ACG CASE REPORTS JOURNAL

CASE REPORT | STOMACH

Gastric Carcinoma With Sebaceous Differentiation and SALL4 Expression

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ABSTRACT

A sebaceous carcinoma is rarely seen in extracutaneous sites. We present a 75-year-old man who was admitted with epigastralgia and melena. Endoscopic examination revealed an ulcer on the posterior wall of the gastric antrum, and distal gastrectomy was performed. Histopathological examination revealed thin to thick trabeculae of polygonal cells with scattered foci of foamy cells, whereas Sudan 3 staining showed lipid vacuoles. Immunohistochemistry was positive for both p40 and SALL4. After considering these findings, we suggest sebaceous differentiation as the diagnosis. To the best of our knowledge, this is the first case of gastric carcinoma with sebaceous differentiation.

KEYWORDS: stomach; AFP-producing adenocarcinoma; sebaceous carcinoma; SALL4

INTRODUCTION

Sebaceous carcinoma (SC) mostly occurs in the head and neck region, with approximately 40% of cases occurring in the eyelid,[1] and rarely arise in sites without sebaceous glands. SC has not been reported in the stomach. Contrastingly, alpha-fetoprotein (AFP)-producing adenocarcinoma (AFP-PA), hepatoid adenocarcinoma, and enteroblastic adenocarcinoma are one of the predominant cancers of the stomach and share nuclear morphology, frequent SALL4 expression, and poor prognosis. We report a case of gastric carcinoma with sebaceous differentiation with SALL4 expression.

CASE REPORT

A 75-year-old man was admitted to our hospital with epigastric pain and tarry stool. He had a history of prostate cancer (curative surgery 15 years before) and a familial malignant history of gastric (father in his 90s) and lung cancer (2 sisters in their 70s and 60s, respectively). Laboratory blood examination showed normal levels of serum carcinoembryonic antigen (0.61 ng/mL) and carbohydrate antigen 19-9 (2.5 U/mL). The serum AFP level was not examined. Upper gastrointestinal endoscopy revealed a 40 mm ulcerated tumor at the gastric antrum (Figure 1), and subsequent biopsy showed poorly differentiated adenocarcinoma. Computed tomography and positron emission tomography showed regional lymph node swelling. Preoperative diagnosis of the tumor stage was T3N2M0 Stage IIIA.

Distal gastrectomy with D2 lymphadenectomy was performed. As broad adhesion was suspected with tumor invasion observed between the gastric antrum and transverse mesocolon during the surgery, transverse colectomy was added. The postoperative course was uneventful, and the patient was discharged on postoperative day 11.

The macroscopic examination showed a 65 × 55-mm ulcerated tumor on the posterior wall of the gastric antrum and a 40-mm submucosal nodule on the pyloric ring (Figure 2). Xanthomatous plaque was not observed on the background gastric mucosa.

ACG Case Rep J 2023;10:e01061. doi:10.14309/crj.0000000000001061. Published online: May 24, 2023

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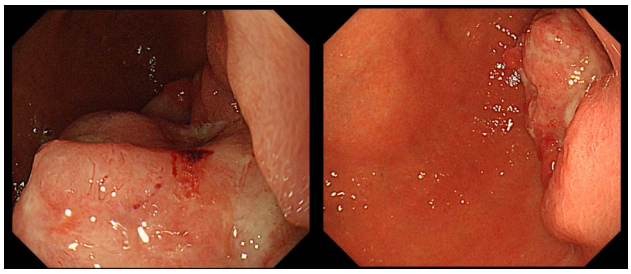

Figure 1. Upper gastrointestinal endoscopy showing a 40 mm ulcerated tumor at the gastric antrum.

Eventually, all mucosa and muscularis propria of the resected distal half of the stomach was sliced into 5-mm strips and submitted for histological specimen. Histological examination revealed the neoplastic lesion was composed of poorly differentiated carcinoma and squamoid carcinoma. Most of the poorly differentiated carcinoma showed sheets of polygonal cells with large round nuclei and prominent central nucleoli (Figure 3). In the poorly differentiated portion, there also were thin to thick trabeculae of polygonal cells with pale to eosinophilic cytoplasm, resembling hepatocellular carcinoma (Figure 3) and small nests of multivacuolated cells resembling sebaceous glands were scattered (Figure 3). The squamoid carcinoma showed a nest of neoplastic cells with abundant eosinophilic cytoplasm, suggesting squamous cell differentiation, although there was not apparent keratinization or presence of intercellular bridges (Figure 3).

The tumor had invaded into the subserosa, but there was no histological invasion into the mesentery or wall of the transverse colon. The pyloric ring nodule penetrating muscularis propria showed almost the same histological features as the main tumor, and was partially surrounded by a lymphoid tissue rim, suggesting lymph node metastasis. Gastric dysplasia or ectopic sebaceous glands were not observed in the background gastric mucosa. Sudan 3 staining of the frozen section showed nests of cells with abundant lipid concentration (Figure 3). Immunohistochemically, the poorly differentiated component showed diffuse positivity for AE1/3, p40, and SALL4 and patchy positivity for Glypican-3 and AFP (Figure 4), and the squamoid component showed diffuse positivity for AE1/3 and p40 and patchy positivity for SALL4, CK5/6, and AFP (Figure 4). Both components were negative for synaptophysin, chromogranin, CDX2, and PSA. Thus, we diagnosed the tumor as a carcinoma with sebaceous differentiation (pT3N1M0, pStageIIIb).

Otorhinolaryngological examination and upper gastrointestinal endoscopy along the mouth to the esophagus did not reveal any yellowish plaque typically suggestive of ectopic sebaceous glands. Similarly, systemic dermatological examination showed the absence of subcutaneal nodules and ulcers that are typically suggestive of sebaceous neoplasm or hyperplasia.

At the 16-month follow-up, without adjuvant therapy, recurrence or distant metastasis was not observed.

DISCUSSION

To the best of our knowledge, SC in the stomach has not been reported until now. SC arising in sites without sebaceous glands has been reported in the thymus, uterine cervix, oral cavity, parotid gland, and larynx, and these cases were suspected to arise from an ectopic sebaceous gland or sebaceous metaplasia.[2–6] Although an ectopic sebaceous gland is sometimes encountered on examination or endoscopy as a single or multiple yellowish white milliary nodule along the oral cavity to esophagus, we could not find literature describing them in gastric cases, despite the same foregut origin. In this case, histological examination throughout the stomach did not reveal any ectopic sebaceous gland or sebaceous metaplasia as a background. Endoscopic, otorhinolaryngologic, and a dermatologic examination also did not reveal any esophageal, oral, or skin lesions, thereby ruling out the possibility of a metastatic origin. Family history and dermatological findings did not suggest hereditary cancer

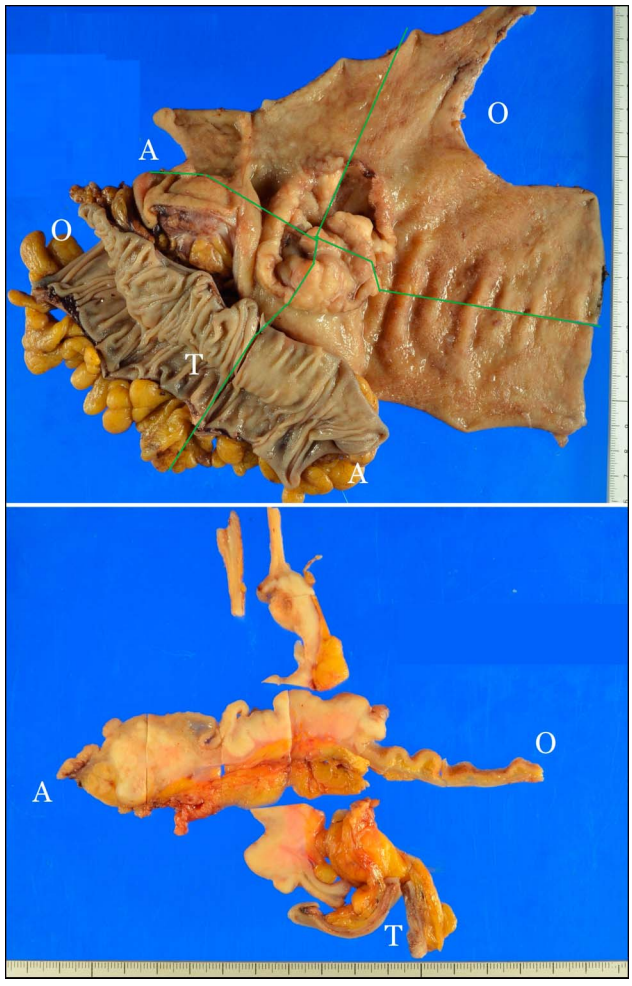

Figure 2. Macroscopic photographs of the resected stomach. The resected stomach was incised through the anterior wall. A 65 × 55-mm seized ulcer was situated across the posterior wall of the antrum. A 40 mm–sized nodule lifted up posterior mucosa of the pylorus ring. The transverse colon (T) and mesocolon were resected together (O, oral; A, anal). Cut surfaces along green lines above are shown below.

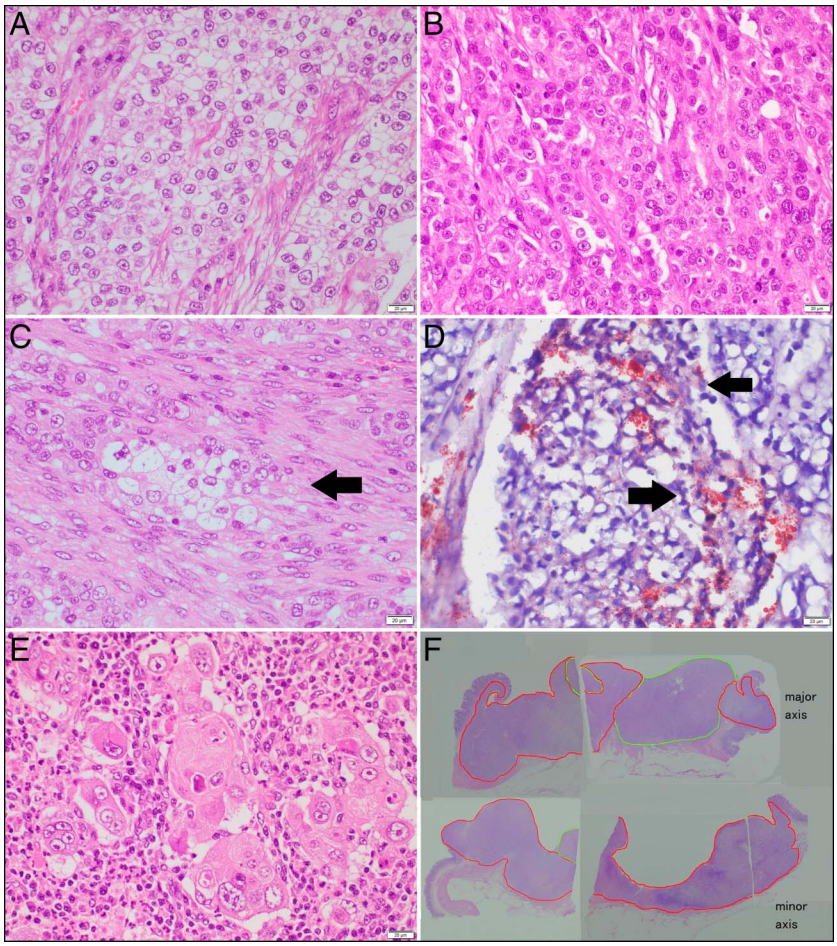

Figure 3. Microscopic photographs of the ulcerated tumor. Most of the poorly differentiated carcinoma shows a sheet of polygonal cells with large round nuclei and prominent central nucleoli (A). Thin to thick trabeculae of polygonal cells with pale to eosinophilic cytoplasm, resembling hepatocellular carcinoma (B). There is a nest of vacuolated cells (arrow), resembling sebaceous glands (C). Sudan 3 staining (D) shows orange lipid droplets (arrows). Tumor cells of some area have abundant eosinophilic cytoplasm, suggesting squamous differentiation (E). Distribution map of poorly differentiated area (red) and squamoid area (green) on the glass slide image (F).

susceptibility, including Muir-Torre syndrome, ie, dermal multiple sebaceous neoplasms associated with visceral malignancy.[7]

Gastric AFP-PA is characterized by elevation of serum AFP levels and/or immunohistochemical positivity for AFP. However, histological AFP expression level is not always associated with serum AFP elevation.[8] AFP-PA shows histological variations such as hepatoid adenocarcinoma (trabeculae with eosinophilic cytoplasm), adenocarcinoma with enteroblastic differentiation (tubules with clear cytoplasm), and yolk sac tumor-like carcinoma. They are believed to be derived from adenocarcinoma of common type because of their frequent coexistence and sharing of gene abnormality.[9] Recently, AFP-PA turned out to show overlap with SALL4-positive adenocarcinoma in the stomach.[10] Although the serum AFP level was not measured, and the histological expression of AFP was only focal in the present report, our case and AFP-PA shared some histological features such as a pale to eosinophilic cytoplasm, large round nuclei with prominent nucleoli, and SALL4 positivity.

Contrastingly, there are reported cases of AFP-PA with neuroendocrine, sarcomatoid, or squamous cell components.[11,12] Although AFP-PA with SC has never been reported, sebaceous differentiation in our case might represent another de-differentiation of AFP-PA.

The prognosis of SC arising in the stomach has not been established. The reported five-year overall survival of AFP-PA and adenocarcinoma of common type are 17.7% and 55.9%, respectively.[8] In the present case, we still continue to carefully follow-up the patient.

DISCLOSURES

Author contributions: T. Nakanishi and Y. Imai wrote the manuscript. M. Akita wrote the clinical findings. K. Kaneda, C. Ichikawa, I. Tamura, Y. Kawata, and M. Takahashi approved the final manuscript. Y. Imai is the article guarantor.

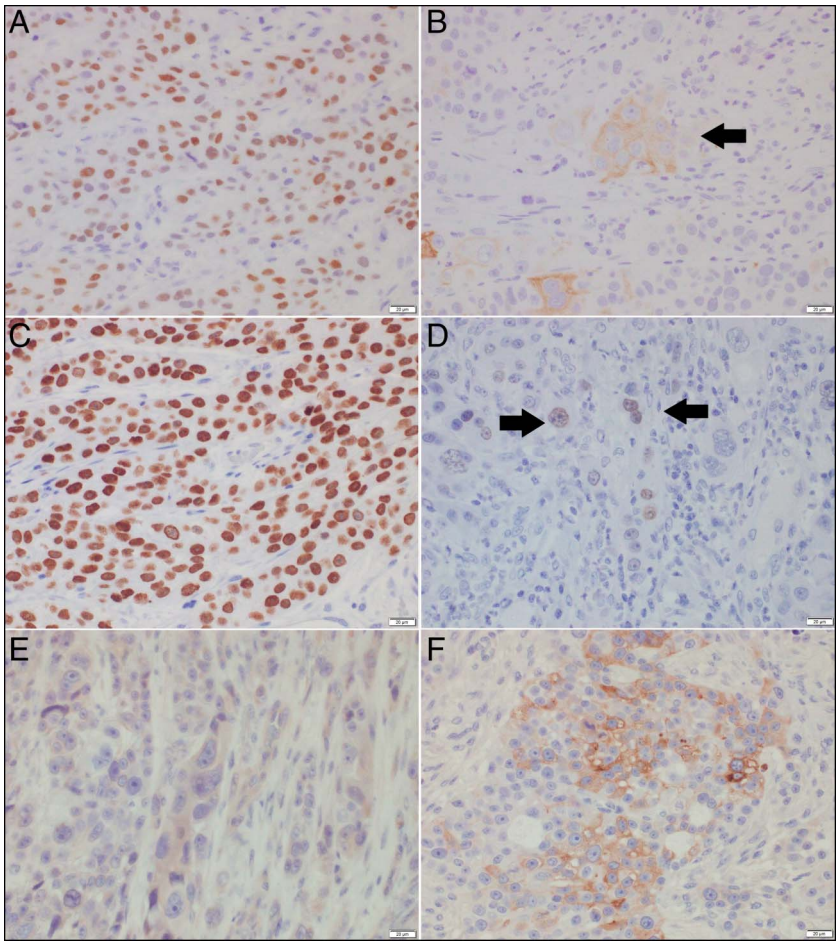

Figure 4. Microscopic photographs of immunohistochemical staining. p40 (A) and SALL4 (C) show diffuse nuclear positivity, and alpha-fetoprotein (E) and Glypican-3 (F) show only focal cytoplasmic positivity in the poorly differentiated component. CK5/6 (B) shows only focal cytoplasmic positivity (arrow), and SALL4 (D) shows patchy nuclear positivity in the squamoid component (arrows).

Financial disclosure: None to report.

Previous presentation: This case was presented at the Japanese Society of Pathology Kinki Branch Conference; December 4, 2021; Kobe, Japan.

Informed consent was obtained for this case report.

Received December 3, 2022; Accepted April 24, 2023

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