Adenocarcinoma coexisting with signet ring cell carcinoma in nonampullary duodenum

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Dear Editor,

Primary duodenal signet ring cell carcinoma (SRCC) is a rare disease and one of the most malignant cancers. In particular, nonampullary SRCC is extremely uncommon; only several cases have been reported to date in the English literature (1-6).

A 66-year-old man with a history of hypertension presented with vomiting and abdominal pain. Two months previously, he had visited our emergency room at KonKuk University Chungju Hospital with similar symptoms, and abdominal computed tomography (CT) without contrast enhancement showed distention of the stomach and stones in the gallbladder. His symptoms improved gradually with conservative management, and laparoscopic cholecystectomy was performed. The pain was tolerable for several weeks after surgery; however, the persistence of symptoms impelled him to visit our hospital again.

Results of blood biochemical tests were unremarkable. Abdominal CT showed marked distention of the stomach, which was filled with a large amount of fluid. Because of the patient's history of allergy to contrast agents, nonenhanced imaging was performed again. To decompress the stomach, drainage was performed with a nasogastric tube. Endoscopic examination revealed a firm, asymmetric stricture with focal nodularity of the mucosa on the proximal second portion of the duodenum (Figure 1). Because of stenosis, the endoscope the endoscope could not be passed to the ampulla of Vater. Histological examination of the biopsy samples from mucosal lesions with nodules of the stenotic duodenum revealed signet ring cell–type adenocarcinoma. SRCC was not detected in the stomach. Subsequent abdominal CT with contrast-enhanced imaging confirmed an enhanced 3-cm mass in the second portion of the duodenum, pancreatic head invasion, and a single enlarged lymph node in the hepatoduodenal chain (Figure 2).

After the diagnosis of duodenal carcinoma with pancreatic head invasion, pancreaticoduodenectomy was performed. Postoperative histologic examination identified a 2.5×1.5×1.4 cm tumor consisting of moderately differentiated adenocarcinoma (55%) with poorly differentiated signet ring cell components (40%), and extracellular mucins (5%) from the duodenum (Figure 3). Lymphovascular invasion, pancreatic invasion (pT4), and metastasis were observed in one of 14 resected lymph nodes (pN1). All resected margins were clear. Immunohistochemically, signet ring cells were positive for cytokeratin 19, cytokeratin 20, caudal-related homeobox transcription factor 2 (CDX2), mucin 2, and E-cadherin and negative for cytokeratin 7, mucin 1, mucin 5A, and mucin 6 (Figure 4).

The patient remains alive and has been disease-free in the 8 months since the surgery. Adjuvant chemotherapy was recommended; however, the patient refused for personal reasons.

Because SRCC is a common tumor in the gastric epithelium, investigators have hypothesized that duodenal SRCC may originate from heterotopic gastric-type mucosa (7). However, primary SRCC has been observed in other organs, including the colorectal region, gallbladder, pancreas, and urinary bladder, which indicates that duodenal SRCC may originate de novo from duodenal mucosa. Maekawa et al. (8), in contrast, proposed that SRCC in the ampullary duodenum in their case might have differenti-

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ated from ordinary adenocarcinoma because no ectopic gastric mucosa or gastric-type metaplasia was found in the peritumoral mucosa. One study revealed that colon adenocarcinoma could be converted to SRCC-like cells by the activation of phosphatidylinositol 3-kinase, which supports Maekawa et al.'s hypothesis (9). In our patient, adenocarcinoma coexisted with SRCC, and no ectopic mucosa or metaplasia was present.

Researchers have attempted to determine the characteristic pattern of SRCC according to cellular origin, on the basis of immunohistochemical mucin profiles. The

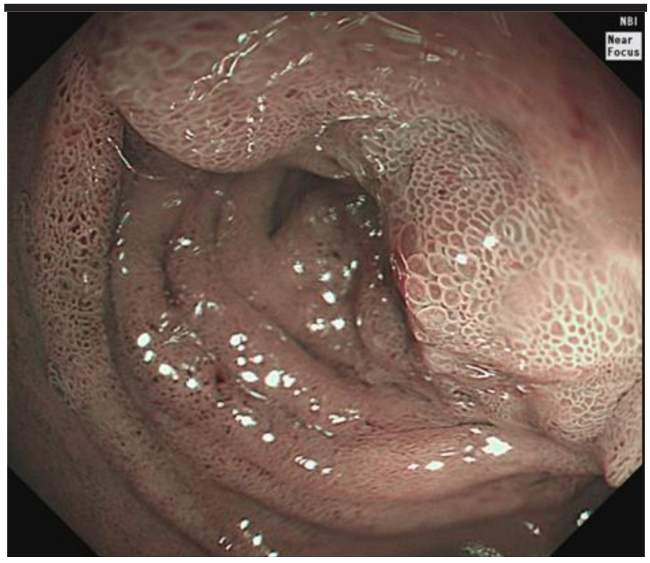

Figure 1. Esophagogastroduodenoscopy with narrow-band imaging shows a firm asymmetric stricture with focal nodularity of the mucosa on the proximal second portion of the duodenum.

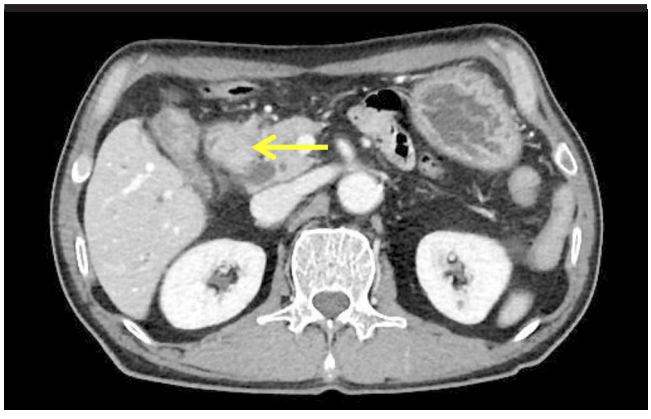

Figure 2. Abdominal computed tomographic scan with contrast enhancement shows focal thickening with prominent enhancement in the proximal second portion of the duodenum.

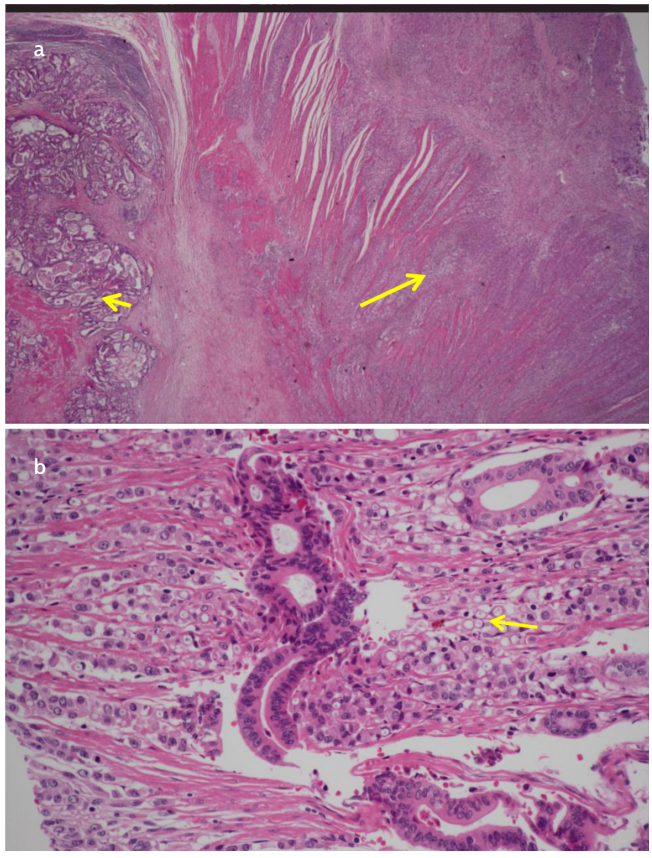

Figure 3. a, b. Histopathological findings of the tumor indicate that it was an adenocarcinoma (hematoxylin and eosin staining [H&E]; magnification, ×12) of varying structure: (a) moderately differentiated (left-sided arrow) or diffuse type (right-sided long arrow); and (b) signet ring carcinoma cells and other cancer glands (H&E; magnification, ×200).

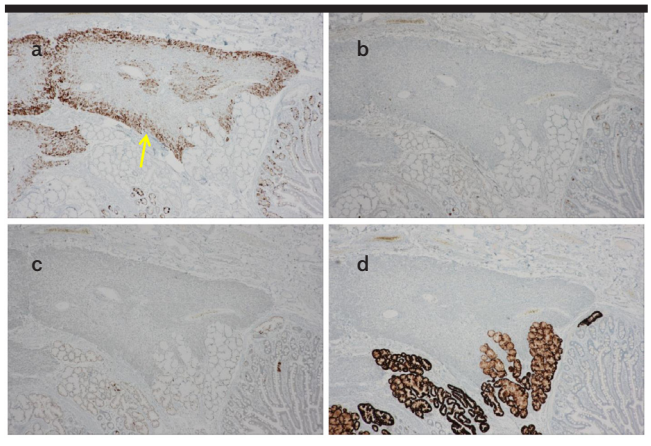

Figure 4. a-d. Immunohistochemical findings. Tumor cells staining positively for mucin 2 (arrow), but negatively for mucin 1, mucin 5A, and mucin 6 (a) mucin 2, b) mucin 1, c) mucin 5A, d) mucin 6).

expression of mucin 2, mucin 5AC, and mucin 6 was consistently recognized in the normal stomach tissue. In the colorectal region, the expression of mucin 2 has been observed in the cryptal epithelial cells (10). Terada (10) found a significant tendency for primary gastric SRCC to express mucin 5AC (67%) and mucin 6 (70%) more frequently than mucin 1 (10%) and mucin 2 (13%) and for primary colorectal SRCC to express mucin 1 (42%), mucin 2 (92%), and mucin 5A (33%), but not mucin 6 . These findings suggest that downregulation or upregulation of mucin expression, as well as its aberrant expression, may be associated with carcinogenesis and malignant potential of SRCC.

Mochizuki et al. (4), Hirano et al. (5), and Carasca et al. (6) reported a case of primary nonampullary duodenal SRCC with mixed gastric foveolar and intestinal phenotypes, in which immunoreactivities of mucin 5AC and mucin 2 were positive. Our patient had only an intestinal, not gastric or pancreaticobiliary, phenotype according to the immunohistochemical results (negativity for cytokeratin 7 and positivity for cytokeratin 20, CDX2, and mucin 2), which suggests that his tumor cells were derived from duodenal goblet cells.

In our patient, the adenocarcinoma was thought to have arisen de novo from duodenal goblet cells, according to the results of immunohistochemical staining. Ampullary SRCC usually manifests in the form of biliary obstruction, as well as epigastric pain and jaundice, whereas nonampullary duodenal SRCC manifests with intestinal obstruction. If the cause of abdominal pain and gallstones is atypical, as in our patient, careful follow-up for detection of any other possible causes is needed.

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