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CASE REPORT

Signet Ring Cell Carcinoma of the Ampulla of Vater. A Case Report

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ABSTRACT

Context Signet ring cell carcinoma of the ampulla of Vater is extremely rare and only 12 cases have previously been described in the English language literature. We report a case of advanced signet ring cell carcinoma of the ampulla of Vater, with invasion of the duodenum and pancreas. **Case report** A 59-year-old man presented at a local hospital with upper abdominal pain and icterus. Obstructive jaundice was diagnosed and he was referred to our hospital. Abdominal computed tomography showed dilatation of the common bile duct and the pancreatic duct. Duodenoscopy indicated an irregularly shaped erosion on the ampulla of Vater. Histological examination of a biopsy revealed adenocarcinoma. Duodenography revealed irregularity of the second portion of the duodenum wall. The diagnosis was carcinoma of the ampulla of Vater, and a pancreaticoduodenectomy was performed. The histopathological findings detected signet ring cell carcinoma. **Conclusion** Although several cases have been reported, the detailed clinicopathological features and prognosis are not clear. Additional reports are warranted.

INTRODUCTION

Tumors of the ampulla of Vater are not common [1]. Most tumors are adenocarcinomas and other histological types are less frequent [2]. Signet ring cell carcinoma of the ampulla of Vater is extremely rare and only 12 cases have previously been described in the English language literature [2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13]. We herein report a case of advanced signet ring cell carcinoma of the ampulla of Vater, with invasion of the duodenum and pancreas.

CASE REPORT

A 59-year-old man presented at a local hospital because of upper abdominal pain and icterus. Obstructive jaundice was diagnosed and he was referred to the National Hospital Organization Disaster Medical Center, Tokyo, Japan. On physical examination, no palpable mass was noted in the abdomen, there was no swelling of superficial lymph nodes, and mucocutaneous jaundice was noted. Laparoscopic cholecystectomy had been performed 6 years earlier to treat cholelithiasis. The patient had no specific family history of related conditions. He had smoked 20 cigarettes each day for 40 years, but had no history of excessive alcohol consumption. Laboratory tests on admission showed hemoglobin 13.8 g/dL (reference range: 13-17 g/dL), total bilirubin 11.4 mg/dL (reference range: 0.2-1.1 mg/dL), alkaline phosphatase 760 IU/L (reference range: 115-359 IU/L), carcinoembryonic antigen 1,000 ng/mL (reference range: 0-5 ng/mL) and carbohydrate antigen 19-9 1.9 U/mL (reference range: 0-37 U/mL). An X-ray of the abdomen was normal. Abdominal computed tomography (CT) showed dilatation of the common bile duct and the pancreatic duct. The tumor, lymph node enlargement and distant metastases were not detected by CT. Duodenoscopy showed an irregularly shaped erosion on the ampulla of Vater and histology of a biopsy revealed adenocarcinoma (Figure 1). Duodenography showed irregularity of the second

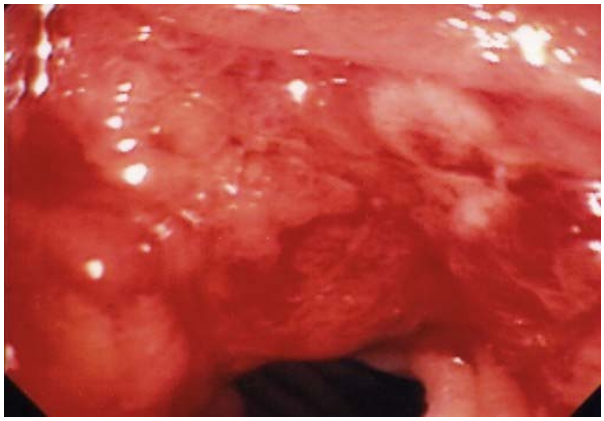

Figure 1. Duodenoscopy disclosed the irregularly shaped erosion on the ampulla of Vater.

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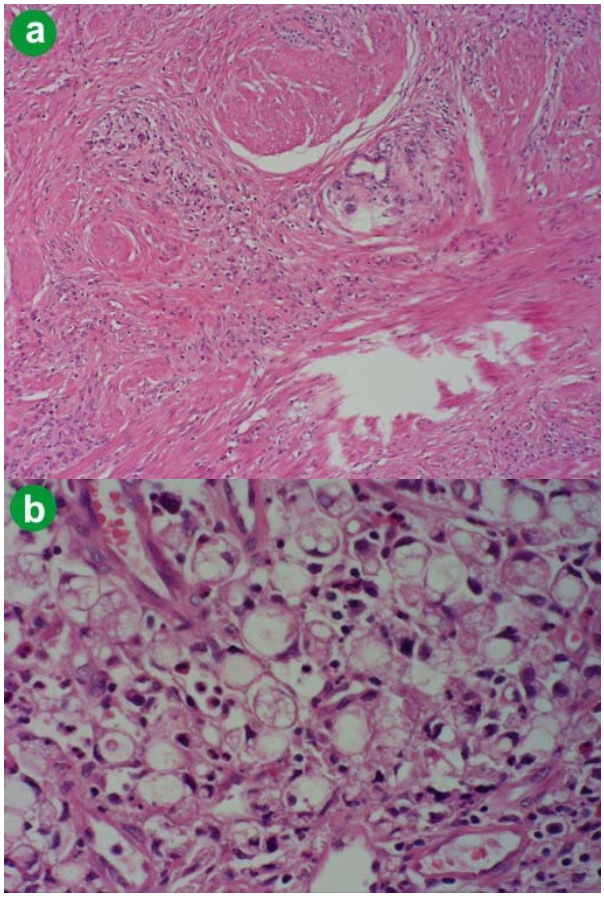

Figure 2. a. The tumor was composed of signet ring cell carcinoma and poorly differentiated adenocarcinoma (H&E x40). **b.** The tumor cells contained abundant intracytoplasmic mucin and the nuclei of the cells were located on one side. These are prominent and typical signet ring features (H&E x400).

portion of the duodenum wall. The diagnosis was carcinoma of the ampulla of Vater.

Pancreaticoduodenectomy and extended lymph-adenectomy (D3) were performed. During surgery, a tumor was palpable in the ampulla of Vater. The pancreas was soft, but inflammatory changes of the pancreas were not present. A slight irregularity of the duodenum wall was found. Macroscopically, the tumor measured 3.0x2.0x2.0 cm, and the cut surface was white. An irregularly shaped erosion was seen on the ampulla of Vater. Histologically, the tumor was classified as a poorly differentiated adenocarcinoma composed mainly of signet ring cell carcinoma. The tumor had invaded the duodenum and the pancreas. The tumor cells contained abundant intracytoplasmic mucin and the nuclei of the cells were located on one side; these are prominent and typical signet ring features (Figure 2). Immunohistochemically, the tumor cells were negative for chromogranin. Tumor cells were not found in the regional lymph nodes. The ampullary carcinoma was diagnosed as T3N0M0, Stage IIA according to the International Union Against Cancer TNM classification (UICC) [14]. Postoperative recovery was good and the patient was discharged on the seventeenth post-operative day. Adjuvant therapy was not administered since the patient did not wish to receive this therapy.

Seventeen months after surgery, the patient was hospitalized because of abdominal pain, weight loss and loss of appetite. CT revealed an excessive amount of ascites, indicating peritonitis carcinomatosa, and the patient died one month after admission.

DISCUSSION

Carcinoma of the ampulla of Vater is a relatively rare neoplasm, comprising 15-37% of surgically resected pancreatoduodenal tumors and 0.2% of routine autopsy cases [1]. Signet ring cell carcinoma occurs most frequently in the stomach and accounts for 15-30% of all gastric cancers. Only a few cases in the esophagus have been reported and the tumor is also uncommon in the colon in which it represents only 1% of all cancers [12]. Signet ring cell carcinoma is extremely rare in the ampulla of Vater. Gardner *et al.* first reported this histological pattern in 1990 and there have been only 12 previously reported cases in the English language literature (Table 1) [2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13]. Including the case reported here, the 13 cases consisted of 6 men and 7 women with ages ranging from 32 to 83 years (mean: 56 years). According to the TNM classification, they were divided between T2N0M0

Table 1. Reported cases of signet ring cell carcinoma of the ampulla of Vater.

Case Study	Age (years)	Sex	TNM stage	Procedure	Outcome
Gardner *et al*., 1990 [3]	69	Female	T3N0M0 Stage IIA	Pancreaticoduodenectomy	Unknown
Tseng *et al*., 2002 [4]	47	Male	T3N0M0 Stage IIA	Pancreaticoduodenectomy	Alive 6 months
Hara *et al*., 2002 [5]	68	Male	T2N0M0 Stage IB	Pancreaticoduodenectomy	Alive 10 months
Nabeshima *et al*., 2003 [6]	49	Male	T3NxM1 Stage IV	None	Dead 12 months
Eriguchi *et al*., 2003 [7]	83	Male	T3N0M0 Stage IIA	Pancreaticoduodenectomy	Alive 18 months
Ramia *et al*., 2004 [2]	67	Female	T2N0M0 Stage IB	Pancreaticoduodenectomy	Alive 12 months
Fang *et al*., 2004 [8]	53	Male	T2N0M0 Stage IB	Pancreaticoduodenectomy	Alive 25 months
Li *et al*., 2004 [9]	56	Female	T2N1M0 Stage IIB	Pancreaticoduodenectomy	Alive 12 months
Purohit *et al*., 2005 [10]	32	Female	TxNxM1 Stage IV	None	Unknown
Bloomstone *et al*., 2006 [11]	58	Female	T2N0M0 Stage IB	Pancreaticoduodenectomy	Alive 134 months
Akatsu *et al*., 2007 [12]	43	Female	T2N0M0 Stage IB	Pancreaticoduodenectomy	Alive 90 months
Gao *et al*., 2009 [13]	38	Female	T3N0M0 Stage IIA	Pancreaticoduodenectomy	Alive 6 months
Present study	59	Male	T3N0M0 Stage IIA	Pancreaticoduodenectomy	Dead 18 months

(Stage IB) (5 cases), T3N0M0 (Stage IIA) (5 cases), T2N1M0 (Stage IIB) (1 case), T3NxM1 (Stage IV) (1 case), and TxNxM1 (Stage IV) (1 case). In our case, the tumor mainly invaded the duodenum wall and pancreas aggressively (T3) but, on the other hand, lymph node metastasis was not found.

The origin of signet ring cell carcinoma in the ampulla of Vater has no clear histological explanation. Two possible theories have been proposed to explain the histological variability. One theory is that signet ring cell carcinoma, which is a common tumor in gastric epithelium, may originate from the heterotopic gastric mucosa in the ampulla of Vater [15]. Some authors have reported the presence of ectopic gastric mucosa contiguous with ampullary tumors [2, 3]. We suggest that the scant presence of ampullary gastric heterotopia accounts for the low number of cases of signet ring cell carcinoma in this location. The other theory suggests that these tumors arise from areas of gastric-type metaplasic epithelia which are considered to be a protective response to elevated acidity and are observable in the duodenal bulb of peptic ulcer patients [16]. The presence of a perivaterian duodenal heterotopia of ulcerous etiology may be the origin of a signet ring cell carcinoma which secondarily invades the ampulla of Vater. In the case reported here, ectopic gastric epithelium was not found and this patient did not have a history of peptic ulcer disease. A histological diagnosis of signet ring cell carcinoma of the ampulla of Vater can be difficult since the tumor must be differentiated from a neuroendocrine tumor. In this context, Gardner *et al.* have reported a double-secreting amphicrine tumor with a large population of neuroendocrine cells [3]. Given the possibility of a mixed tumor cell population, immunohistochemical staining for chromogranin was performed to examine the possible presence of a neuroendocrine component in the tumor. However, the staining was negative in all areas which showed that, in our case, the tumor did not have a neuroendocrine component.

Among the reported cases of signet ring cell carcinoma of the ampulla, 11 underwent pancreatico-duodenectomy, but surgery was not performed in two cases because of metastatic disease (Nabeshima *et al*., diagnosed by autopsy [6]; Purohit *et al*., diagnosed by histology using samples from an endoscopic biopsy [10]). In our case, the preoperative diagnosis was an advanced tumor with invasion of the duodenum wall, so a pancreaticoduodenectomy and extended lymphadenectomy were performed. In patients with an early carcinoma of the ampulla of Vater, a pyrolus-preserving pancreaticoduodenectomy is recommended because the preservation of the whole stomach and pyloric ring is thought to reduce the occurrence of postoperative complications, without decreasing curability [7]. To date, no standard postoperative adjuvant therapy regimen has been established for patients with this tumor. Nabeshima *et al*. reported that 5-fluorouracil and leucovorin were effective in increasing the survival time with a good quality of life [6]. In our case, the patient did not wish to receive adjuvant therapy, so this therapy was not performed postoperatively.

Signet ring cell carcinoma localized in other digestive organs has a poor prognosis. For example, the 5-year survival rate of patients with diffusely infiltrating carcinoma of the stomach (the majority of which consists of cases of signet ring cell carcinoma or poorly differentiated adenocarcinoma) is extremely poor, even after radical gastrectomy; an analysis of data collected through a nationwide registry in Japan revealed a 5-year survival rate of only 16.2% [17]. On the other hand, experience from previously reported cases of carcinoma of the ampulla of Vater suggests a good prognosis, provided there is no metastasis at the time of surgery. The follow-up period of the 10 cases which underwent a pancreaticoduodenectomy ranged from 6 to 134 months (mean: 33 months). On the other hand, a case with stage IV carcinoma died 12 months after diagnosis. In the present case, lymph node metastasis and distant metastasis were not found at the time of surgery, but the tumor had invaded the duodenum and pancreas aggressively. Thus the prognosis for our case was not good and 18 months later, he died from peritonitis carcinomatosa.

In conclusion, we have presented a rare case of signet ring cell carcinoma in the ampulla of Vater with invasion of the duodenum and pancreas. Although several cases have been reported, the detailed clinicopathological features and prognosis are not clear.

Conflict of interest The authors have no potential conflicts of interest

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