Glomus Tumor of the Stomach: A Clinicopathologic Analysis of 10 Cases and Review of the Literature

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Background/Aims: Gastric glomus tumors are extremely rare, and presurgical confirmation is often impossible. The identification of clinical and radiologic characteristics of this tumor type is important for preoperative diagnosis and treatment planning. Methods: In this study, we analyzed 10 cases of gastric glomus tumors resected at a single institute over 9 years. Results: Eight of the patients were men and 2 were women, with a mean age of 49 years. Five patients presented with abdominal discomfort or pain, 1 presented with anemia, and the remaining 4 cases were found incidentally during endoscopic examinations. The most common location of the tumor was the antrum (n=7), followed by the low (n=2) and high body (n=1). Although the endoscopic ultrasonography findings were variable, contrast-enhanced computed tomography generally showed a strong homogeneous enhancement. The resected tumors were well-demarcated solid masses with sizes ranging from 1.0 to 3.6 cm. Microscopically, the masses were composed of abundant vascular channels with clusters of uniform and round glomus cells. There was no evidence of recurrence after complete surgical resection. Conclusions: Gastric glomus tumors are unusual, distinct lesions that should be considered in the differential diagnosis of a gastric submucosal mass. Unlike their deep soft tissue counterparts, most glomus tumors in the stomach are benign. (Gut Liver 2012;6:52-57)

Key Words: Glomus tumor; Stomach; Endoscopy; Pathology; Radiology

INTRODUCTION

Glomus tumor is a mesenchymal tumor composed of modified smooth muscle cells representing a neoplastic counterpart of the perivascular glomus bodies. These tumors usually occur in peripheral soft tissue, especially in the distal part of extremities. In the gastrointestinal tract, glomus tumors are most commonly found in the stomach, and present as submucosal masses that project into the lumen or out onto the serosa. Histologically, it consists of vascular channels lined by endothelial cells surrounded by mantle of uniform small, round glomus cells with centrally placed nucleus lacking cellular atypia. Gastric submucosal tumors (SMTs) encompass both nonneoplastic and neoplastic conditions of various etiologies. They arise from the submucosa or muscularis propria of the gastric wall and usually spare the overlying mucosa. Currently, the main diagnostic modalities for evaluating SMTs are endoscopic ultrasound (EUS) and computed tomography (CT). The former has an advantage in identifying the layer of tumor origin, and the latter is advantageous in tumor characterization with the use of contrast enhancement. Among gastric SMTs, gastrointestinal stromal tumors (GISTs) are the overwhelming majority and the top candidate for malignancy. Therefore, the main purpose of diagnostic strategy is to differentiate GIST from other SMTs and to define the risk of malignancy. Prior imaging studies of SMTs have focused on differentiating between benign and malignant lesions, and mainly have dealt with radiologic-pathologic correlation of each disease entity. In this point of view, identifying clinicopathologic and radiologic characteristics of gastric glomus tumor is important for proper diagnosis and management. For this purpose, we present clinicopathologic features of 10 gastric glomus tumors, and describe the image findings of EUS and CT scan with regard to their role in preoperative diagnosis.
MATERIALS AND METHODS

Ten gastric glomus tumors were retrieved from the surgical pathology files between January 2001 and December 2009. During this period, 393 GISTs and 45 schwannomas were surgically resected and diagnosed. The approximate incidence of glomus tumor is 2.2% among gastric SMTs. The clinicopathologic data and follow-up information were obtained by medical record review. The patients were diagnosed with gastric SMTs on upper gastrointestinal endoscopy and underwent contrast-enhanced CT examination. EUS was also performed in 5 of the patients to evaluate depth and origin of the tumor. The tumors were removed by wedge resection of the stomach, and follow-up was available in all patients.

All hematoxylin and eosin-stained slides were reviewed for each case. The histologic features, including mucosal erosion or ulceration, transmural extent of tumor, nuclear atypia and presence of hemorrhage, necrosis or calcification, were assessed in all cases. Mitotic figure was counted in 50 consecutive high-power fields (HPFs) from the most cellular areas. Four-μm sections were cut from the representative blocks of each case, followed by deparaffinization and rehydration. The slides were immunostained with α-smooth muscle actin (1:100, monoclonal; DAKO, Carpinteria, CA, USA), vimentin (1:200, clone Vim3B4; DAKO), h-caldesmon (1:200, clone h-CD; DAKO), CD34 (1:100, clone QBEnd10; DAKO), and KIT (1:250, polyclonal A4502; DAKO) using BOND-MAX System (Leica Microsystems, Wetzlar, Germany). Diaminobenzidine was used as a chromogen.

RESULTS

The clinicopathologic and radiologic findings of glomus tumors are summarized in Table 1. The patients consisted of 8 men and 2 women with age ranging from 37 to 72 years (mean, 49 years). Five had abdominal discomfort or epigastric pain, one presented with anemia, and the remaining 4 were found incidentally during endoscopic examination. Upper gastrointestinal endoscopy revealed submucosal mass with normal appearing mucosa in 9 patients, and the biopsies of these lesions were nondiagnostic (Fig. 1A). The patient (case no. 9) with anemia had mucosal ulceration (Fig. 1B). The most common location was the antrum (n=7), followed by low body (n=2) and high body (n=1). On EUS, they appeared as well-demarcated masses

Table 1. Clinicopathologic and Radiologic Findings of 10 Glomus Tumors in the Stomach

| Case No. | Age, yr | Gender | Site     | Size, cm | Location of Tumor | Hemorrhage/Calcification | Endoscopic ultrasonography | Computed tomography       |
|----------|---------|--------|----------|----------|-------------------|--------------------------|---------------------------|---------------------------|
| 1        | 37      | M      | Antrum   | 1.7      | MP                | -/-                      | Not performed             | Homogeneous/Well demarcated |
| 2        | 46      | M      | Low body | 2.0      | SM                | +/-                      | Homogeneous/Hypoechoic (3rd layer) | Homogeneous/Well demarcated |
| 3        | 41      | M      | Antrum   | 1.5      | MP                | +/+                      | Homogeneous/Hypoechoic (4th layer) | Homogeneous/Well demarcated |
| 4        | 54      | F      | Antrum   | 3.2      | MP+SM             | +/-                      | Inhomogeneous/Central hyperechoic (3rd layer) | Heterogeneous/Well demarcated |
| 5        | 38      | M      | Antrum   | 2.5      | MP+SM             | +/-                      | Not performed             | Homogeneous/Well demarcated |
| 6        | 72      | F      | Low body | 2.5      | MP+SM             | +/-                      | Not performed             | Homogeneous/Well demarcated |
| 7        | 38      | M      | High body| 1.6      | MP                | -/-                      | Not performed             | Homogeneous/Well demarcated |
| 8        | 63      | M      | Antrum   | 1.9      | MP+SM             | -/-                      | Not performed             | Homogeneous/Well demarcated |
| 9        | 50      | M      | Antrum   | 3.6      | MP+SM             | +/+                      | Inhomogeneous/Hyperechoic (4th layer) | Heterogeneous/Relatively well demarcated |
| 10       | 54      | M      | Antrum   | 1.0      | MP+SM             | +/-                      | Inhomogeneous/Hypoechoic (4th layer) | Homogeneous/Well demarcated |

SM, submucosa; MP, muscularis propria.

Fig. 1. (A) Gastrointestinal endoscopy showing a round elevated lesion with an overlying normal mucosa. (B) In case number 9, a mucosal ulceration is observed.
Fig. 2. (A) Endoscopic ultrasonography in case number 4 shows a hypoechoic mass. (B) Case number 9 shows heterogeneous echogenicity due to internal hemorrhage and calcification. (C) A computed tomography (CT) scan demonstrates a homogeneously enhanced ovoid mass in the anterior wall of the stomach. Perigastric fat infiltration or lymph node enlargement was not noted. (D) The CT scan of case number 9 reveals a heterogeneously enhanced mass in the posterior wall, which may have been caused by hemorrhage or necrosis.

Fig. 3. Case number 9 has an infiltrative margin (A, H&E stain, ×4) and reveals hemorrhagic necrosis (B, H&E stain, ×10; C, H&E stain, ×20) with foci of calcification (D, H&E stain, ×20).
in the 3rd or 4th layer of the gastric wall with hypoechoic pattern (Fig. 2A). However, 3 tumors showed heterogeneous echogenicity, which corresponded to hemorrhage or calcification on pathologic examinations (Fig. 2B). Contrast-enhanced CT in 8 patients demonstrated a well-demarcated, homogeneously enhancing round mass in the submucosal layer (Fig. 2C). Two tumors, those greater than 3 cm in diameter, showed heterogeneous enhancement signifying areas of hemorrhage or necrosis (Fig. 2D).

The resected tumors were grossly well-circumscribed, solid masses with size ranged from 1.0 to 3.6 cm (median, 2.0 cm). One tumor was located in the submucosa and 6 involved both submucosal and muscular layer. In spite of relatively small size, hemorrhage or calcification within the tumor was found in 5 cases. One (case no. 9) showed an infiltrative growth with hemorrhagic necrosis in the central portion of the tumor (Fig. 3A-C). Dense calcification was also observed in this case (Fig. 3D). However, all glomus tumors showed typical histologic features characterized by central round to oval nucleus with inconspicuous nucleoli and clear to eosinophilic cytoplasm with distinct cell borders. According to the subclassification by Tsuneyoshi and Enjoji, the cases consisted of 7 solid, 2 angiomatous and one mixed solid and angiomatous type (Fig. 4A and B). Nuclear atypia was minimal, and mitotic count was less than 2/50 HPFs. Immunohistochemical study revealed diffuse strong staining for α-smooth muscle actin and vimentin, weak positive staining for h-caldesmon, and negative staining for CD34 and KIT (DAKO) (Fig. 4C and D). None of 10 tumors has shown metastasis or recurrence of disease after a median follow-up of 44.5 months (range, 15 to 116 months).

**DISCUSSION**

Current imaging studies, including EUS and CT, have limitations in the diagnosis of SMTs due to overlapping features. Although EUS helps identifying the layer of origin, there are no specific findings that would allow for a convincing preoperative diagnosis of glomus tumor. EUS features suggestive of malignancy in GISTs may be present in benign glomus tumors. These features include irregular border, necrotic or cystic areas and echogenic foci. In this study, we first confirmed that heterogeneous echogenicity found within glomus tumors

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**Fig. 4.** Representative photomicrograph of a solid growth pattern (A, H&E stain, ×10) and an angiomatous pattern (B, H&E stain, ×10). The tumors are positive for smooth muscle actin (C, ×20) and vimentin (D, ×20).
Table 2. Clinical Features of Gastric Glomus Tumors in This Series Compared with Previously Reported Cases

| Feature                      | Present series (n=10) | Miettinen et al.²,¹ (n=52) | Appleman et al.¹² (n=12) | Review by Kanwar et al.¹⁷ (n=52) |
|------------------------------|-----------------------|----------------------------|--------------------------|--------------------------------|
| M:F                          | 8:2                   | 18:34                      | 7:5                      | 25:27                          |
| Age (median), yr             | 37-72 (48)            | 19-90 (54)                 | 30-74 (55)               | 18-89 (53)                     |
| Tumor size (median), cm      | 1.0-3.6 (2.0)         | 1.3-7.0 (2.5)              | 1.0-4.0 (2.6)            | 0.8-22.0 (3.0)                 |
| Ulceration                   | 1/10                  | 20/52                      | 6/12                     | 4/52                           |
| Gastrointestinal bleeding    | 1/10                  | 21/52                      | 5/12                     | 12/52                          |
| Epigastric pain              | 5/10                  | 14/52                      | Often                    | 18/52                          |
| Incidental                   | 4/10                  | 9/52                       | 3/12                     | 16/52                          |

corresponds to the hemorrhagic or calcified foci. EUS will usually show a well-circumscribed hypoechoic mass located in the 3rd and/or 4th layer.²⁶ However, heterogeneous echogenicity caused by hemorrhage or calcification can occur. Thus, the EUS findings are insufficient to establish a diagnosis of glomus tumor. It is important for endoscopists not to be influenced by unusual findings to ignore the possibility of benign lesions such as glomus tumor in the differential diagnosis. On arterial phase of CT, all tumors showed strong enhancement with relatively sharp demarcation, reflecting their hypervascular nature. CT is practically unable to differentiate glomus tumor from other well-enhancing submucosal lesions, such as carcinoid, ectopic pancreas and some GISTs, and also reveals a different attenuation depending on size.¹¹-¹⁴ Both EUS and CT are insufficient to establish a diagnosis of SMT, and cannot be used to predict the malignant potential of a tumor as described earlier.²⁵ Further intensive study with large number of cases is needed to find specific radiologic findings.

Due to intramural location, which precludes a diagnosis by endoscopic biopsy, and lack of characteristic radiologic features, glomus tumors are commonly diagnosed histologically after surgical resection. Recently, EUS-guided fine-needle aspiration is widely used to diagnose and stage mediastinal, pancreaticobiliary, and some retroperitoneal neoplasms. Although the assessment of clinical behavior cannot be fully reached by aspiration cytology, this method may be helpful in the preoperative evaluation of SMTs, sparing a patient from extensive surgical resection. EUS-guided aspiration has been reported to successfully diagnose glomus tumors with cytologic and immunohistochemical analysis.²³ However, amount of tissue acquisition and risk of bleeding or other complications will be a major limitation when we apply the technique to this highly vascular tumor.

The clinicopathologic features in this and previous series are summarized in Table 2. The gastric antrum or prepylorus was the most commonly involved area of the gastrointestinal tract.²,¹³ Many patients recorded in the literature had gastrointestinal bleeding and various symptoms of peptic ulcer such as epigastric pain, nausea, vomiting, and anorexia.²,¹⁶,¹⁷ Nevertheless, these symptoms can be caused by any gastric mass pressing on the mucosa, probably resulting in secondary ulceration and hemorrhage.¹⁶ The previous series documented the occurrence in adults of all ages, and showed a nearly equal gender distribution.² We cannot explain a male predominance (80%) in our patients, but this may be affected by selection bias.

Folpe et al.¹⁸ proposed criteria for malignancy in glomus tumors, including deep location, size greater than 2 cm and combination of high nuclear grade and mitotic activity (>5/50 HPFs), and classified gastric site as deep-seated. However, there seems to be a marked difference in clinical behavior between glomus tumors in deep peripheral soft tissue and those in the stomach.¹ Gastic glomus tumors are usually small, with median size ranging from 2 to 3 cm, but the tumors that metastasized were 6.5 and 8.5 cm.²,¹⁶-¹⁸ The evaluation of nuclear atypia may be subjective, and the previously described metastatic glomus tumors showed only mild nuclear atypism with a few mitoses (1-3/50 HPFs). Therefore, absence of nuclear atypia and paucity of mitotic activity do not rule out malignant potential, and the size greater than 5 cm might be a more appropriate indicator of risk for gastric glomus tumor.¹

We also confirmed that gastrointestinal glomus tumors are histologically and immunophenotypically fully comparable with the tumors of peripheral soft tissues as previously reported.¹,¹³,²⁰ The tumors are positive for α-smooth muscle actin, vimentin and h-caldesmon, and negative for CD34 and KIT. These immunohistochemical findings may help distinguishing glomus tumor from other histologically similar tumors.

In summary, we have analyzed the clinicopathologic and radiologic features of 10 gastric glomus tumors in Korean population. Gastric glomus tumors are most commonly located in the antrum, and occur in adults of all ages with male predominance in our case series. As most gastric glomus tumors are small in size and clinically benign, they should not be equated with the tumors occurring in deep soft tissue. Overall diagnostic accuracy can be improved by comprehensive interpretation of endoscopic and radiologic findings under the recognition of this rare but distinctive lesion in the stomach.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was
reported.

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