

[CASE REPORT]

Gastric Metastasis from Salivary Duct Carcinoma Mimicking Scirrhou Gastric Cancer

Kenichi Kishimoto¹, Kotaro Shibagaki², Asuka Araki³, Kotaro Murakami¹,
Yusuke Takahashi¹, Satoshi Kotani¹, Akihiko Oka¹, Tomotaka Yazaki¹, Nobuhiko Fukuba¹,
Yoshiyuki Mishima¹, Naoki Oshima², Kousaku Kawashima¹, Norihisa Ishimura¹,
Kyuichi Kadota³ and Shunji Ishihara¹

Abstract:

A 59-year-old man underwent submandibular gland excision for salivary duct carcinoma (SDC). One year later, esophagogastroduodenoscopy indicated gastric diffuse mucosal thickening with luminal contraction, mimicking scirrhou gastric carcinoma. Biopsy specimens showed dense proliferation of neoplastic cells expressing androgen receptor and human epidermal growth factor 2, indicating SDC. Gastric diffuse infiltrative metastasis is generally characteristic of gastric metastasis from invasive ductal carcinoma, which shows histologic features similar to SDC. This is the first known report of gastric diffusely infiltrating metastasis in an SDC patient. Rapidly progressing, diffuse gastric wall thickening should also be considered indicative of salivary tumor-associated gastric metastasis.

Key words: gastric metastasis, scirrhou gastric cancer, salivary duct carcinoma

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Introduction

Metastatic tumors to the stomach are very rare and reportedly occur in 1.7-5.4% of all gastric tumor cases (1-3). The primary tumor in affected patients is frequently a malignant melanoma related to lung or breast cancer (1, 2, 4). Endoscopic findings of gastric metastasis primarily show solitary lesions with a submucosal tumor-like form, followed by a primary gastric cancer-like form, with occurrence usually in the middle or upper third of the stomach (5). As a special metastatic form, approximately 30% of breast cancer cases exhibit a diffusely infiltrating metastasis that is very similar to scirrhou gastric cancer (6).

Cases of salivary duct carcinoma (SDC) are very rare, as they reportedly account for 5-10% of all salivary gland tumors (7, 8), although they show an aggressive nature with high rates of local recurrence and distant metastasis (9). Histologically, SDC resembles a high-grade mammary ductal

carcinoma characterized by tumor cell proliferation with comedonecrosis and cribriform growth pattern findings (10). SDCs primarily metastasize to the lungs, bone, and brain, whereas gastric metastasis is extremely rare.

We herein report the details of the first known reported case of diffusely infiltrating gastric metastasis from SDC showing a scirrhou gastric cancer-like appearance.

Case Report

A 59-year-old man underwent submandibular gland excision and cervical lymph node dissection for a right submandibular gland tumor, shown histologically to consist of pleomorphic tumor cells arranged in sheets that strongly expressed androgen receptor (AR) and human epidermal growth factor receptor type 2 (HER2) (Fig. 1). Diagnosed with primary SDC stage IVB (pT3, pN3, bcM0), the patient thereafter underwent postoperative radiation chemotherapy with 5-fluorouracil and cisplatin. One year later, bone me-

¹Department of Gastroenterology, Faculty of Medicine, Shimane University, Japan, ²Department of Endoscopy, Shimane University Hospital, Japan and ³Department of Pathology, Faculty of Medicine, Shimane University, Japan

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Correspondence to Kotaro Shibagaki, kotaro@med.shimane-u.ac.jp

Table. Laboratory Data.

WBC	7,390 / μ L	LDH	194 U/L
Neut	77.7 %	Amylase	59 U/L
Lympho	10.4 %	BUN	16.9 mg/dL
Mono	8.9 %	Creatinine	0.96 mg/dL
RBC	4.28×10^6 / μ L	Sodium	138 mEq/L
Hemoglobin	13.4 g/dL	Potassium	4.2 mEq/L
Hematocrit	38.6 %	Chloride	101 mEq/L
Platelet	9.1×10^4 / μ L	Calcium	8.9 mEq/L
Total protein	5.8 g/dL	CRP	0.58 mg/dL
Albumin	3.7 g/dL	SCC	1.1 ng/mL
Total bilirubin	0.7 mg/dL	CEA	1.9 ng/mL
AST	18 U/L	<i>Helicobacter pylori</i> IgG	<3 U/mL
ALT	28 U/L		

WBC: white blood cell, RBC: red blood cell, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, BUN: blood urea nitrogen, CRP: C-reactive protein, SCC: squamous cell carcinoma, CEA: carcinoembryonic antigen

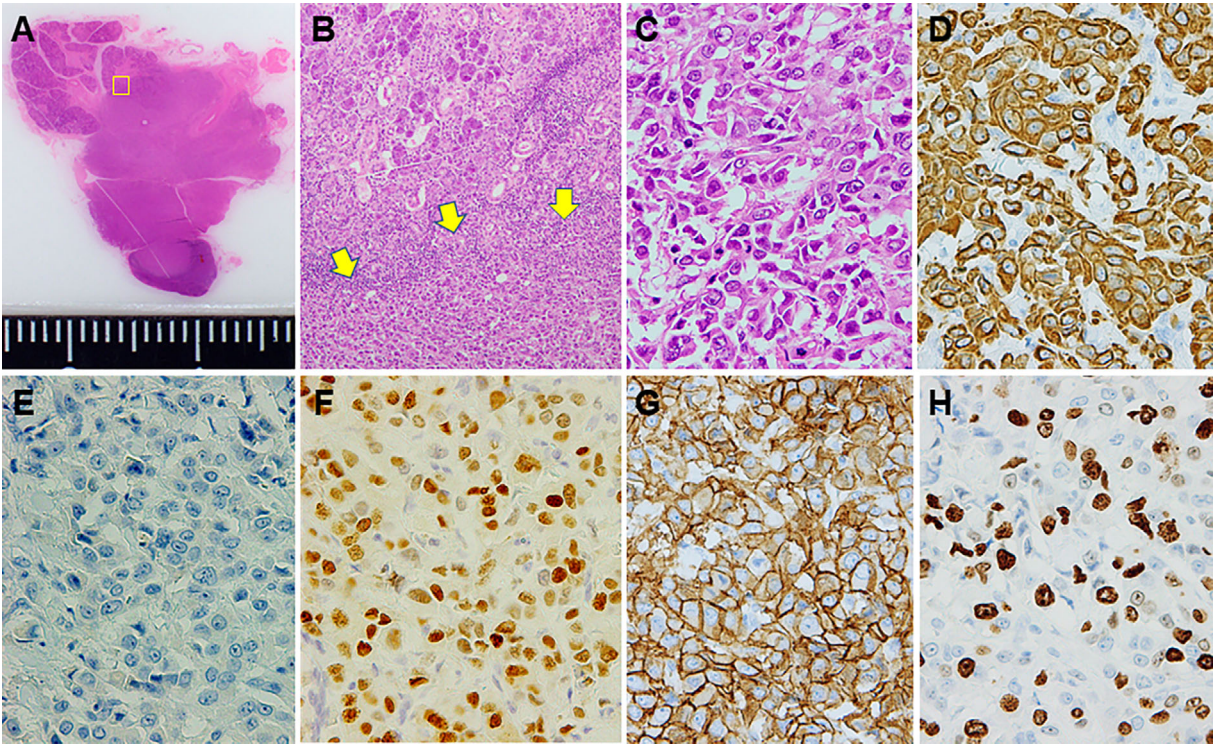


Figure 1. (A) Representative section of resected submandibular gland, with boundary area of normal and neoplastic tissue indicated by yellow box. (B) Neoplastic tissue adjacent to normal salivary gland with amorphous structure (yellow arrows). (C) High magnification showing a tumor comprised of pleomorphic neoplastic cells with vesicular nuclei and prominent nucleoli arranged in sheets. Neoplastic cells showing (D) strong expression of CK7 and (E) negative expression of CK20. Strong expression of (F) androgen receptor and (G) human epidermal growth factor receptor type 2 in neoplastic cells was noted, suggesting primary salivary duct carcinoma. (H) The Ki-67 labeling index was approximately 40%, indicating high cell proliferation.

tastasis was detected, and systemic combined chemotherapy using docetaxel and trastuzumab was started. However, one year after starting chemotherapy treatment, the patient complained of postprandial nausea.

There were no abnormal findings in the abdominal physi-

cal examination, as follows: blood pressure: 136/92 mmHg, heart rate: 105 beats/min, oxygen saturation: 98% (room air), body temperature: 36.4°C. Laboratory data showed appropriately normal findings (Table). The patients previously underwent eradication therapy for *Helicobacter pylori*, and

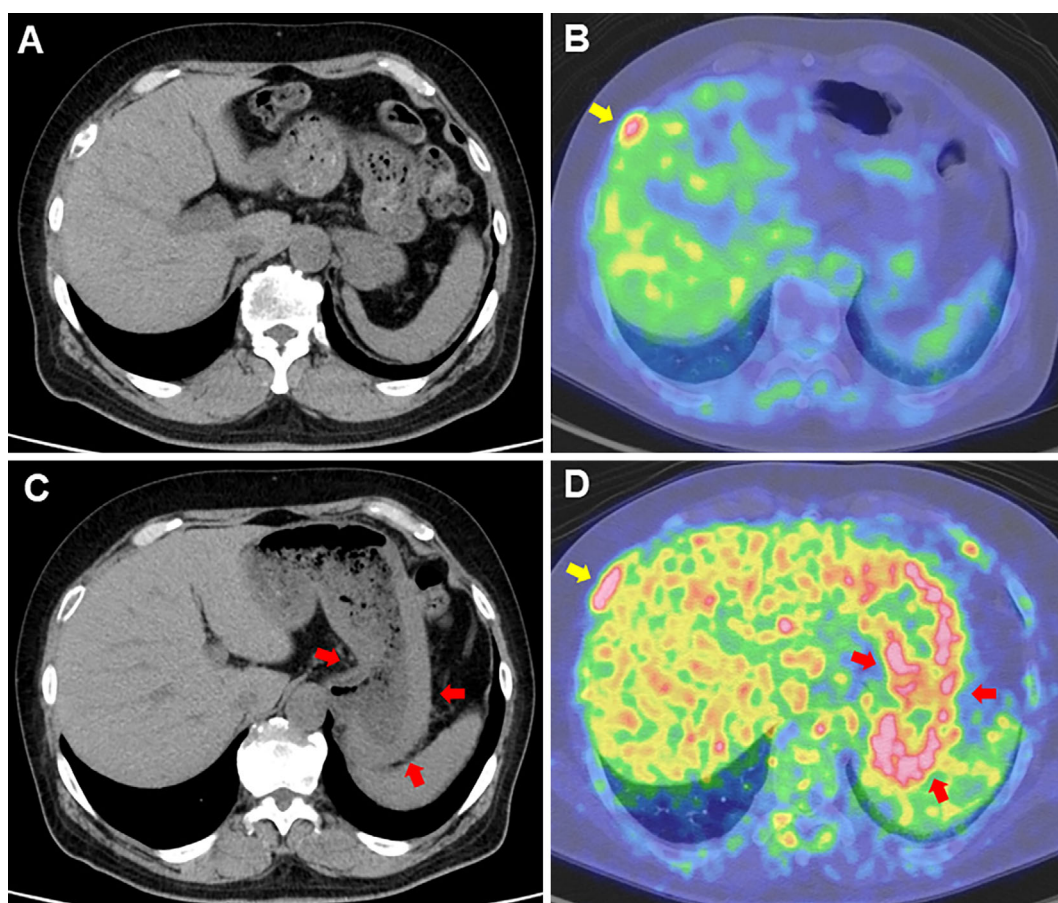


Figure 2. Representative images of computed tomography (CT) and positron emission tomography (PET)-CT. Six months prior to referral to our department, (A) abdominal CT showed no thickening of the gastric wall, and (B) PET-CT showed the accumulation of fluorodeoxyglucose (FDG) in the right rib and bone metastasis (yellow arrow). (C) At the time of referral to our department, abdominal CT showed circumferential thickening of the gastric wall (red arrows), and (D) PET-CT showed progression of bone metastasis (yellow arrow) and an intensive FDG accumulation in the thickening gastric wall and gastric metastasis (red arrows).

the serum anti-*Helicobacter pylori* IgG antibody titer was < 3 U/mL. Computed tomography and positron emission tomography showed a rapidly progressing, diffuse wall thickening of the gastric body with an intensive spot of fluorodeoxyglucose (Fig. 2). Furthermore, esophagogastrroduodenoscopy indicated diffuse mucosal thickening with an exudate and luminal contractions in the oxyntic gastric compartment, along with a scirrhous gastric carcinoma-like appearance (Fig. 3).

Biopsy specimens from the thickened gastric mucosa were obtained, and histological results showed densely proliferating neoplastic cells with pleomorphic hyperchromatic large nuclei arranged in sheets. Immunohistochemical findings were positive for both AR and HER2 in neoplastic cells, as well as the primary salivary tumor, suggesting gastric metastasis from SDC (Fig. 4).

There is no established regimen of chemotherapy for SDC, so the patient received S-1 (tegafur, gimeracil, and oteracil potassium) plus oxaliplatin and trastuzumab according to the regimen for HER2-positive gastric cancer, although he died from tumor progression 10 months later.

Discussion

Gastric metastasis from a salivary gland tumor is extremely rare. There are only two known case reports of salivary gland tumors, both of which presented with histological findings of SDC developing from the parotid gland. Each showed common endoscopic features of gastric metastasis, one with a multiple submucosal tumor-like form (11) and the other with an advanced gastric cancer type 2 (ulcerative type)-like form (12). To our knowledge, the present case is the first reported case of diffuse infiltrative gastric metastasis from a salivary gland tumor with a primary scirrhous gastric cancer-like appearance.

Diffuse infiltrative invasion into the stomach wall is a representative form of gastric metastasis from breast cancer. Invasive ductal carcinoma is the most common histologic type of breast cancer, followed by lobular carcinoma (13), with 38.9% (14/36) of lobular carcinomas and 30% (3/10) of ductal carcinomas found to exhibit diffusely infiltrating gastric metastasis (6). SDC generally presents histopathological

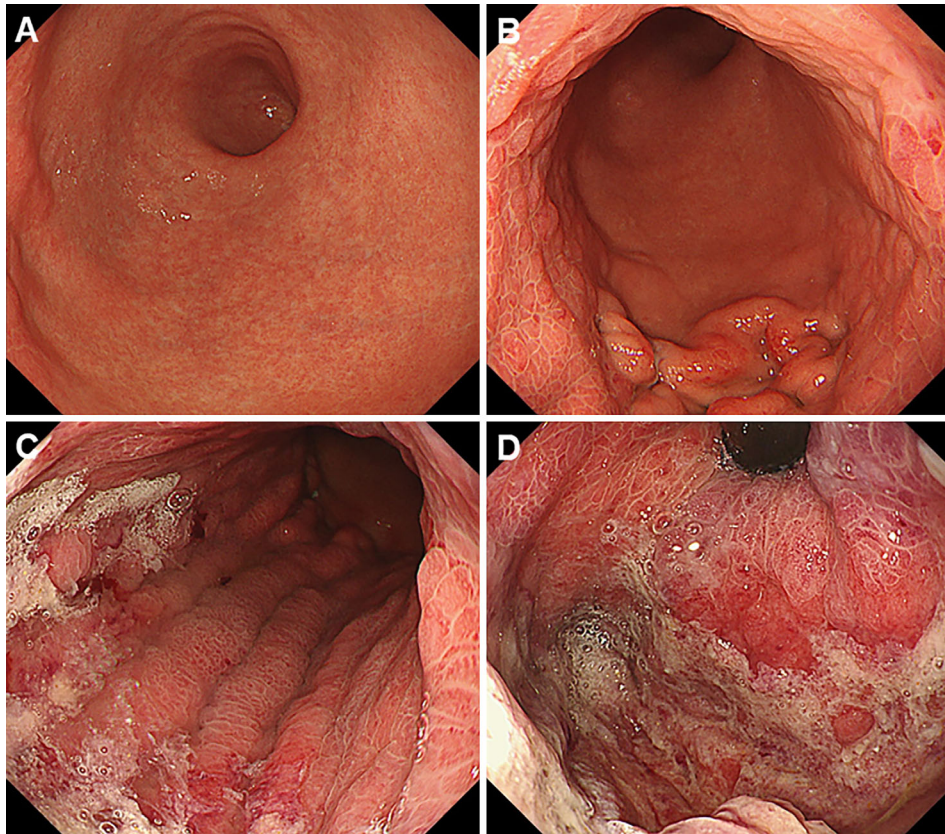


Figure 3. (A) Esophagogastroduodenoscopy findings showing atrophic gastritis in the gastric antral compartment. (B) Mucosal findings showing a scirrhus gastric carcinoma-like appearance, including drastic changes at the angular incisure and diffuse mucosal thickening with an exudate and luminal contraction in the (C) gastric body and (D) fornix.

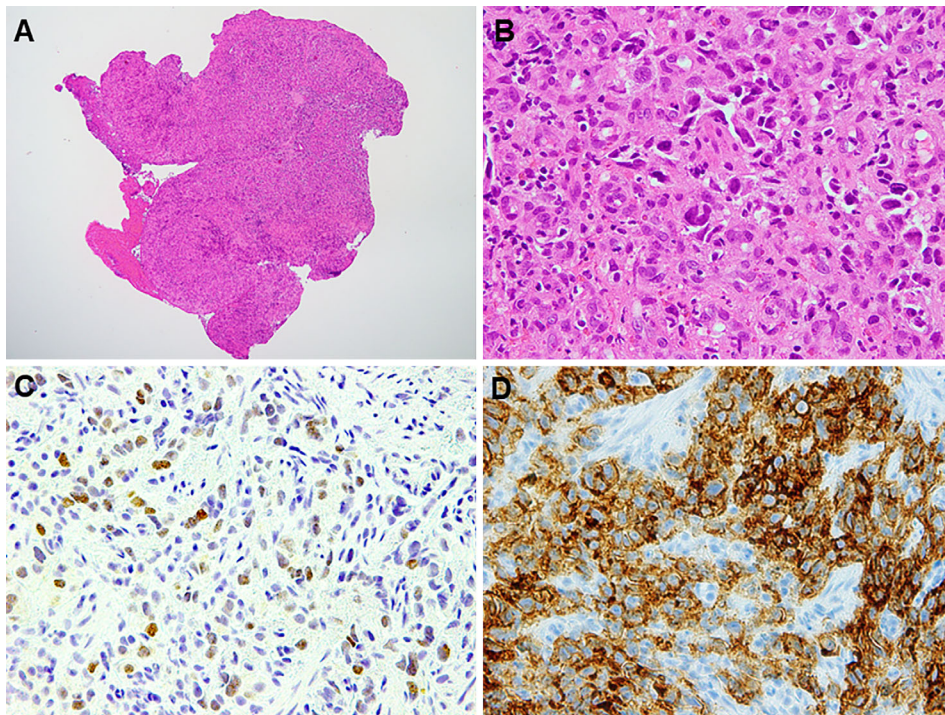


Figure 4. (A) Biopsy specimen from gastric mucosa. (B) High-magnification image showing dense proliferation of neoplastic cells with pleomorphic hyperchromatic large nuclei arranged in sheets. In neoplastic cells, (C) androgen receptor and (D) human epidermal growth factor receptor type 2 were both partially positive, suggesting gastric metastasis from salivary duct carcinoma.

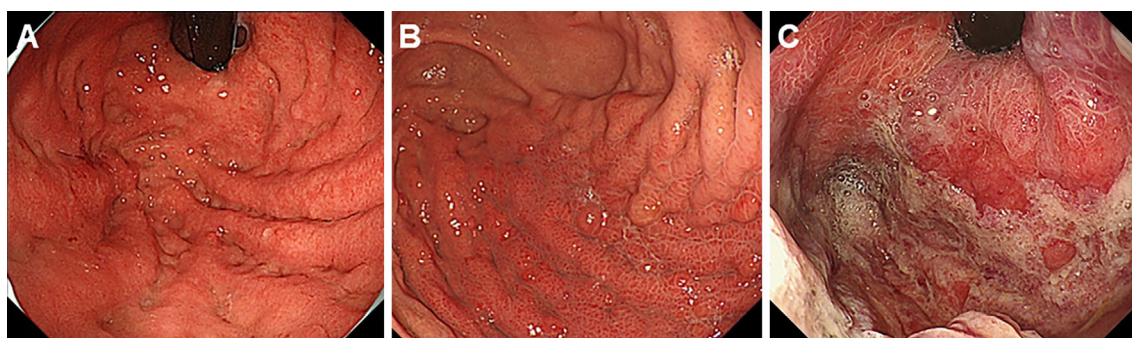


Figure 5. Our cases of diffuse-type gastric cancer and diffusely infiltrative gastric metastasis cases; (A) scirrhous gastric carcinoma (59-year-old woman), (B) gastric metastasis of invasive ductal carcinoma of the breast (52-year-old woman), and (C) gastric metastasis of salivary duct carcinoma (the present case).

characteristics similar to those of invasive ductal carcinoma, with AR being a specific immunohistochemical marker for both, showing a positive ratio of 72.5-93.1% in invasive ductal carcinoma and 56-100% in SDC cases (14-17). HER2 is also likely expressed in both types of tumors, with reports showing positive ratios of 20-27% and 16-83%, respectively (14-16). Interestingly, malignant tumors with similar histologic features appearing in different tissues, such as mammary and salivary glands, show a similar special type of gastric metastasis that resembles primary scirrhous gastric cancer (Fig. 5).

There are four pathways that may be involved in the metastatic spread of primary tumors to the stomach: direct tumor invasion, peritoneal dissemination, lymphatic spread, and hematogenous dissemination (18). When metastasis occurs via lymphatic channels, tumor cells likely develop locally in the submucosal layer, showing a submucosal tumor-like form or an advanced gastric cancer-like form. Hematogenous dissemination occurs as distant metastasis, and tumor cells in the blood are trapped in the submucosal or subserosal layer, where they induce submucosal localized growth or diffuse infiltration that is composed of poorly differentiated carcinoma, as in the present case. Thus, the morphologic characteristics of gastric metastasis are affected by the metastatic pathway and cellular differentiation of the primary tumor.

Based on histological findings obtained by Hematoxylin and Eosin staining alone, gastric diffusely infiltrating metastasis is difficult to differentiate from diffuse-type primary gastric cancer due to morphologic similarities; thus, an immunohistochemical analysis is required for a differential diagnosis (19). Some cases of breast cancer with gastric diffusely infiltrating metastasis were reportedly misdiagnosed as primary gastric cancer (20, 21). The present patient was initially treated for an advanced-stage salivary tumor, and gastric metastasis was not suspected because of the unique endoscopic features. A pathologist was requested to perform a differential diagnosis examination for primary gastric cancer and gastric metastasis from potential male breast cancer, with the correct diagnosis ultimately being reached based on

the histologic similarities of mammary and salivary tumors. Thus, it is necessary to provide clinical information to the attending pathologist to ensure a proper histologic diagnosis of diffusely infiltrating gastric metastasis. When a histologic diagnosis by a conventional biopsy is difficult due to metastatic tumor growth in the submucosal or subserosal layer, a boring biopsy or endoscopic ultrasound-guided fine needle aspiration may be useful for a tissue diagnosis (22). In addition, when the primary site is difficult to detect, positron emission tomography is reportedly helpful for estimating the primary site (18).

In conclusion, when a rapidly progressive gastric tumor that shows a primary scirrhous gastric cancer-like appearance is encountered, it is necessary to consider the possibility of not only primary gastric cancer or gastric metastasis from breast cancer but also gastric metastasis from a salivary tumor.

The authors state that they have no Conflict of Interest (COI).

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