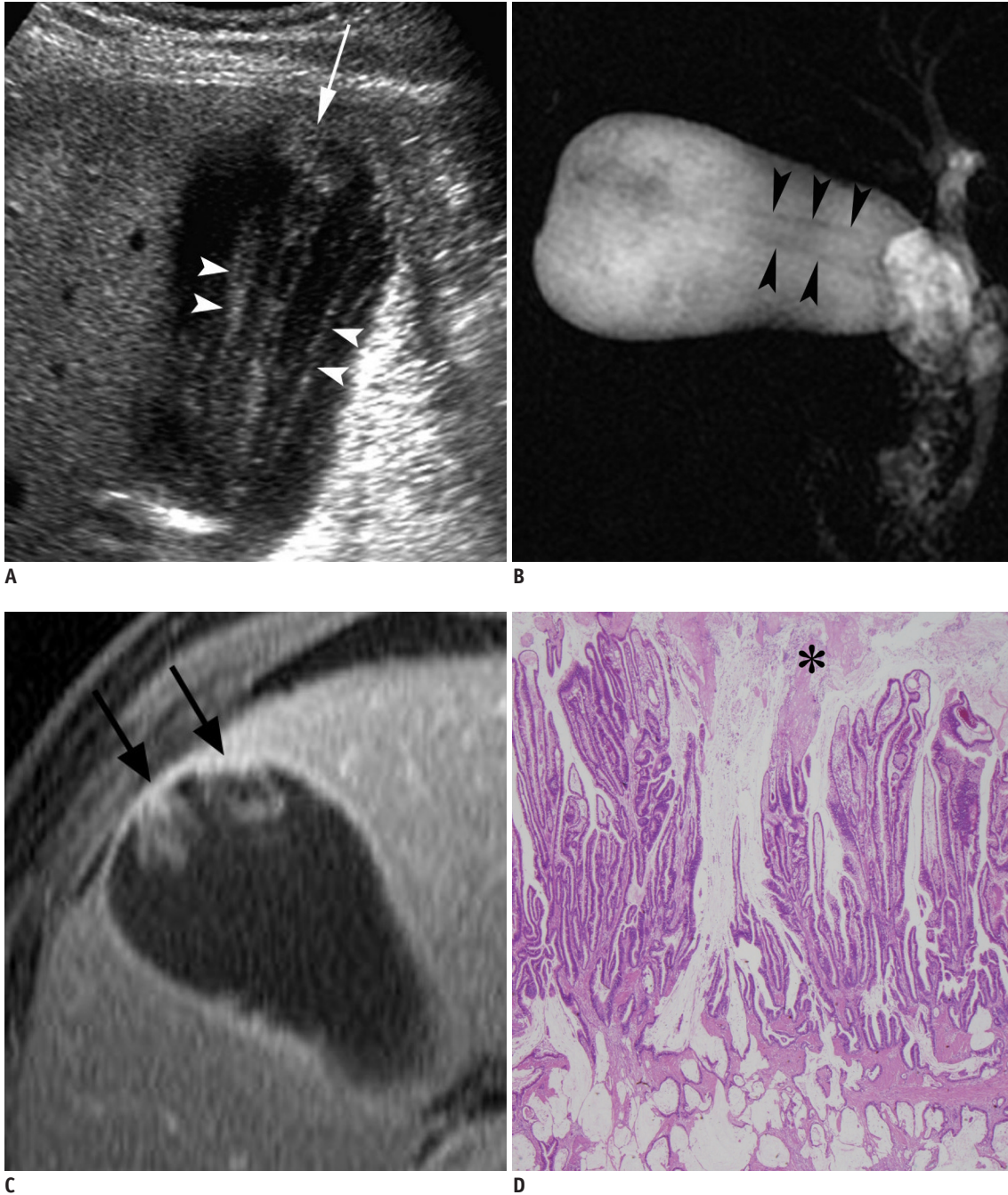


Fig. 1. Intracystic papillary adenocarcinoma in 59-year-old man.

A. Right intercostal Ultrasonography performed with 5.0 MHz probe demonstrates that tumors in fundus (arrow) and several striations of variable width (arrowheads) are almost same echogenicity. **B.** Thick-slab magnetic resonance cholangiopancreatography (repetition time msec/echo time msec, infinite/1023 [effective]; 60-mm-thick slab) depicts some fine hypointense striations (arrowheads) in moderately enlarged gallbladder showing marked hyperintensity. **C.** Axial T1-weighted fat-saturated gradient-recalled echo (175/2.1; flip angle, 70°) obtained 3 min after Gd-DTPA injection reveals well-enhanced papillary projections (arrows) in fundus that could be clearly differentiated from mucus striations. **D.** Microscopically, significant mucin (asterisk) sticks to surface of papillary carcinoma, and floating in mucin are clumps or strands of epithelium, some of which contain malignant cells (Hematoxylin & Eosin staining; original magnification x 200).

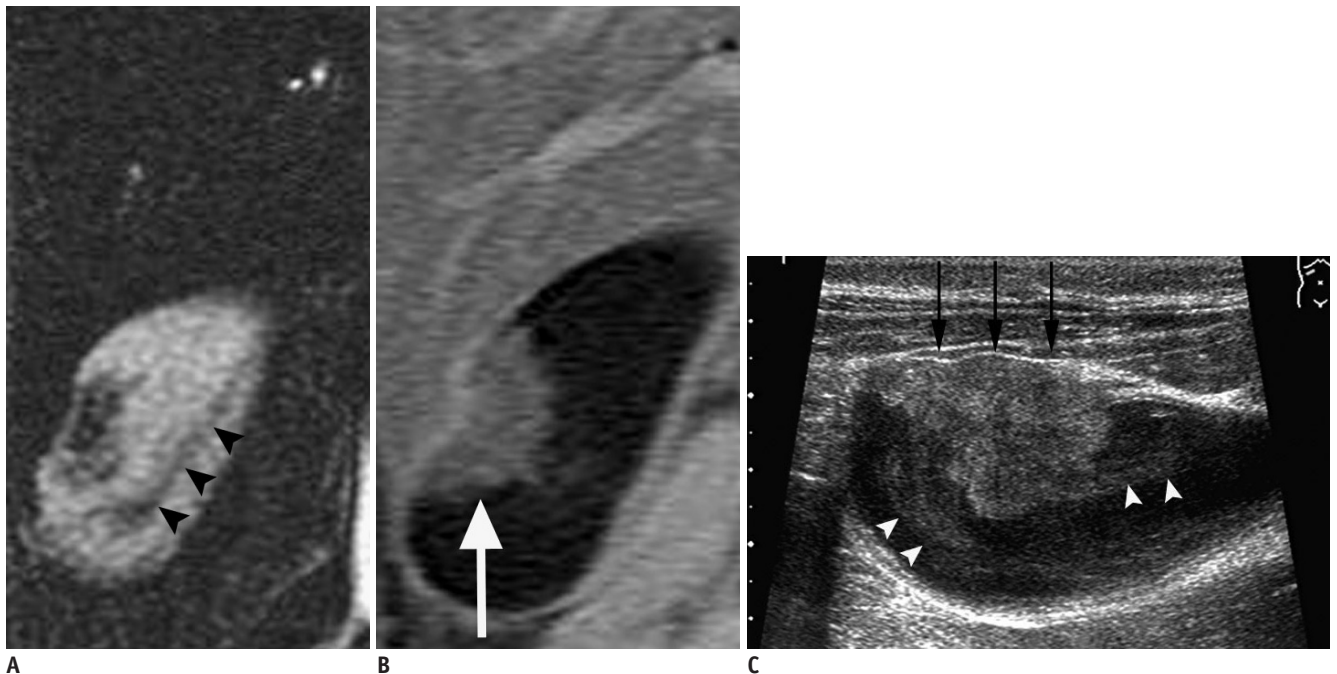


Fig. 2. Papillary adenocarcinoma invading subserosal layer with lymph node metastasis in 53-year-old woman.

A. Coronal thin-section magnetic resonance cholangiopancreatography (MRCP) (infinite/99.6 [effective], 4-mm-thick sections) clearly shows some striations running along long axis (arrowheads) of gallbladder. **B.** Coronal gadolinium-enhanced T1-weighted image (150/1.8; flip angle, 70°) anterior to **(A)** demonstrates protruding lesion (arrow) in body of enlarged gallbladder. **C.** Subcostal ultrasonography performed with 9.0 MHz probe reveals hyperechoic polypoid lesion with papillary surface (arrows) that seems to produce threading striations (arrowheads) similar to those visualized on MRCP images.

coil, we performed T1-weighted gradient-recalled echo (GRE) images before and after the administration of gadopentetate dimeglumine, and T2-weighted fast spin echo (FSE) images. Both thick-slab and thin-section MRCP images were obtained with a single-shot FSE sequence. MRCP disclosed some streaks of hypointensity extending from the tumor to the neck of the gallbladder (Fig. 1B). Unenhanced T1-weighted GRE images and T2-weighted FSE images did not show the tumor or any other findings in the enlarged gallbladder. Gadolinium-enhanced GRE images demonstrated irregular papillary enhancement in the fundus (Fig. 1C).

A cholecystectomy with wedge resection of the liver bed (CWL) and regional lymphadenectomy were performed and the gallbladder was found to be filled with 100 mL of greenish viscous mucin. A papillary tumor 4 cm in size was found in the fundus. Histologically, adenocarcinoma cells were demonstrated to have proliferated intraluminally with papillary formation, shallow invasion into the mucosa, and a few muscular and subserosal layers. Many striations protruded from the papillary proliferation of the adenocarcinoma, and the striations consisted of thick mucus bundle with detached cells (Fig. 1D). No recurrence has been observed 78 months after the operation.

Case 2

A 53-year-old woman was referred to our hospital with pain in the right hypochondrium. Laboratory tests were normal except for an elevated CEA level. Both CT and MR images revealed a 3-cm eccentric mass in the fundus of the dilated gallbladder and lymph node adenopathy in the hepatoduodenal ligament. MRCP showed many hypointense striations in the lumen, running from the tumor surface to the neck and along the long axis of the gallbladder (Fig. 2A). The mass showed moderate enhancement on gadolinium-enhanced T1-weighted images (Fig. 2B). US also depicted a mass and many hyperechoic striations moving in a wave-like manner (Fig. 2C).

Cholecystectomy with wedge resection of the liver bed and pylorus-preserving pancreaticoduodenectomy with regional lymph node dissection were performed. The gallbladder was enlarged and filled with excess mucin. Histologically, the intraluminal nodular tumor, whose luminal surface was covered by mucin, consisted of the papillary adenocarcinomatous proliferation. The adenocarcinoma had also infiltrated into the subserosal connective tissue, where the tumor was a mucinous carcinoma partly associated with tubular adenocarcinoma. No recurrence has been observed 72 months after the operation.

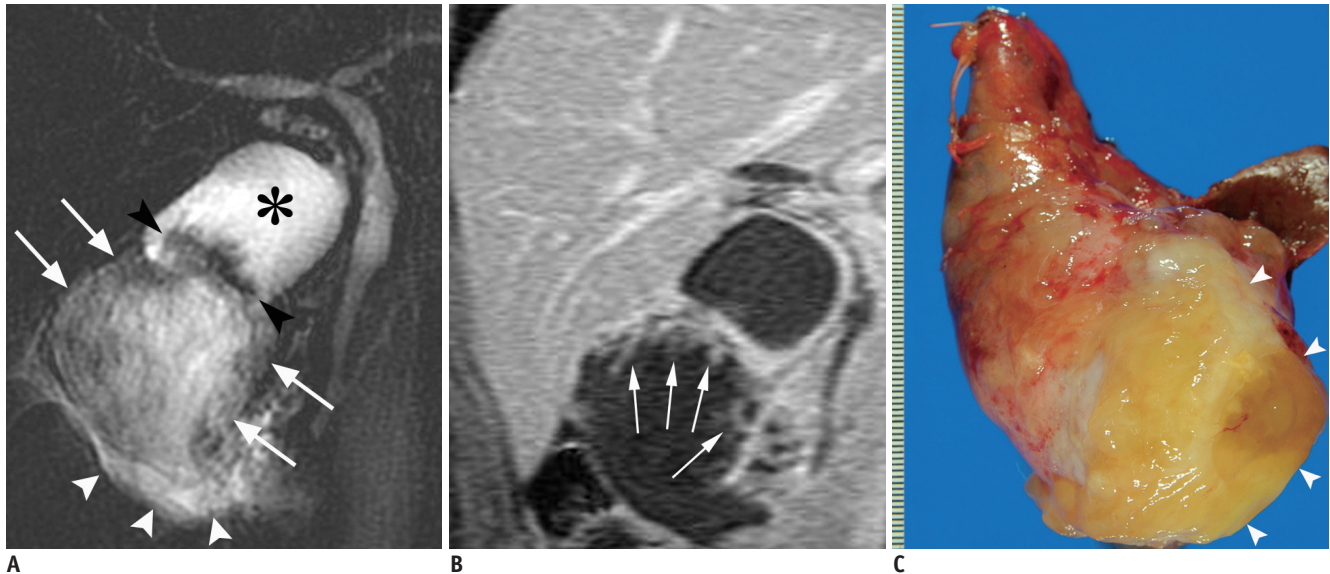


Fig. 3. Mucinous carcinoma with peritoneal dissemination in 48-year-old woman.

A. Thick-slab magnetic resonance cholangiopancreatography (infinite/1023 [effective], 60-mm-thick slab) shows two separate compartments of gallbladder. Markedly hyperintense portion near cystic duct (asterisk) corresponds to native lumen of gallbladder, while weakly hyperintense fundic part (arrows) filled with mucus materials shows hypointense streaks of mucinous carcinoma extending to highly thickened wall. Separation between two parts is seen as localized wall thickening with papillary surface observed as luminal lesion in fundus (black arrowheads). Poorly formed area of hyperintensity surrounds gallbladder (white arrowheads), which is indicative of pooled mucin due to perforation. **B.** Coronal gadolinium-enhanced T1-weighted image (150/1.8; flip angle, 70°) shows several papillary enhancements with irregularly thickening wall (arrows). **C.** Macroscopically, fundus of enlarged gallbladder was covered thickly with overflowing gelatinous mucin (arrowheads).

Case 3

A 48-year-old woman presented with pain in the right abdomen. Laboratory tests were normal except for markedly elevated serum levels of CA19-9. CT showed an enlarged gallbladder filled with irregular septa with varying degrees of thickening near the center of the body. MRCP showed an octagonal gallbladder with heterogeneous hyperintensity and some hypointense streaks running from the gallbladder to the abdominal cavity (Fig. 3A). On coronal thin-section MRCP, the outer wall of the fundus was partially discontinuous and surrounded by an irregular-shaped hyperintense area, which was suspected to be a mucin collection caused by a perforation (not shown). Gadolinium-enhanced T1-weighted images demonstrated an irregular-surfaced tumor (Fig. 3B).

A CWL was performed. The gallbladder had a 3-cm diameter hole in the fundus, from which yellowish and glistening mucus material was overflowing (Fig. 3C) and spreading to the surrounding peritoneal surface and disseminated on the diaphragm. Histologically, the original gallbladder cavity was not so enlarged and the papillary adenocarcinoma was present on the fundus. The tumor had largely invaded the muscle layer and proliferated in the deep layer. It contained mucus nodules of varying sizes, which were demonstrated in the histology of the mucinous

carcinoma. The patient died of recurrent peritoneal dissemination 14 months after the operation.

DISCUSSION

Mucin-producing carcinoma of the gallbladder is considered to be a subtype of two major histological types of gallbladder carcinoma: well-differentiated adenocarcinoma (intracystic papillary adenocarcinoma) and mucinous carcinoma (4). Gallbladder carcinomas are commonly biologically aggressive tumors, whereas the biological behavior of MPGBC itself is still unknown. Some authors consider it to be highly aggressive and invasive, as demonstrated in one of our reported cases with perforation (1, 4, 6). However, the majority of the reported MPGBC cases so far have presented with clinical symptoms linked to enlargement of the gallbladder and the viscous mucin, such as abdominal pain, discomfort, fever and jaundice (3-7). As a result, it may be possible to detect these tumors at an earlier stage, while the prognosis still remains reasonable.

In our series with MPGBC, MRCP showed linear or curvilinear striations in the gallbladder, running more or less along the long axis of the gallbladder. The signal intensity of these striations was less than that of the bile in the lumen, but greater than that of the liver. We called this

characteristic pattern of striations a “mucus thread” sign, which corresponded microscopically to a thick mucus bundle including some cellular components. This observation was proven by a MRCP image-pathologic correlation. Huang et al. (6) also reported visualizing laminated streaks of fluid inside the gallbladder without evidence of obstruction of the cystic duct in their case on MRCP. We speculated that this finding is associated with the flow of the highly viscous mucin secreted from the surface of the tumor in the gallbladder cavity. In addition, we observed some threads showing an irregular arrangement in a mucus lake associated with mucinous carcinoma.

The mucus thread sign was observed on MRCP with a single-shot FSE sequence in all the three patients in our series, and was seen more clearly on MRCP images than on T2-weighted FSE images. On the other hand, visualization of mucus material from mucin-producing tumors, such as intraductal papillary mucinous tumors of the pancreas, has not been reported on MRCP using a FSE sequence in previous publications (7). We speculate the reasons for our successful visualization of the mucus thread sign as follows: First, the parameters used for MRCP using a single-shot FSE sequence in this study relied on more heavily-T2 weighted imaging than on FSE imaging (8, 9). Second, we used a phased-array torso coil and a large matrix size to obtain higher space resolution (8, 9). In addition, MRCP allows a direct optimized plane of acquisition, enabling precise evaluation of this sign; this plane should be arranged with its long axes parallel to the long axis of the gallbladder.

The papillary projections and solid components of the tumors were more clearly visualized on the gadolinium-enhanced MR images, by virtue of their moderate to marked enhancement, than by other modalities in all the three patients. Since unenhanced T1- or T2-weighted images sometimes do not show thin papillary projections in the gallbladder, as in Case 1, it would appear that gadolinium-enhanced MR imaging is essential to confirm the diagnosis of MPGBC. Moreover, since mucus threads do not show enhancement, gadolinium-enhanced MR imaging could be useful for differentiating them from tumorous lesions.

The mucus thread sign was also seen on US. Two patients preoperatively examined by US with a 5.0 or 9.0 MHz probe showed a linear or curvilinear hyperechoic bundle of streaks. Intraoperative US with a 7.5 MHz probe in the three patients demonstrated a bundle of mucus threads within the lumen of the gallbladder in two patients and a mucus lake-destroyed wall in one. Ozeki et al. (5) reported the same

findings, called tree-like sludge echoes, in intraoperative US, although they missed them in conventional extracorporeal US. Therefore, higher frequency echo probes of 5.0 MHz or more may be useful for a detailed visualization of the structure of not only the tumor itself, but also of the hypersecreted mucus and its course, although it might still may be possible in thin patients only. On the other hand, intraoperative US with a high-frequency probe may be more helpful, regardless of patient body type.

Computed tomography demonstrated MPGBC as a solid mass of 3-cm or more in size that shows enhancement in the enlarged gallbladder in two patients. However, in the remaining patient with thin papillary projections, both unenhanced and contrast-enhanced CT failed to show the projections or the tumor itself. Since the tumors are thin projections and contain significant mucin, it may be difficult on CT images to distinguish between a low-attenuation lesion similar to water and bile-containing gelatinous mucin (10, 11). Radiologists must bear in mind that the diagnosis of MPGBC may be easily missed by CT alone.

Differentiating mucus threads from stones, sludge or hematomas, which can obstruct the cystic duct and are often associated with the retention of mucus, is important in clinical practice. Stones are oval or round and often have calcification. Sludge and hematomas usually show higher intensity than dilute bile on T1-weighted images and layers beneath the dilute bile due to its greater specific gravity. The mucus thread sign of MPGBC should be carefully evaluated for the size and length of the mucus bundle, the appearance of the arrangement and direction, and the continuity with tumorous lesions.

In conclusion, MRCP may demonstrate hypointense striations in the enlarged gallbladder in patients with MPGBC. Careful assessment of this sign can be helpful for early detection and accurate preoperative diagnosis of this type of malignancy of the gallbladder. Also, gadolinium-enhanced MR imaging is mandatory for precise characterization of the lesions.

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