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CASE REPORT | STOMACH

Metastatic Small Cell Carcinoma of the Stomach

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ABSTRACT

Primary gastric small cell carcinoma (GSCC) is an extremely rare type of small cell carcinoma. Its aggressive nature with early widespread metastasis and late detection gives it a poor prognosis with overall survival of <12 months. GSCC is a type of neuroendocrine tumor, and because of its histopathological similarity to small cell lung carcinoma (SCLC), treatment regimen of GSCC includes the same chemotherapy agents as SCLC. We report a case of a 57-year-old man who presented with signs of partial gastrointestinal obstruction and was found to have a primary stage IV GSCC with metastasis to the liver.

KEYWORDS: small cell carcinoma; gastric small cell carcinoma; neuroendocrine tumor; extrapulmonary small cell carcinoma; gastrointestinal cancer

INTRODUCTION

In 2018, the World Health Organization reported about 1 million new cases resulting from gastric cancer alone.[1] Globally, gastrointestinal malignancy contributes to an estimated 35% of all cancer-related deaths.[1] Gastric small cell carcinoma (GSCC), a subtype of extrapulmonary small cell carcinoma, accounts for less than 0.1% of extrapulmonary small cell carcinoma making it an especially rare malignancy.[2] Matsusaka et al are the first to report GSCC in 1976.[3] Extrapulmonary SCC involving the gastrointestinal tract has an aggressive course and commonly presents with widespread metastatic disease at the time of diagnosis making the overall prognosis poor.[3,4] Thus, it is highly important to address the modifiable risk factors such as nicotine use, high salt diet, and *Helicobacter pylori* infection. Here, we present a rare case of a 57-year-old man who presented with abdominal pain and was found to have stage IV primary GSCC with metastasis to the liver.

CASE REPORT

A 57-year-old man with a medical history significant for gastroesophageal reflux disease, hepatic steatosis, and remote history of minimal tobacco use disorder presented to his primary care physician with complaints of 1-year history of worsening abdominal pain, poor appetite, early satiety, and bloating. He denied the presence of weight loss, fever, or melena. The patient was referred to his gastroenterologist for an esophagogastroduodenoscopy (EGD) for further evaluation. On endoscopic examination, he was found to have an obstruction preventing entry into the duodenum with a notable gastric mass at the gastric antrum and retained gastric contents. The gastric body and antrum biopsies were negative for *H. pylori* infection; however, gastric antrum biopsy at the site of the mass was positive for intestinal metaplasia. His last EGD 12 years ago had no findings of a mass, and he had no risk factors for gastric carcinoma. The patient was sent to the emergency department for further imaging and medical management.

Although in the hospital, abdominal and pelvic computed tomography (CT) with contrast showed a 10.1 × 9.9 × 9.0-cm heterogenous exophytic mass arising from the distal stomach extending into the porta hepatis, in addition to a moderate fluid-filled stomach proximal to the mass consistent with likely gastric outlet obstruction (Figure 1). Imaging also showed the presence of perigastric lymphadenopathy, with the largest lymph node measuring 3.7 × 2.2 cm (Figure 1).

Advanced interventional gastroenterology was consulted for EGD with endoscopic ultrasound and stent placement. EGD revealed a large fungating circumferential infiltrative mass with ulceration and stigmata of recent bleeding on the posterior wall of the gastric

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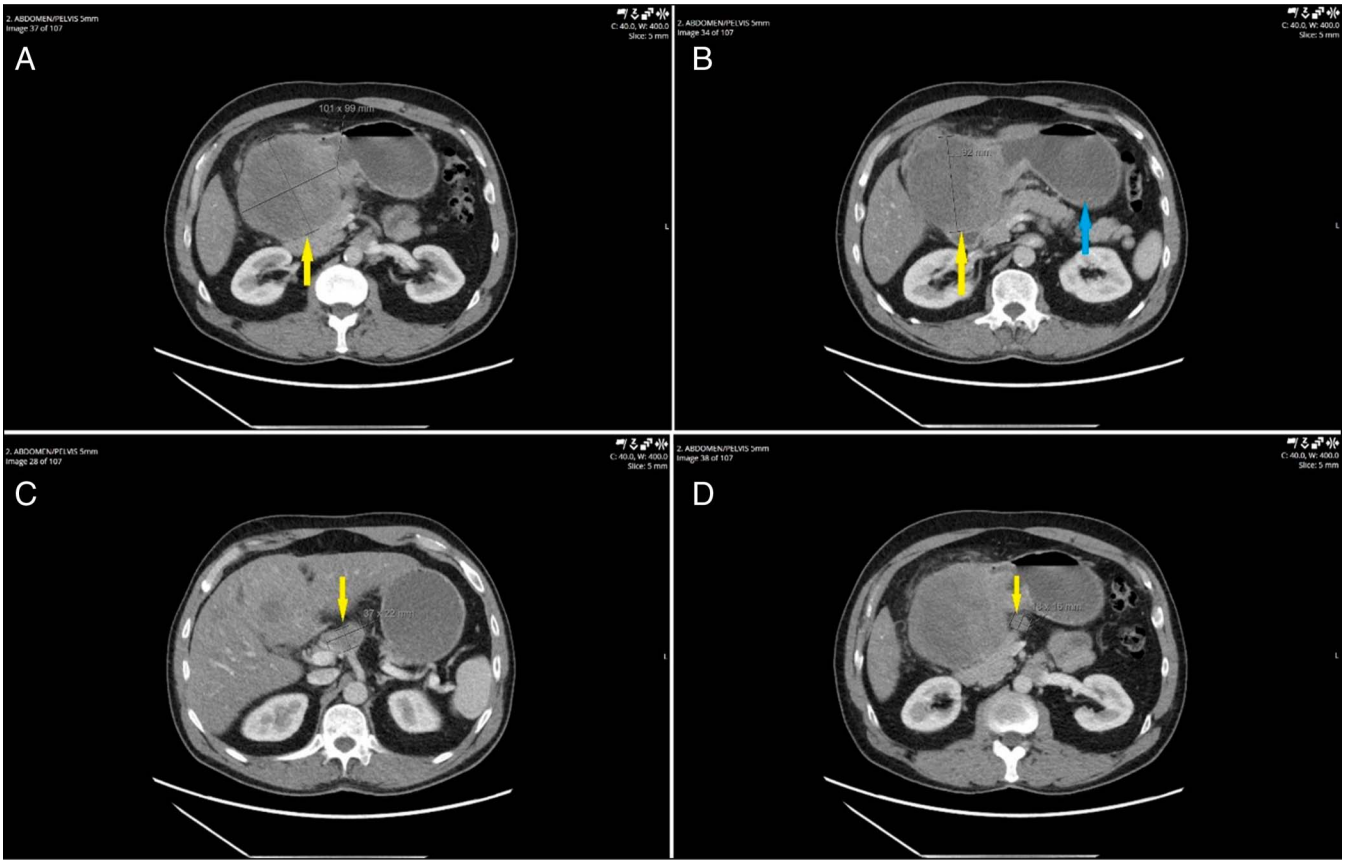

Figure 1. Abdominal and pelvic computed tomography showing gastric mass and lymph nodes. (A and B) Large heterogenous exophytic gastric mass measuring 10.1 × 9.9 × 9.2 cm (yellow arrows) with moderate fluid-filled stomach (blue arrow). (C and D) Presence of perigastric lymphadenopathy measuring 3.7 × 2.2 cm and 1.8 × 1.6 cm, respectively (yellow arrows).

antrum (Figure 2). Biopsies of the gastric wall and mass were taken with cold forceps, and a 22-mm × 6-cm nitinol self-expandable stent was placed across a stenotic prepyloric region under fluoroscopic guidance. On endoscopic ultrasound, a hypoechoic mass measuring 82 × 80 mm with erosion through the serosa with adjacent lymph node involvement was identified (Figures 3 and 4). The mass was staged T4N2MX by endosonographic criteria. Chest CT was obtained for staging and

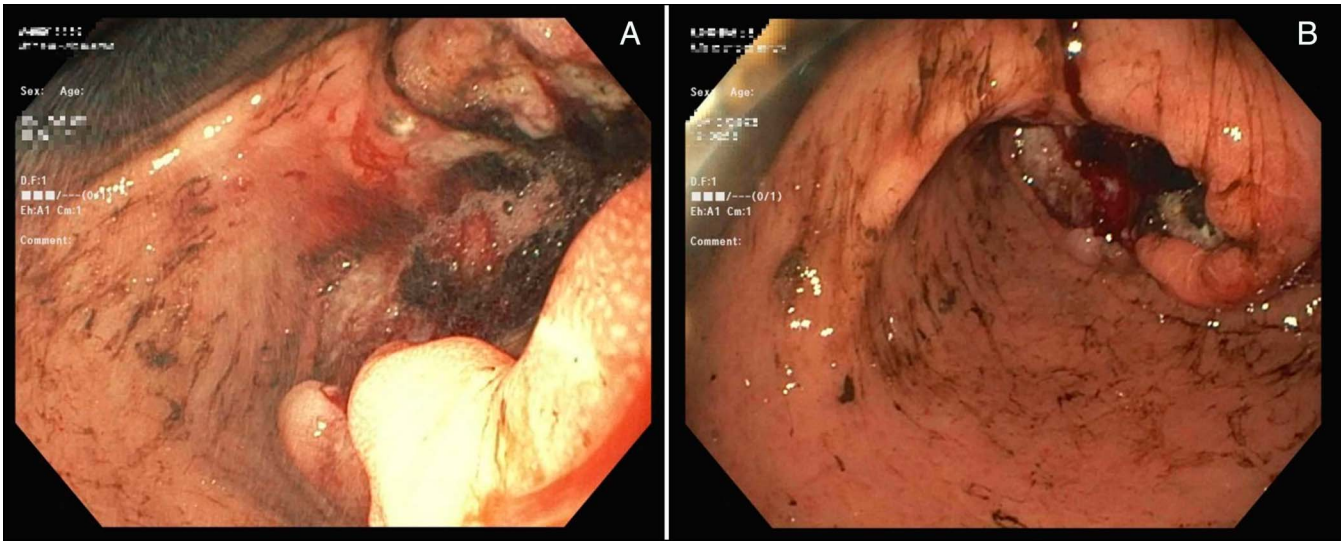

Figure 2. (A and B) Esophagogastroduodenoscopy view of the gastric mass at the posterior wall of the gastric antrum. Ulceration and stigmata of recent bleeding are seen.

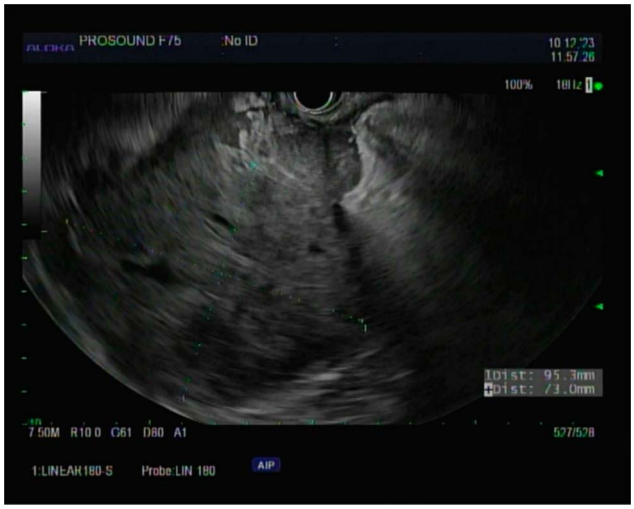

Figure 3. Endoscopic ultrasonographic view of large hypoechoic mass with erosions through the serosa.

showed no evidence of thoracic metastasis, but there were multiple liver lesions suspicious for hepatic metastasis (Figure 5).

Carcinoembryonic antigen level was <0.5 μg/L, and carbohydrate antigen 19-9 level was 9.8 U/mL. Gastric wall biopsies taken during EGD were negative for *H. pylori* infection. The pathological sections of the gastric mass were demonstrating sheets of round cells with scant cytoplasm and small- to medium-sized nuclei with finely dispersed chromatin (Figure 6). Tumor cells were positive for cytokeratin OSCAR, insulinoma-associated protein 1 (INSM1), and synaptophysin (Figure 6). There was focal weak expression of pancytokeratin (AE1/AE3) with Ki-67 proliferation index at 99%. These findings in combination were consistent with small cell carcinoma of gastric origin. Chemotherapy was started immediately with carboplatin and etoposide. Six months after initiation of

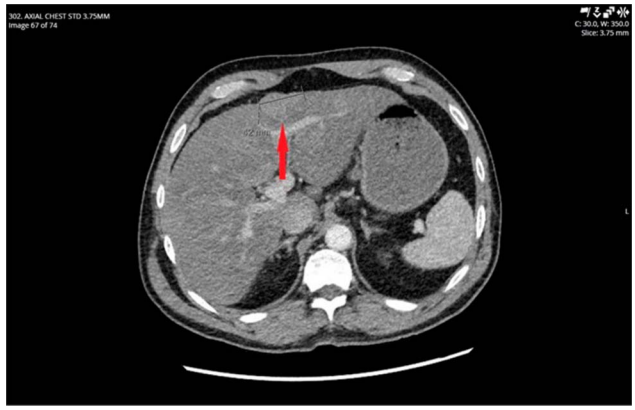

Figure 5. Chest computed tomography showing a 4.2-cm anterior left hepatic lobe lesion, suspicious for hepatic metastasis (red arrow).

chemotherapy, the patient showed excellent tolerability and response with improvement in lymphadenopathy and size of the mass to 5.7 × 4.6 × 3.6 cm.

DISCUSSION

Small cell carcinoma is most commonly found in the lungs. However, extrapulmonary locations have been documented and comprise approximately 3% of small cell carcinomas.[5] GSCC is a type of neuroendocrine tumor that is positive for chromogranin, synaptophysin, and pancytokeratin, analogous to SCLC, as these are markers of epithelial tumors.[6] As seen in our case, the histology of these tumors typically shows small, round, or oval lymphocyte-like cells with hyperchromatic nuclei, scant cytoplasm, and frequent mitoses.[7]

Clinical features of GSCC are nonspecific and typically include localized symptoms of epigastric discomfort or fullness, nausea,

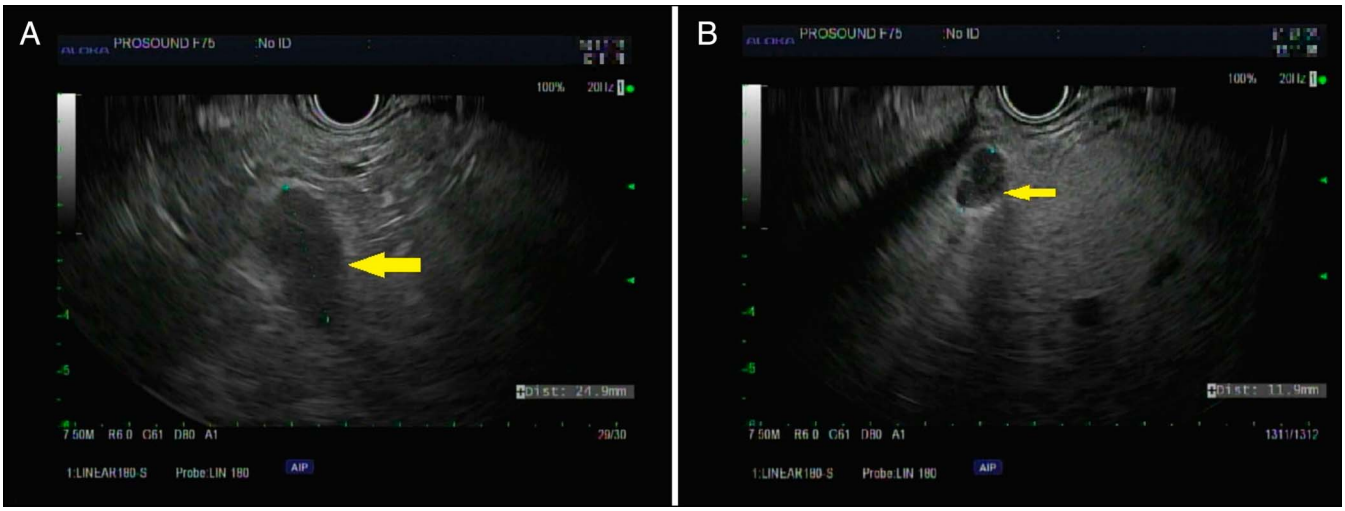

Figure 4. (A and B) Endoscopic ultrasonographic view of malignant-appearing lymph nodes (yellow arrows) in the perigastric and celiac region.

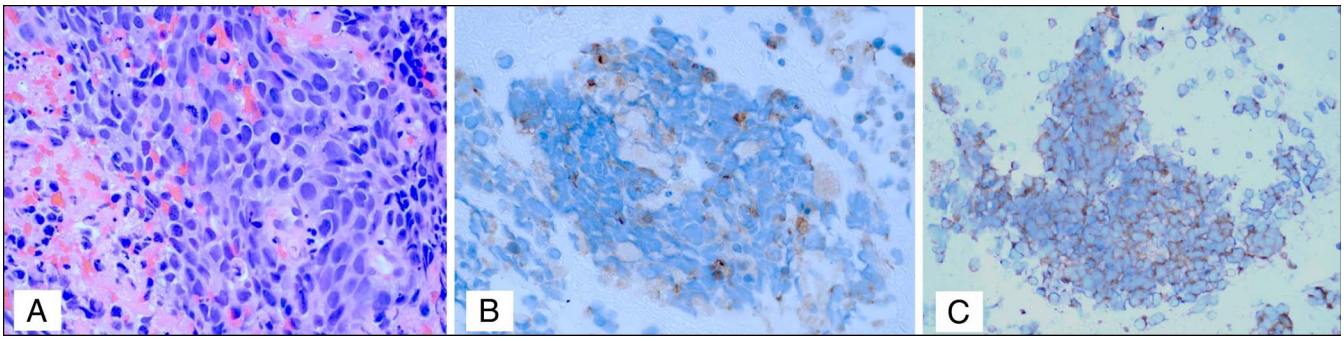

Figure 6. The histologic appearance of gastric small cell carcinoma. (A) Hematoxylin and eosin–stained biopsy of the gastric mass at 60× magnification. (B) Positive immunohistochemistry staining of the gastric mass for cytokeratin OSCAR antibody at 40× magnification. (C) Positive immunohistochemical staining of the gastric mass for the neuroendocrine marker synaptophysin at 40× magnification.

and weight loss.[8] When gastric cancer is suspected, abdominal CT imaging, barium studies, and/or upper endoscopy are useful in evaluation and diagnosis. It can, however, be difficult to diagnose GSCC through endoscopic biopsy because it tends to grow beneath the mucosa, and there may be difficulties obtaining adequate tissues by endoscopic biopsies.[9]

The survival of GSCC in treated patients is reported to be less than 12 months.[10] Between the years of 2012 and 2018, 5-year relative survival rate in people with metastatic gastrointestinal neuroendocrine tumor was found to be 68% according to National Cancer Institute Surveillance, Epidemiology, and End Results statistics.[11] The treatment of GSCC is comparable with that of SCLC because of similar histopathological findings and includes resection and/or chemotherapy depending on the stage and extent of the disease. Chemotherapy is usually a platinum-based regimen with etoposide,[12] and our patient had an excellent response to this first-line therapy regimen.

Early detection and diagnosis of GSCC is challenging and requires a multimodal approach. CT imaging, endoscopic evaluation with ultrasound, and biopsy can provide insight into the extent of tumor invasion and histopathological identification of GSCC; however, because of the vague nature of the clinical presentation and poor prognosis, suspicion for GSCC needs to be high. In addition, early initiation of chemotherapy, resection, and/or radiation is essential in managing patients with GSCC because of its aggressive nature.

DISCLOSURES

Author contributions: M. Gunay participated in writing, editing, and organizing the manuscript. C. Leone participated in writing the manuscript and collecting the images. O. Albayati participated in writing and editing the manuscript. A. Mohamed participated in editing the manuscript, clinically evaluating the patient, and performing the endoscopic interventions. N. Anyadike reviewed the manuscript, clinically evaluated the patient, and performed the endoscopic interventions. M. Gunay is the article guarantor.

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Informed consent was obtained for this case report.

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