Clinical Case Report

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Primary gastric squamous cell carcinoma presenting as a large submucosal mass

A case report and literature review

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Abstract

Rationale: Primary gastric squamous cell carcinoma (SCC) is rarely encountered clinically. SCC, which presents as a submucosal tumor, is even rarer. Without the support of pathological evidence, it is difficult to make a correct preoperative diagnosis. Due to limited clinical data, the pathogenesis and treatment of gastric SCC remain unclear.

Patient concerns: A 69-year-old man was admitted to our hospital with unexplained weight loss. Endoscopy revealed a submucosal mass without any ulcer on its surface located on the body of the stomach. The results of 2 gastroscopic mucosal biopsies were chronic inflammation.

Diagnoses: The clinical diagnosis by computed tomography (CT) and gastroscopy was gastrointestinal stromal tumor (GIST) preoperatively. The postoperative pathological examination demonstrated this tumor as moderately differentiated SCC.

Interventions: Total gastrectomy, distal pancreatectomy, and splenectomy were performed.

Outcomes: The patient was discharged 7 days after the surgery without any complications. The follow-up CT scan showed no evidence of metastatic disease 6 months after surgery.

Lessons: Large primary gastric SCC could present as a submucosal mass. Gastroscopic mucosal biopsy may not be able to get tumor tissue due to inflammatory reaction.

Abbreviations: AC = adjuvant chemotherapy, AP = abdominal pain, AR = adjuvant radiotherapy, CD = cluster of differentiation, CK = cytokeratin, CT = computed tomography, ESD = endoscopic submucosal dissection, F = female, GIST = gastrointestinal stromal tumor, GSCC = gastric Squamous cell carcinoma, M = male, NA = not available, NAC = neoadjuvant chemotherapy, RS = radical surgery, SCC = squamous cell carcinoma, WL = weight loss.

Keywords: diagnosis, gastric neoplasms, gastrointestinal stromal tumor, prognosis, squamous cell carcinoma

1. Introduction

Primary gastric squamous cell carcinoma (GSCC) is a rare malignancy, only accounts for 0.2% of all gastric neoplasms.[1] Less than 100 primary GSCCs have been reported so far.[2–4] In compliance with the Japanese Society of Gastric Cancer, primary GSCC was defined as the squamous cell carcinoma (SCC) originating entirely from the stomach without any adenocarcinoma components.[5] The symptoms of primary GSCC are similar to those of gastric adenocarcinoma such as abdominal pain and weight loss. However, patients with primary GSCC usually had a poorer prognosis than those with adenocarcinoma.[6] Due to limited clinical data, the standard treatment for primary GSCC had not come to an agreement. It is currently believed that radical surgery can benefit patients.

The majority of primary GSCCs reported presented as ulcer lesions. We experienced a case of large primary GSCC presenting as a large submucosal tumor, which was rarely reported. Without pathological evidence, we misdiagnosed the tumor as gastrointestinal stromal tumor (GIST) preoperatively. This study provided an extremely rare case and reviewed 25 cases of primary GSCC published, which could provide help for the diagnosis and treatment of primary GSCC.

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LG and XT contributed equally to this article.

This study was in accordance with the Declaration of Helsinki and approved by the ethics committee of Qilu Hospital of Shandong University.

Written informed consent was obtained from the patient for the publication of this case report.

The authors have no conflicts of interests to disclose.

The datasets generated during and/or analyzed during the current study are publicly available.

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2. Case presentation

A 69-year-old man came for consultation due to an unexplained weight loss of 3 kg in 2 months. He denied other symptoms such as anorexia, nausea, vomiting, fatigue, or melena. The laboratory tests were normal. Computed tomography (CT) showed a heterogeneously enhanced tumor mass (Fig. 1A) located between the pancreas and the stomach, and no evidence of metastasis was found in other parts of the body. Endoscopy revealed a submucosal mass without any ulcer on its surface located on the body of the stomach (Fig. 1B). The first gastroscopic mucosal biopsy showed chronic inflammation, so we performed the second biopsy and the result were consistent with the first. The third mucosal biopsy was refused by the patient. The clinical diagnosis by CT and gastroscopy was GIST. Therefore, laparoscopic exploration was performed, which revealed a large and exophytic mass originating from the posterior wall of the stomach and invading the pancreas and splenic vessels (Fig. 2). The tumor was completely dissected using total gastrectomy, distal pancreatectomy, and splenectomy. The intraoperative rapid frozen pathology found SCC. The postoperative pathological examination found moderately differentiated SCC in the resected specimen (Fig. 3A-C). No metastasis was observed in the 19 dissected lymph nodes. Immunohistochemistry markers were positive for P63 and cytokeratin (CK) 5/6 and negative for the cluster of differentiation (CD) 117 (Fig. 3D-F). No evidence of SCC in other organs was reported. Therefore, the postoperative diagnosis was primary GSCC. According to the Eighth Edition AJCC Cancer Staging Manual, it was diagnosed as T4bN0M0, pStage IIIA. The patient was discharged 7 days after surgery without any complications and referred to the medical oncology to receive adjuvant chemotherapy, but he refused. The follow-up CT scan showed no evidence of metastatic disease 6 months after the surgery.

3. Discussion and conclusions

GSCC is characterized by keratin pearls, mosaic cell arrangement, intercellular bridges, and a high concentration of sulfhydryl and/or disulfide groups.[7] Most gastric SCCs are located on the esophagogastric junction. Primary GSCC is rarely encountered clinically. The Japanese Society of Gastric Cancer provided the concept of "primary".[5] The tumor was not located on cardia and did not invade into the esophagus. No evidence of SCC in any other organs was reported. In our cases, endoscopy showed that the tumor was located on the body of the stomach and did not invade the esophagus. Thoracic, abdominal, and pelvic of contrast-enhanced CT showed no evidence of metastatic lesions. Therefore, the diagnosis was primary GSCC.

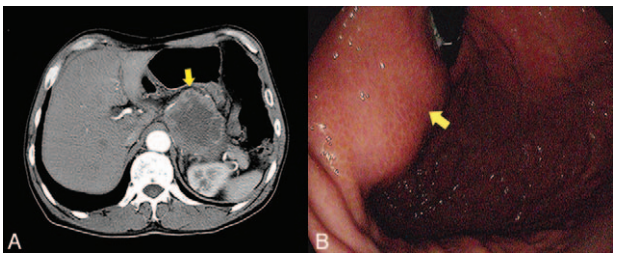

Figure 1. Images of CT and gastroscopy. Contrast-enhanced CT showed a large exophytic mass (yellow arrow) on the body of the stomach (A). The gastroscopy indicated a submucosal mass (yellow arrow) (B).

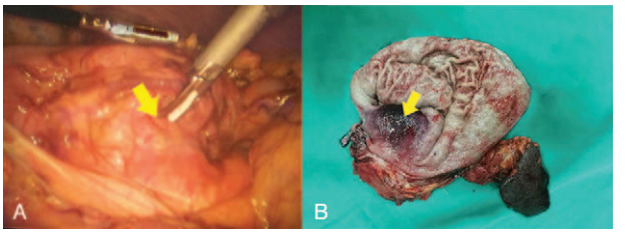

Figure 2. Images of laparoscopic exploration and the specimen. Laparoscopy revealed a large exophytic mass (yellow arrow) originating from the stomach and invading into the pancreas (A). Resected specimen showed the submucosal tumor (yellow arrow) (B).

The pathogenesis of primary GSCC remains unclear. Several theories about the origin of primary GSCC have been proposed, including squamous differentiation followed by adenocarcinoma, squamous metaplasia of gastric mucosa, multipotent capability of stem cells, nests of ectopic squamous epithelium in the gastric mucosa, and malignant transformation of gastric vascular endothelial cells.[8,9]

Fewer than 100 cases of primary GSCC have been reported.[2] However, it is difficult to detect accurate clinical features of this disease. A total of 25 case reports in the English literature published in the last 10 years were reviewed.[2–4,8–29] The clinical data are shown in Table 1. The mean age at the onset was 64 years, and the male-to-female ratio was 19:6. The most common symptoms were abdominal pain (13/25) and weight loss (12/25). Most tumors exceed 5 cm and were diagnosed in an advanced stage.

GSCC presenting as a submucosal mass occurred in only 1 of 25 cases.[2] It should be differentiated from other neoplasms, including GIST, carcinoids, melanomas, lymphomas, and leiomyosarcomas. The most common submucosal tumors are GIST. The CT scan for GSCC usually shows a heterogeneously enhanced mass.[13,14,17] The same performance is reflected on huge GIST due to necrosis, hemorrhage, or degenerative components.[30] Gastroscopic mucosal biopsy could help in identifying the submucosal tumors. However, a preoperative biopsy was not recommended for the tumors that were clinically highly suspected of GIST and could be completely removed.[31] We support the idea of preoperative biopsy, because the preoperative diagnosis is important to decide surgical method. Endoscopic ultrasound-fine needle autopsy should be considered when no abnormalities are found in the first biopsy. CK 5/6, P63, and CD117 are immunohistochemical markers that help distinguish between SCC and GIST.[32,33] Therefore, large primary GSCC, which resembles a submucosal mass, could be misdiagnosed as GIST in the absence of pathological evidence.

The prognosis of gastric SCC was dismal.[1,34] The study by Caixia Dong et al analyzed the prognostic characteristics of primary GSCC.[1] It was reported that 47.2% of patients were diagnosed at stage IV. The median survival for gastric adenocarcinoma in this study was 19 months, while the primary GSCC was only 8 months. The 5-year overall survival for primary GSCC was 32.7%, respectively, and patients in stage I, II, III, and IV was 80.0%, 67.5%, 39.7%, and 6.0%, respectively. More importantly, their study indicated the prognosis of the surgical group and the non-surgical group was significantly different. The median survival for the surgery

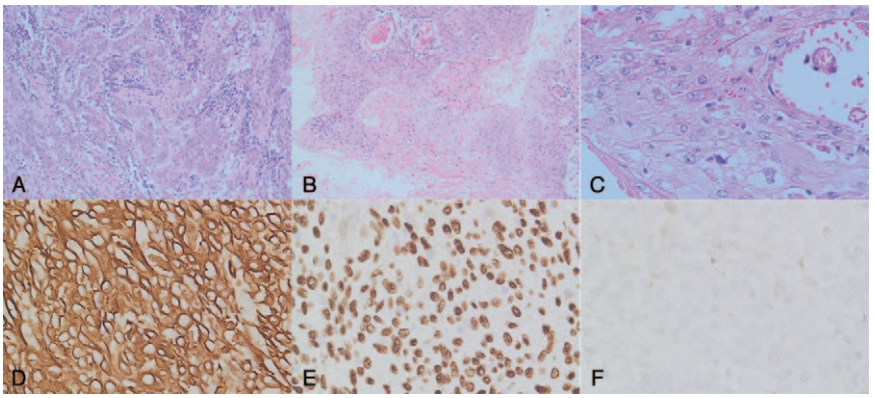

Figure 3. Histological and immunohistochemical (H&E) examination. H&E examination showed a moderately differentiated SCC (A, ×20 magnification) with keratin pearls (B, ×10 magnification) and intracellular bridges (C, ×40 magnification). Immunohistochemical staining displayed that the tumor cells were positive for CK 5/6 (D, ×40 magnification) and P63 (E, ×40 magnification) and negative for CD117 (F, ×40 magnification).

group was 133 months, and the 5-year survival rate was 59.2%. However, the median survival for non-surgery group was 2 months, and the 5-year survival rate was 17.4%.

Phases 2 and 3 randomized controlled trial proved that chemoradiotherapy followed by surgery improved the survival of patients with SCC in the esophagus and esophagogastric junction compared with surgery alone.[35,36] Due to limited data, no guideline exists for primary GSCC. Surgery combined with chemotherapy is the most common treatment.

The majority of primary GSCC presented as ulcer lesion. By endoscopy and biopsy, it was not hard to make a correct diagnosis preoperatively. Our case indicated that primary GSCC could present as submucosal tumor. The extremely rare case, combined with the inflammatory reaction around the tumor, made us not get the correct diagnosis until the postoperative histopathological examination was completed. When it was difficult to obtain lesion tissue, multi-point sampling should be considered or with the help of endoscopic ultrasonography. Preoperative diagnosis is important to decide surgical method. Therefore, repeated biopsy is useful for diagnosis of submucosal tumor.

In conclusion, a rare case of primary GSCC presenting as a submucosal tumor was reported, and 25 case reports in the English literature published in the last 10 years were reviewed.

Table 1

Case reports of primary gastric squamous cell carcinoma published in the last 10 years.

Author	Year	Age (year)	Sex	Symptom	Location	Size (cm)	Stage	Treatment	DFS (m)	OS (m)
Yamagata et al[10]	2019	60	M	AP	Lower	4	III	RS + AC	5	17
Rojas et al[11]	2018	66	M	Bloating	Upper	2.5	I	RS + AC	NA	NA
Lopez et al[12]	2018	78	F	AP, vomiting, WL	Lower	NA	NA	Stent	NA	NA
Sanchez et al[13]	2017	52	F	AP, WL	Upper	10	IV	RS + AC	36	40
Wu et al[14]	2016	59	M	AP	Upper	6	IIB	RS + AC	10	16
Segura et al[15]	2016	64	F	AP	Upper	NA	IV	Chemotherapy	NA	NA
Gulcicek et al[16]	2016	49	M	AP, nausea, vomiting, WL	Lower	10	III	RS + AC + AR	NA	NA
Chang et al[17]	2016	65	M	AP, WL	Middle	10	IIB	RS + AC	NA	52*
Gao et al[22]	2015	50	M	AP	Lower	12	III	RS + AC	3	NA
Waagner et al[18]	2015	70	M	WL	Upper	7	III	RS + AC	3	27
Patnayak et al[19]	2015	80	F	AP, WL	Lower	4	NA	RS	NA	NA
Hamzaoui et al[21]	2015	55	M	AP, vomiting, WL	Upper	6	IV	None	NA	0.3
Modi et al[20]	2015	55	M	Hematemesis, WL	NA	8	I	NAC + RS + AC	NA	NA
Sakemi et al[24]	2014	81	M	No symptom	Upper	1.3	NA	ESD	NA	NA
Hwang et al[2]	2014	61	M	WL	Upper	7	III	RS + AC	4	6
Wakabayashi et al[8]	2014	69	M	Dysphagia, melena	Upper	9	IV	RS	18	36
Xu et al[23]	2014	66	M	Hematemesis	Upper	1.8	IV	None	NA	2
Erkol et al[25]	2014	45	M	Hematemesis	Upper	NA	IIIA	RS + AC	NA	NA
Mardi et al[26]	2013	42	M	AP, vomiting, constipation	Lower	4	IV	NA	NA	NA
Mhairi et al[3]	2013	73	M	Hematemesis	Lower	8	III	RS + AC	NA	6*
Tokuhara et al[4]	2012	67	M	Dysphagia	Middle	6	IV	RS + AC	6	13
Guttmann et al[27]	2012	81	F	AP	Pylorus	4	NA	NA	NA	NA
Karaca et al[28]	2011	68	M	WL, melena	Upper	10	NA	RS	NA	10*
Amuluru et al[29]	2010	78	F	Vomiting, WL	Middle	1.5	NA	Gastrojejunostomy	NA	NA
Callacondo et al[9]	2009	83	M	AP, vomiting, WL	Lower	15	I	RS	NA	24*

AC = adjuvant chemotherapy, AP = Abdominal pain, AR = adjuvant radiotherapy, ESD = endoscopic submucosal dissection, F = female, M = male, NA = not available, NAC = neoadjuvant chemotherapy, RS = radical surgery, WL = weight loss.
* alive.

Primary GSCC could present as a submucosal tumor, and gastroscopic mucosal biopsy may not be able to get tumor tissue due to inflammatory reaction. Surgery combined with chemotherapy is the most common treatment. The prognosis of primary GSCC is poor.

Author contributions

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Writing – review & editing: Lei Gao, Xiaolong Tang, Hui Qu.

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