Malignant neoplasms arising from the small bowel are relatively rare, accounting for only 2% of all GI cancers [1]. Due to the small number of cases, study about prognosis of patients with small intestinal cancer has been limited. There are several subtypes among these small intestinal cancers, including adenocarcinoma (40-50%), carcinoid (30%), lymphoma (14%), and sarcoma (11%) [2]. They account for approximately 98% of small-bowel malignancies. Each subtype has its own distinct clinical behavior and needs a different treatment approach. Adenocarcinoma is the most common type of small intestine cancer, frequently arising in the duodenum and jejunum. It develops in the glandular cells of the lining of the small intestine. Primary duodenal adenocarcinoma was first described by Hamburger in 1746 [3]. It accounts for less than 0.5% of all gastrointestinal cancers. Gastrointestinal carcinomas with squamous differentiation are adenosquamous carcinoma, adenoscaanthoma, and squamous cell carcinoma [4]. They are extremely rare, and only a few cases have been reported [5-7]. To our knowledge, no adenosquamous carcinoma been reported to arise from the duodenal third portion. We herein report an exceedingly rare case.

CASE REPORT

A 67-year-old man was healthy before. Recently, he had suffered from exertional dyspnea and epigastralgia intermittently. Melena was found occasionally and 2 kilograms of body weight was lost in the past 6 months. Otherwise, no poor appetite, dizziness, palpitation, nausea, or vomiting was noted during this period. Due to worsening symptoms with presence of general weakness during the preceding 5 days, this man visited our emergency department for help. On examination, the patient’s face was pale. The rest of the physical examination was unremarkable, especially without prominent abdominal tenderness or distension. Laboratory investigations revealed severe anemia (hemoglobin 5.1 g/dL). Both γ-glutamyl transpeptidase (22 IU/L) and alkaline phosphatase (60 IU/L) levels were normal. Bile duct obstruction could be excluded initially. Total leucocyte count (9,600/μL) was mildly elevated, with neutrophilic predominance (93.4%).

Due to severe anemia and intermittent epigastralgia, the patient underwent panendoscopy. An ulcerative mass lesion was noted in the duodenum (Fig. 1). Abdominal CT scan
Adenosquamous carcinoma

revealed a huge isodense enhancing tumor in the duodenal 3rd portion, measuring 8.1 × 5.3 cm, with anterosuperior displacement and suspicious invasion of the pancreatic head (Fig. 2). Several small (< 1 cm) lymph nodes were found in the peri-pancreatic and peri-duodenal regions. Otherwise, no prominent liver metastases or intestinal obstruction was noted on this abdominal CT.

Pancreateicoduodenectomy, cholecystojejunostomy, and pancreateicojejunostomy were done. The pathologic diagnosis was adenosquamous carcinoma of the duodenum, which had invaded to the pancreas. The tumor was made up of biphasic components, including poorly differentiated adenocarcinoma and moderately differentiated squamous cell carcinoma. These two components were mixed together without clear border (Fig. 3a). The poorly differentiated adenocarcinoma was composed of single cells or signet ring cells containing intracytoplasmic mucin, and the moderately differentiated squamous cell carcinoma revealed keratinized polygonal cells arranged in nests (Fig. 3b). Immunohistochemically, the tumor cells were diffuse positive for cytokeratin 7, and the squamous part was reactive for cytokeratin 5/6 and p63. The special stain of d-PAS demonstrated the intracytoplasmic mucin in the signet ring cells. The immunophenotype was also compatible with adenosquamous carcinoma.

DISCUSSION

Cancers of the small intestine are relatively uncommon diseases among all gastrointestinal cancers. The most common types of small intestinal cancer include adenocarcinoma, lymphoma, sarcoma, and carcinoids. Diagnostic image examinations usually include a barium contrast study, upper GI tract endoscopy, and computed tomography of abdomen. Biopsy is often required to reach a final diagnosis.

Approximately 50% of small intestinal adenocarcinomas arise in the duodenum. About 45% of duodenal adenocarcinomas arise from the third and fourth portions [8]. Although most cases are sporadic, associations with Crohn's disease, celiac disease, Peutz-Jeghers syndrome, or familial adenomatous polyposis (FAP) have been reported. On fluoroscopy, duodenal adenocarcinomas may have various appearances, including ulcerated mass, polypoid mass, annular constricting “apple-core” lesion, etc. Discrete mass or irregular thickening of the duodenal wall with concentric luminal narrowing and local lymphadenopathy may be found on CT. The tumor is more likely to cause intestinal obstruction.

Lymphoma accounts for approximately 14% of small-bowel malignancies [2]. On UGI series, duodenal lymphoma may be a smooth or loculated submucosal mass involving the distal stomach and duodenum. Bulky hypovascular soft tissue mass infiltrating submucosa of the stomach and duodenum may be represented on contrast-enhanced CT.

Sarcomas account for approximately 11% of small-bowel malignancies [2]. They are mesenchymal neoplasms of the GI tract believed to be derived from the interstitial cells of Cajal, the pacemaker cells that regulate peristalsis of the digestive tract. Recently, they have been named GI stromal tumors (GISTs). On image examination, a
Figure 2. Adenosquamous carcinoma of the duodenal 3rd portion. a. Axial unenhanced CT image shows a huge homogeneous isodense mass lesion (arrows) in the right anterior pararenal space. b. Arterial phase contrast-enhanced CT image shows anterior displacement of the pancreatic head (arrows) by the mass lesion. Several small (< 1 cm) regional lymph nodes were also noted. c. Delayed-phase contrast-enhanced CT image shows heterogeneous enhancement of the mass lesion. d. Coronal reformatted CT image shows the tumor arising from the duodenal 3rd portion. e. Coronal reformatted CT image shows indistinct margin (arrows) between the tumor and pancreatic head. Pancreatic invasion was suspected. No prominent intestinal obstruction was noted on this abdominal CT.
well-circumscribed submucosal mass extending exophytically from GI tract is the typical presentation of GIST.

On the abdominal CT of our patient, a huge isodense mass lesion was seen arising from the duodenal 3rd portion, with exophytic growth pattern and anterosuperior displacement of the pancreatic head. Several small (short-axis diameter < 1 cm) regional lymph nodes were also noted on this CT. After contrast administration, the lesion showed heterogeneous enhancement. Focal necrosis was suspected. The margin between the pancreatic head and the tumor was partially unclear. Invasion of the pancreatic head or partial volume effect could not be well clarified. Otherwise, no prominent intestinal obstruction was noted on this abdominal CT. Under these image findings, submucosal tumor (such as GIST, etc) was suspected initially. After operation, the histopathologic diagnosis was adenosquamous carcinoma of the duodenal 3rd portion with pancreatic invasion.

Adenosquamous carcinomas are extremely rare tumors. They have been reported in various organs, including lung, esophagus, stomach [9], duodenum [4, 5], gallbladder [10], common bile duct [11], pancreas [12], and colorectum [13]. Few cases have been reported to arise from the duodenum. In our case, the adenosquamous carcinoma arises from the duodenal third portion.

According to the WHO definition, adenosquamous carcinoma should consist of both adenocarcinoma and squamous cell carcinoma components in different quantity. There may be a transitional area between these two components, or these two components may be separated completely. In our case, the adenocarcinoma and squamous cell carcinoma components were mixed together without clear border.

As to the origin of these tumors, it has not been clarified yet. Several theories have been proposed to explain the histopathogenesis of both glandular and squamous epithelia in the same tumor. One hypothesis is that the tumor may be a result of overgrowth from or inclusion of adjoining different epithelium. But the nearest structure normally lined by squamous epithelium is the esophagus; the distance between these two locations is too far to admit of the possibility [6]. Wood et al [14] proposed that adenosquamous carcinoma may originate from stimulation of undifferentiated basal cells of the intestine. These cells appear at the base of normal mucosal crypts [15], and they can differentiate into glandular and squamous epithelia. On the other hand, metaplasia may offer another possible explanation, since it may occur in chronically inflamed tissues, especially when they are subjected to chemical or mechanical irritation [6]. Other possible origins that have been proposed include embryonic rests, endothelial cells of regional vessels, prosoplasia, totipotential undifferentiated cell, and squamous differentiation in a pre-existing adenocarcinoma [4].

In some exocrine glands, adenosquamous carcinoma may be regarded as mucoepidermoid carcinoma. The tumor originates from the ductal epithelium of these glands. Brunner’s glands are duodenal submucosal glands that excrete mucus to protect the duodenal wall from the digestive

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**Figure 3**

3a. Photomicrograph (original magnification, x100; hematoxylin-eosin stain) The tumor was composed of both poorly differentiated adenocarcinoma (black arrow) and moderately differentiated squamous cell carcinoma (white arrow) which revealed no clear border.

3b. Photomicrograph (original magnification, x400; hematoxylin-eosin stain) The poorly differentiated adenocarcinoma (black arrow) is composed of signet ring cells. The squamous cell carcinoma (white arrow) shows marked keratinization.
juices. They are found in the portion of duodenum above the sphincter of Oddi. In our case, the tumor arose from the duodenal third portion. Theoretically, there are no Brunner’s glands in this portion. Microscopically, no Brunner’s glands can be identified in the tumor part as well as in the adjacent normal duodenal submucosal layer. The possibility of tumor arising from Brunner’s glands can be excluded in our case. The true histopathogenesis of this tumor still remains to be clarified.

Surgical resection is one choice to treat duodenal adenosquamous carcinoma. Due to limited number of these cases, there is no effective pre- or post-operative adjuvant therapy documented in the literature. On the basis of pre-operative findings, our patient received pancreati-coduodenectomy, cholecystojejunostomy, and pancreatico-jejunotomy. Pancreatic invasion and lymph node metastasis were also noted during the operation. They are usually associated with a poor prognosis. In comparison with corresponding adenocarcinoma, many studies revealed poorer prognosis of adenosquamous carcinoma in the stomach [9], gallbladder [10], common bile duct [11], and colorectum [13]. The squamous component has a greater proliferative capacity than the granular component. Among the gallbladder tumors, adenosquamous carcinoma has a shorter doubling time compared to adenocarcinoma [16]. That is, it is more malignant than common adenocarcinoma. However, there are only a few cases of duodenal adenosquamous carcinoma reported in the literature. The true prognosis of a tumor in duodenum remains to be investigated after more cases are reported.

In conclusion, we have reported an extremely rare case of duodenal adenosquamous carcinoma. The histopathogenesis, image findings, and clinical behaviors of the tumor are of interest to clinicians.

REFERENCES