Case Report:
Signet-Ring Cell Carcinoma of the Ampulla of Vater

Lin Li,1 Qiang-Hua Chen,1 James D. Sullivan,2 and Frank U. Breuer1
Departments of 1Pathology and 2Surgery, North Shore University Hospital, Manhasset, New York

Abstract: Signet-ring cell carcinoma (SRCC) of the alimentary canal is a variant of adenocarcinoma that has a poor clinical prognosis. SRCC of the ampulla of Vater is extremely uncommon with <12 cases reported in the literature. SRCC of the ampulla of Vater occurs in an older age group (mean age 60 yr) when compared to SRCC of the stomach (under 45 yr), but is similar to SRCC of the large intestine. We report a case of SRCC of the ampulla of Vater with unusual histopathologic features in a 56-yr-old woman who presented with a small tumor at the orifice of the ampulla, associated with extensive lymphovascular invasion and multiple regional lymph node involvement. (received 4 May 2004, accepted 25 August 2004)

Keywords: ampulla of Vater, adenocarcinoma, signet-ring cell carcinoma

Introduction

Adenocarcinoma of the ampulla of Vater is rare, with an incidence of <6 cases per million persons per year [1]. It accounts for 0.2% of all gastrointestinal malignancies and 6% of periampullary malignancies, which include tumors of the pancreatic head, distal common bile duct, ampulla of Vater, and duodenum [2,27]. Signet-ring cell carcinoma (SRCC) of the ampulla of Vater is an uncommon histologic type at this site. It was first described by Sekoguchi et al [3] in 1979. Nine more cases have been reported [4-10,26,28]. We report a woman with signet-ring cell carcinoma in the ampulla of Vater.

Case Report

A 56-yr-old woman presented with pruritus, weight loss, and obstructive jaundice. Abdominal ultrasound examination revealed obstruction and dilatation of the common bile duct (CBD) at the level of the head of the pancreas. Helical computed tomography (CT) showed a dilated CBD without a mass lesion (Fig. 1). Endoscopic retrograde cholangiopancreatography (ERCP) showed a patent but ulcerated ampulla. A biopsy taken during ERCP was diagnosed as intramucosal signet-ring cell carcinoma. Imaging studies (ie, mammography, computer-aided detection (CAD), CT of chest and abdomen, magnetic resonance imaging (MRI) of the abdomen) did not reveal any visceral or breast malignancy. The patient underwent a Whipple resection. Following surgery, she received radiation (total dose of 5040 cGy) and chemotherapy, which was completed in March 2004. The patient is clinically well at one yr after surgery.

Pathological Findings

The Whipple resection specimen showed a 1.5 x 1.0 cm sessile ulcerated polypoid mass encroaching upon the orifice of the ampulla of Vater at the insertion of the distal common bile duct. Proximally, the lumen of the common bile duct was dilated to 1.4 cm and the wall of the common bile duct was markedly thickened. The head of the pancreas and the stomach were apparently free of lesions. The cut surface of the tumor was tan and firm; the tumor infiltrated into the wall of the duodenum.
Fig. 1. Computerized tomogram (CT) showing markedly dilated common bile duct (1a) at the level of pancreatic head (1b). No mass lesion was noted. Du: duodenum; CBD: common bile duct; Pan: pancreas.

Fig. 2. Ampulla of Vater demonstrating intramucosal SRCC (2a, 100 x); higher magnification showing characteristic signet-ring cells with eccentrically located, hyperchromatic nuclei, and abundant intracytoplasmic mucin (2b, 400 x); admixture of signet-ring cells with infiltrating adenocarcinoma (2c, 400x); regional lymph node showing metastatic adenocarcinoma without SRCC component (2d, 100x).
Histologically, an in situ signet-ring cell carcinoma and an infiltrating adenocarcinoma admixed with numerous signet-ring cells were found (Fig. 2a-2c). The tumor involved the entire muscularis propria of the ampulla and focally extended into adjacent peritoneal adipose tissue. The infiltrating tumor showed >60% diffusely distributed signet-ring cells that contained abundant intracytoplasmic mucin and typical eccentric nuclei (Fig. 2c). The intracytoplasmic mucin stained positively with mucicarmine and D-PAS stains. The common bile duct, stomach, and pancreas were free of tumor. Lymphovascular invasion was present within the tumor. Eight of 12 peripancreatic lymph nodes were positive for metastatic adenocarcinoma without a signet-ring cell component (Fig. 2d).

Discussion

Signet-ring cell carcinoma (SRCC) is a variant of adenocarcinoma recognized by the presence of >50% of the characteristic signet-ring cells with intracytoplasmic mucin and typical eccentrically located, crescent shaped nuclei seen by light microscopy [11,27]. Clear cell carcinoma such as renal cell carcinoma, clear cell type, can mimic SRCC histologically. However, the glycogen-rich cytoplasm in clear cell carcinoma is easily distinguished from the mucin-rich cytoplasm in signet-ring cell carcinoma by mucin and D-PAS stains, which were diffusely positive in our case.

Adenocarcinoma of the ampulla is unique due to its special epithelial composition. There are 3 different types of epithelium (ie, duodenum, pancreatic duct, and common bile duct) that become confluent in a narrow region of the ampulla of Vater [21,27]. Several large series of ampullary adenocarcinomas have been published [2-3,16-19,28-29]. However, SRCC in this location has rarely been discussed. Seifert et al [28] described 1 case in a series of 35 carcinomas of the papilla of Vater. Blackman and Nash [29] found 2 anaplastic carcinomas that contained signet ring cells. However, the extent of the signet ring cells in these carcinomas was unclear from the paper. As mentioned previously, >50% of tumor must comprise signet ring cells to qualify as a signet ring cell carcinoma.

Nine well-documented cases of SRCC of the ampulla of Vater are summarized in Table 1. Of the 9 cases, 8 were male. Seven of the patients were Asian, including 6 from Japan. The mean age at presentation was 60 yr (25 to 83 yr). This is 15 yr older than SRCC of the stomach, but similar to SRCC of the large bowel [13-15,23-24]. SRCC of
the ampulla of Vater has generally been described without lymph node involvement or distant metastasis at the initial presentation. Furthermore, of 7 patients (including the current case) with documented follow-up information, 6 were alive without disease for periods of 6 to 24 mo at the time of publication. One patient presented initially with a bone marrow metastasis by a poorly differentiated adenocarcinoma with signet-ring cell features. The primary site was identified as the ampulla of Vater at autopsy [4].

Our case showed unusual clinical and pathological features. First, a distinct in situ SRCC component was noted. Intramucosal SRCC has not been previously described in ampullary SRCC. The signet-ring cells in our case were diffusely admixed with a moderately differentiated infiltrating adenocarcinoma. However, only adenocarcinoma without signet-ring cell was found in metastatic lymph nodes. Second, although it is believed that most cancers of the small bowel arise within a preexisting adenoma or are associated with atypical epithelium [13,18,25, 27-28], none of the previous cases of SRCC of the ampulla identified an adenomatous or dysplastic precursor lesion in the adjacent mucosa of the duodenum, common bile duct, or cystic duct. Our case raises a question whether the in situ signet-ring cell component may be a true precursor lesion. Third, our case presented with a small tumor (1.5 x 1.0 cm) but had extensive lymphovascular invasion and involvement of multiple regional lymph nodes by metastatic adenocarcinoma without signet-ring cells. In 8 of 9 previously described cases, neither lymph node nor distant metastases were found.

SRCC can arise in many organs, particularly in the alimentary tract, where it occurs most frequently in the stomach and large bowel [12-13]. In contrast to SRCC of the ampulla of Vater, SRCC of the stomach appears to arise from nonmetaplastic foveolar or mucous neck cells that proliferate as single cells or in small clusters with admixture of glandular elements in the deeper portions of the tumor [11]. A 26% incidence of SRCC in early gastric adenocarcinoma has been reported in a large series [12] in Japan. It has a tendency to develop in a younger age group (<45 yr) and is associated with a poor prognosis [11].

SRCC is an uncommon subtype of colorectal adenocarcinomas [13-14], although an increasing trend of signet-ring cell carcinoma in the colon was observed by Henson [30]. Several large series reported a frequency rate of approximately 1% of SRCC in large bowel carcinomas [13,15,23-24]. Unlike SRCC of the stomach, the mean age for SRCC of the large bowel ranged from 59 to 63.5 yr [15,23-24]. An increased frequency of exophytic or well-circumscribed SRCC has been associated with hereditary non-polyposis colorectal cancer syndrome (HNPPC) and in sporadic colorectal cancers displaying DNA microsatellite instability (DMI) [13]. The prognosis of colorectal SRCC is extremely poor [13-14,23-24]. The origin of SRCC of the large bowel is uncertain. Mai et al [15] reported that SRCC may arise from conventional adenocarcinoma, adenoma, “atypical” epithelium, or a combination of these epithelia, that is, a transformation at any level of a neoplastic colonic mucosa.

In summary, we report a unique case of signet-ring cell carcinoma of the ampulla of Vater with an intramucosal signet-ring cell component and extensive regional lymph node involvement. SRCC of the ampulla of Vater occurs in an older age group than SRCC of stomach but is similar to the age group of SRCC of the large bowel. Henson et al [30] reported an increasing incidence of diffuse type of gastric carcinoma, signet ring cell carcinoma in particular, in the United States during 1973-2000 based on data from the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute. We believe that the biologic behavior and pathogenetic mechanisms of ampullary signet-ring cell carcinoma need to be investigated further.

Acknowledgements

The authors thank Myron Susin, M.D., for advice and assistance.

References

Signet cell carcinoma of the ampulla of Vater


