Total gastrectomy and extended D2 lymphadenectomy for primary gastric squamous cell carcinoma: A case report

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Abstract. Primary gastric squamous cell carcinoma (PGSCC) is a rare form of gastric malignancy. The etiology remains unclear and no standardized treatment protocol or consensus has been established. The current study presents a rare case of PGSCC treated by total gastrectomy and extended D2 lymphadenectomy, alongside a review of related clinical literature. A 57-year-old man was diagnosed with primary SCC located at the lesser curvature of the gastric body. The patient underwent a total gastrectomy and extended D2 lymphadenectomy. Postoperative pathology confirmed a moderately differentiated SCC with perineural invasion, classified as stage T4bN2M0. Treatment strategies for PGSCC remain controversial, underscoring the need for further studies with larger sample sizes to clarify therapeutic approaches.

Introduction

Primary gastric squamous cell carcinoma (PGSCC) is a rare gastric malignancy, accounting for only 0.04-0.07% of all gastric cancers (1), with ~100 cases documented in the literature (2). The incidence ratio of men to women is 5:1 (1), and the disease predominantly affects patients >60 years old. The exact etiology remains unknown; however, previous studies have suggested an association with long-term smoking (3,4). Therefore, PGSCC may be more commonly found in male patients. There is no standardized treatment protocol for PGSCC, and it often carries a poor prognosis due to its typical late-stage diagnosis. The median survival time for patients with PGSCC has been reported to be as short as 7 months (5), reflecting the aggressive nature of this tumor. This poor prognosis is primarily attributed to the non-specific symptoms of PGSCC, such as dysphagia, weight loss and epigastric pain, which are often mistaken for other gastric conditions. To date, to the best of our knowledge, no research has definitively clarified the pathogenesis of PGSCC (2). The primary aim of the present case report was to contribute to the limited knowledge of PGSCC and explore the potential treatment options, including surgery, in managing this rare disease.

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Case report

The patient, a 57-year-old man with a 30-year history of smoking and tobacco pipe use (~20 cigarettes per day), presented with epigastric pain and 6 kg of weight loss over the past 3 months. The patient was admitted to the Vietnam National Cancer Hospital (Hanoi, Vietnam) in March 2023. A physical examination revealed no notable abnormalities. Upper gastrointestinal endoscopy demonstrated a large, ulcerated lesion, ~5 cm in size, located at the posterior wall of the gastric body, with gastrointestinal bleeding classified as Forrest class IIB originating from the tumor (Fig. 1). Computed tomography identified a tumor at the lesser curvature of the stomach, measuring ~40 mm in length and 20 mm in maximal thickness. Strong contrast enhancement following injection, surrounding infiltration and an enlarged lymph node near the lesser curvature measuring 14x15 mm were observed (Fig. 2). The tumor was classified as cT4N1M0 (American Joint Committee on Cancer/International Union Against Cancer, 8th edition) (6). A preoperative biopsy previously performed at an external hospital confirmed the diagnosis of PGSCC.

The patient underwent open surgery at 7 days post-admission. Intraoperative findings included no peritoneal effusion or peritoneal metastasis. The tumor was located at the lesser curvature, posterior to the gastric body, and measured 5x6 cm, with invasion into the peritoneum covering the pancreas (Fig. 3). Lymph nodes in groups 7, 8a, 9, 10, 11p and 11d, ranging from 1 to 1.5 cm in size, were suspected of metastasis.

Due to the aggressive nature of PGSCC, a total gastrectomy was performed along with an omentectomy, a bursectomy of the peritoneum covering the pancreas and an extended D2 lymph node dissection (D2 + 10, 12a, 12p, 13 and 16). A Roux-en-Y anastomosis was completed and a gastric tube was

placed to facilitate early postoperative feeding. The patient recovered well with no complications reported. A postoperative barium swallow study demonstrated normal findings 1 week after surgery, allowing for nasogastric tube removal. The patient was discharged 3 days later.

Pathological examination (10% neutral-buffered formalin at 20-25˚C for 24 h; 4-μm thick sections; hematoxylin and eosin staining processed using automatic HE Staining on Dako Systems; Olympus BX53 microscopy) reported a moderately differentiated primary SCC (Fig. 4), with peritoneal and perineural invasion. Metastatic nodes were found in groups D1 (2/8) and D2 (2/9), with no metastatic nodes found in group D2+ (0/7). This result was thoroughly discussed with the pathologist, who affirmed that additional immunohistochemical staining was not required to establish the diagnosis. Accordingly, the postoperative stage was classified as pT4bN2M0.

The patient began an adjuvant chemotherapy regimen at 1-month post-surgery with capecitabine and oxaliplatin (XELOX) for a total of eight cycles. The XELOX regimen consisted of oxaliplatin at a dose of 130 mg/m^2 administered intravenously on day 1, and capecitabine at a dose of 1,000-1,250 mg/m^2 taken orally twice daily on days 1-14 of a 3-week cycle. Follow-up was conducted every 3 months, with no recurrence or metastasis detected after 1 year of follow-up.

Discussion

PGSCC comprises 0.04-0.07% of all gastric cancers (1), with only ~100 cases recorded in the literature to date (2). The incidence ratio of male to female patients is ~5:1 (1), with most cases of disease occurring in patients >60 years old. Despite its rarity, PGSCC is often diagnosed at an advanced stage due to the lack of specific symptoms and reliable biomarkers for early detection. The aggressive nature of this tumor is reflected in its poor prognosis, with a median survival time of only 7 months reported (5). The present case shares several characteristics commonly described in other reports on PGSCC. For instance, in a study of 21 PGSCC cases by Chen *et al* (3), 85.7% were male patients, with two-thirds of tumors located in the upper third of the stomach, and 62% of patients had a history of smoking. Long-term tobacco use can lead to chronic inflammation and oxidative stress in the gastric mucosa, contributing to genetic mutations and carcinogenesis (7). This finding suggests a potential association between prolonged tobacco use and the occurrence of PGSCC, similar to lung or esophageal cancers. This observation aligns with the present case, as the patient was a 69-year-old male with a marked history of smoking, further supporting the potential association between prolonged tobacco use and the development of PGSCC.

The etiology of PGSCC remains uncertain despite several hypotheses. Mori *et al* (8) identified an adenocarcinoma component in the histology of three PGSCC cases, leading to the hypothesis that PGSCC might originate from adenocarcinoma. Takita *et al* (9) utilized polymerase chain reaction to detect Epstein-Barr virus (EBV) infection in surgical specimens of the tumor. The findings proposed that EBV infection could play a role in the pathogenesis of PGSCC in some cases.

Typically, PGSCC is diagnosed as SCC based on biopsy samples from an upper gastrointestinal endoscopy. However, postoperative pathological findings often reveal gastric adenosquamous carcinoma or SCC extending from the esophagus. Therefore, clear diagnostic criteria for PGSCC are essential to differentiate it from other cases. Parks (10) proposed the following diagnostic criteria: i) The tumor should not be located at the cardia; ii) it should not be esophageal cancer spreading to the stomach; and iii) there should be no SCC in other organs (such as the uterus, lung, bronchus or pancreas). Additionally, the Japanese Gastric Cancer Association (JGCA) suggested the following criteria (8): i) All tumor cells must be squamous cells without glandular elements; and ii) there must be evidence that the tumor originated from the gastric mucosa. The present case met both Parks' and JGCA criteria.

Currently, there are no standardized treatment protocols for PGSCC due to limited data on surgical, chemotherapeutic and radiotherapeutic approaches for this rare disease (1). Gastrectomy and lymphadenectomy remain the primary treatments. Postoperative adjuvant chemotherapy, including regimens based on 5-fluorouracil, is administered similarly to gastric adenocarcinoma treatment. Alternative regimens include fluorouracil + oxaliplatin + calcium folinate (FOLFOX) or capecitabine + oxaliplatin (XELOX). As with chemotherapy, the role of radiotherapy in PGSCC has not been established; however, some cases have utilized combined chemoradiotherapy. Schmidt *et al* (11) reported a PGSCC case with a 5-year disease-free survival following surgery, radiotherapy and chemotherapy. However, Wakabayashi *et al* (1) reported a case treated solely with surgery and chemotherapy. Postoperative follow-up for this patient for the first 18 months was uneventful. However, the patient subsequently developed multiple liver metastases and para-aortic lymph node metastases. Neoadjuvant chemotherapy may be effective for some patients with PGSCC (12), although its indications and role remain uncertain (3). Therefore, further studies with a larger patient population are needed to thoroughly evaluate appropriate treatment strategies for PGSCC.

In the present case, a total gastrectomy, omentectomy and lymphadenectomy were performed as recommended by the JGCA for advanced gastric cancer. A bursectomy was conducted due to the location of the tumor at the posterior gastric body with invasion into the anterior pancreatic peritoneum. Typically, the JGCA recommends a D2 lymphadenectomy in cases of locally advanced disease with suspected lymph node metastasis (13). In the present case, an extended D2 lymphadenectomy (D2+) was chosen, including hepatic pedicle nodes (12a, 12p and 12b), groups 10, 13 and 16. Given the poor prognosis associated with PGSCC and its high malignancy, along with the advanced stage of the tumor, including perineural and adjacent organs invasion, it was reasonable for extensive surgery combined with more extensive lymphadenectomy to be performed.

PGSCC is often diagnosed at an advanced stage, frequently presenting with lymph node or liver metastases. This may be due to its rarity and non-specific symptoms, which overlap with other more common gastric conditions. Additionally, the lack of specific biomarkers for early detection contributes to the difficulty in diagnosing PGSCC at an earlier stage. Therefore, endoscopic screening programs, especially in high-risk populations, such as those with a history of smoking, should also be considered.

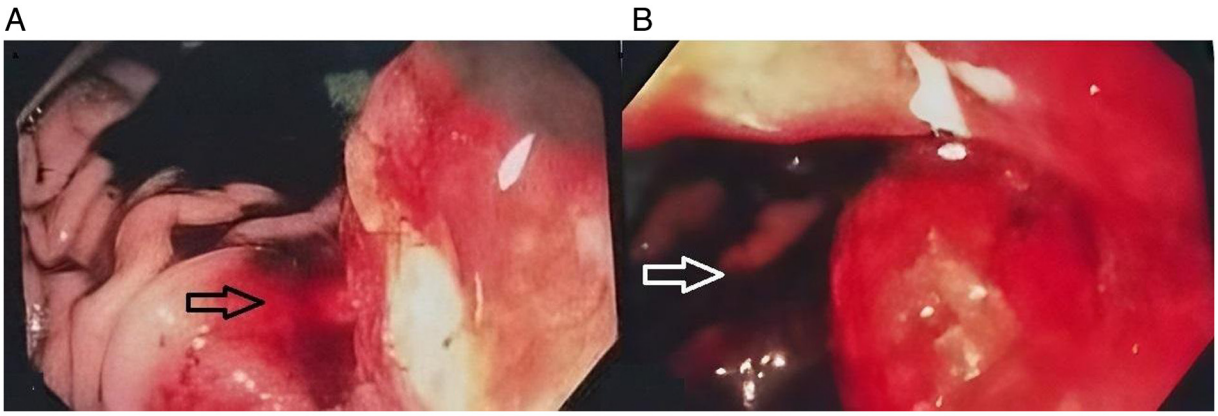

Figure 1. Endoscopic image showing (A) an ulcerative bleeding lesion at the lesser curvature with adherent blood clots (black arrow) and (B) gastric aspirate that contains dark specks of old blood (white arrow).

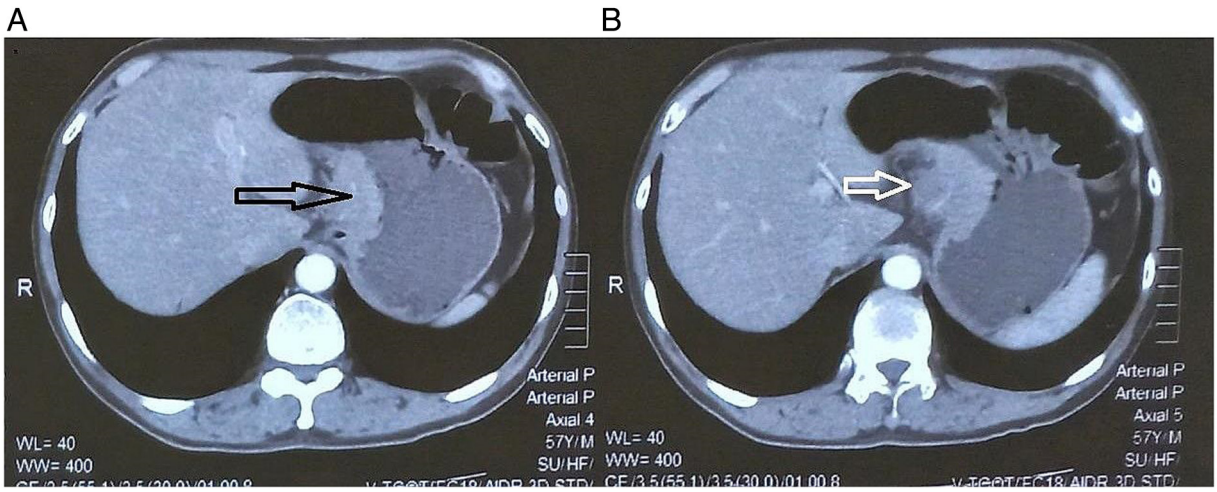

Figure 2. Preoperative multi-slice computed tomography scan showing (A) a thickened gastric wall lesion measuring ~2.5 cm at the lesser curvature near the cardia (black arrow) and (B) an enlarged group 3A lymph node measuring ~2x2 cm (white arrow).

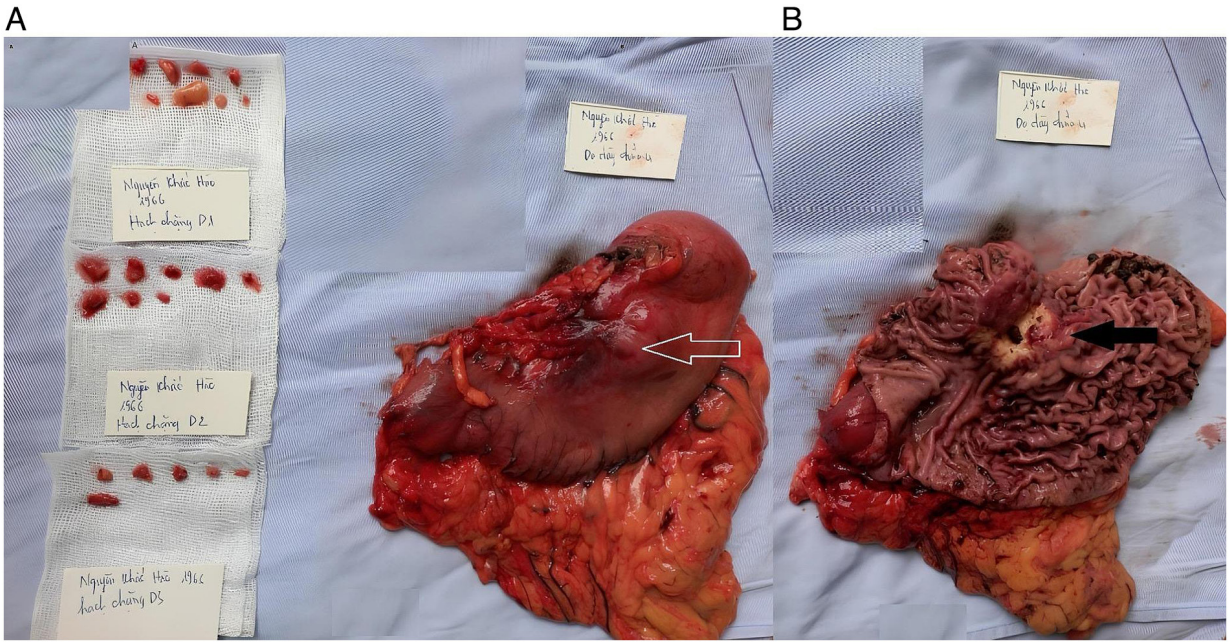

Figure 3. (A) Whole stomach specimen with a ~5x6-cm lesion located at the lesser curvature (white arrow). (B) The opened stomach, revealing an ulcerative lesion (black arrow).

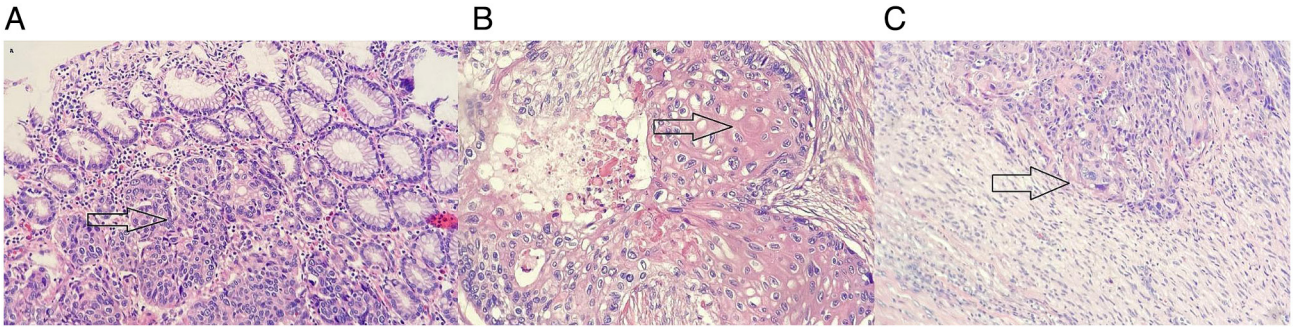

Figure 4. Histological images (hematoxylin and eosin) of the sample sourced from the lesion at the lesser curvature, illustrating features consistent with moderately differentiated squamous cell carcinoma. (A) Disorganized arrangement of tumor cells (black arrow) (magnification, x200). (B) Clusters of tumor cells with keratin pearls and irregular arrangement (black arrow) (magnification, x400). Tumor cells exhibit round nuclei with hyperchromasia, prominent nucleoli, a high nuclear-to-cytoplasmic ratio, and evidence of mitotic activity. (C) Evidence of perineural invasion (black arrow) (magnification, x200).

Compared with adenocarcinoma, PGSCC is more aggressive and has a higher risk of lymph node metastasis (the present case was classified as pT3N2M0 with four metastatic lymph nodes and perineural invasion) (2). Therefore, PGSCC often has a poor prognosis. Meng *et al* (5) conducted a retrospective study showing that PGSCC has a worse prognosis than gastric adenocarcinoma, with a median survival time of only 7 months. Meanwhile, advanced gastric adenocarcinoma typically has a median survival time of 11-17 months with standard treatment (14). This difference further underscores the aggressive nature and poor prognosis of PGSCC. Each case represents a valuable opportunity to explore adjuvant or alternative treatment strategies. The decision to proceed with upfront surgery, followed by postoperative adjuvant therapy, is also a strategy that could be proposed. However, further studies with larger sample sizes are needed to clarify this approach.

To conclude, PGSCC is a rare form of gastric malignancy that is often diagnosed at an advanced stage. Gastrectomy combined with D2 lymphadenectomy remains the standard treatment approach, with the use of chemotherapy and radiotherapy remaining contentious. Additional research with larger sample sizes is essential to accurately evaluate the optimal therapeutic regimen for PGSCC.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

Conception and design was performed by BVP, DDN, MDT, TDN, ADT, BTN and KVL. Administrative support was provided by BVP, TDN, ADT, BTN, KVL and HTTN. Provision of study materials of patients was performed by BVP, DDN, MDT, ADT, KVL and HTTN. Collection and assembly of data was performed by BVP, DDN, MDT, TDN, ADT and HTTN. Data analysis and interpretation was performed by BVP, DDN, ADT, BTN and HTTN. The manuscript was written by all authors. All authors read and approved the final version of the manuscript. BVP and HTTN confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The present study was conducted with informed patient consent to participate and received the requisite ethical approval from the Scientific Council of Vietnam National Cancer Hospital (Hanoi, Vietnam; approval no. 3366/BVK-HDDD; dated February 3, 2023). The council comprises expert representatives from relevant specialties, including gastrointestinal surgeons, radiologists, oncologists, gastroenterologists and pathologists. Their comprehensive review and endorsement ensured adherence to the highest ethical standards throughout the research process. The procedures adhered to the Declaration of Helsinki.

Patient consent for publication

Written informed consent was obtained from the patient for publication of the case report and any accompanying images.

Competing interests

The authors declare that they have no competing interests.

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