

## Original Article

# Features of gastric glomus tumor: a clinicopathologic, immunohistochemical and molecular retrospective study

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**Abstract:** Glomus tumor (GT) of the stomach is a rare mesenchymal tumor. There have been few detailed studies on these tumors. A total of 1894 cases of resected gastric mesenchymal tumors were collected and eleven confirmed gastric GTs were studied. The clinical, pathological, immunohistochemical, ultrastructural and molecular characteristics of the tumors were analyzed through a retrospective study. Histologically, most tumors had gastric smooth muscle immediately adjacent and surrounding the tumor. Tumor cells around blood vessels were small, uniform, and round. Foci of hyaline and myxoid changes were observed. Prominent clear cell features were observed in two tumors. Positive expression of  $\alpha$ -smooth muscle actin ( $\alpha$ -SMA), laminin, collagen type IV, and vimentin was detected by immunohistochemical analysis in all patients. However, in clear cell areas the expression of  $\alpha$ -SMA, laminin, and type IV collagen were mild, while Syn was positive. Moreover, myofibrils and neuroendocrine granules were also present in the cytoplasm of these cells. No C-kit or PDGFR- $\alpha$  genetic mutations were detected in all patients. To conclude, Our results show that GTs in the stomach are histologically and immunophenotypically fully comparable with the glomus tumors of peripheral soft tissues. Neuroendocrine granules and neuroendocrine differentiation were identified in some of the gastric GT cells. Thus, a novel subtype of gastric glomus tumor expressing neuroendocrine cell markers may exist.

**Keywords:** Glomus tumor, immunohistochemistry, ultrastructure: stomach, diagnosis

## Introduction

Glomus tumor (GT) is a neoplastic lesion of mesenchymal origin arising from the neuro-myoarterial canal (the canal of Sucquet-Hoyer) or glomus body [1-4]. Although most GTs occur in the peripheral soft tissue and extremities, these tumors can grow anywhere in the body [1-4]. GTs seldom occurs in internal organs, as glomus bodies are absent or rarely exist in these organs [5].

GT in the stomach is rare. The first case of gastric GT was reported in 1951 [6]. The frequency of gastric glomus tumors is estimated to be 100 times less than that of gastrointestinal stromal tumors (GIST). The prevalence of gastric GT is dominant in females in the fifth or sixth decade, but a wide range of ages has been encountered [2, 7]. GT typically appears as a solitary, submucosal nodule or mass in the stomach antrum without specific clinical manifestations [1, 3]. The vast majority of gastric

GTs are benign, and the malignant form is exceedingly rare, with only a few malignant cases documented in the literature [8-11].

Most patients with gastric GT are asymptomatic, and the identification of this tumor is usually incidental. The most frequent complaints associated with gastric GT include epigastric pain, discomfort, upper gastrointestinal bleeding and ulcerous syndrome with or without nausea or vomiting [12-14]. The gross appearance of tumor usually presents as a polypoid lesion with intact surface mucosa. Microscopic examination reveals a distinct morphology characterized by round, uniform glomus cells and hypervascular structure. Tumor cells are positive for mesenchymal markers, e.g.  $\alpha$ -smooth muscle actin ( $\alpha$ -SMA), laminin, collagen type IV, and vimentin [12-14].

Because gastric GT lacks specific clinical and/or endoscopic characteristics, it is difficult to be distinguished from other gastric submucosal

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**Table 1.** Primary antibodies used in this study

Antigen	Source	Clone	Dilution
Vimentin	Amersham	V9	1:100
α-smooth muscle actin	Dako	IA4	1:100
Melanoma-associated antigen (MAA)	Dako	HMB-45	1:40
CD34	Dako	Qbend/10	1:20
Laminin	Dako	LAM-89	1:400
Collagen I	Dako	IV	1:400
CD117	Dako	Poly	1:50
Desmin	Dako	D33	1:100
S100 protein	Dako	4C4.9	1:100
Melan-A	Dako	A103	1:40
Synaptophysin	Dako	snp88	1:50
Chromogranin	Dako	Poly	1:200
CD56	Dako	Poly	1:100
Keratin 18	Novocastra	DC-10	1:50

**Table 2.** Primer sequences for genetic analysis of *C-kit* and *PDGFR-α*

Gene	Exon		Primers
<i>C-kit</i>	9	Forward	5'-CCTAGAGTAAGCCAGGGCTT-3'
		Reverse	5'-TGGTAGACAGAGCCTAAACATCC-3'
	11	Forward	5'-CTATTTTCCCTTCTCCCC-3'
		Reverse	5'-TACCCAAAAGGTGACATGG-3'
	13	Forward	5'-GCTTGACATCAGTTGCCAG-3'
		Reverse	5'-AAAGGCAGCTTGGACACGGCTTTA-3'
	17	Forward	5'-TTTCTCCTCCAACCTAATAG-3'
		Reverse	5'-CCTTTGCAGGACTGTCAAGC-3'
<i>PDGFR-α</i>	12	Forward	5'-TCCAGTCACTGTGCTGCTTC-3'
		Reverse	5'-GCAAGGGAAAAGGGAGTCTT-3'
	18	Forward	5'-ACCATGGATCAGCCAGTCTT-3'
		Reverse	5'-TGAAGGAGGATGAGCCTGACC-3'

neoplasms before operation. The diagnosis of GT largely depends on the pathological and immunohistochemical findings after the surgical resection and tissue biopsy [12-14].

In this study, we analyzed the clinical, pathological, immunohistochemical, ultrastructural and molecular characteristics of gastric GT in eleven confirmed patients, with the aim of more rigorously understanding of this rare lesion.

### Materials and methods

#### *Patient information*

A total of 1894 cases of gastric mesenchymal tumors which underwent surgical resection from April 1988 to October 2013 were collect-

ed from the General Hospital of People's Liberation Army. There were 1604 cases of gastrointestinal stromal tumor (GIST) and 11 cases of gastric GT. The clinical information collected from patients with gastric GT included gender, age, clinical symptoms, tumor location, and tumor size. The clinical data from the records were reviewed. All patients were followed up through phone calls, and the follow-up information was obtained from the hospital records. The ultrasound endoscopy, computed tomography (CT), and magnetic resonance imaging (MRI) examinations were performed in an outpatient facility. The results were collected from the records.

#### *Histopathologic examination*

All hematoxylin and eosin-stained slides were reviewed for each case. The histologic changes were evaluated under a light microscope by experienced pathologists. Mitoses were counted from 50 consecutive high power fields (HPFs) from the most cellular or mitotically active areas. The following histologic characteristics were recorded in all patients: mucosal erosion or ulceration, transmural extent of tumor, nuclear atypia, and presence of hemorrhage, necrosis or calcification.

#### *Immunohistochemistry*

Immunohistochemical staining of the formalin-fixed and paraffin-embedded tissue was conducted using an EnVision kit (DAKO, Denmark). The slides were photographed using a light microscope equipped with a digital camera. The antibodies and the dilutions were listed in **Table 1**.

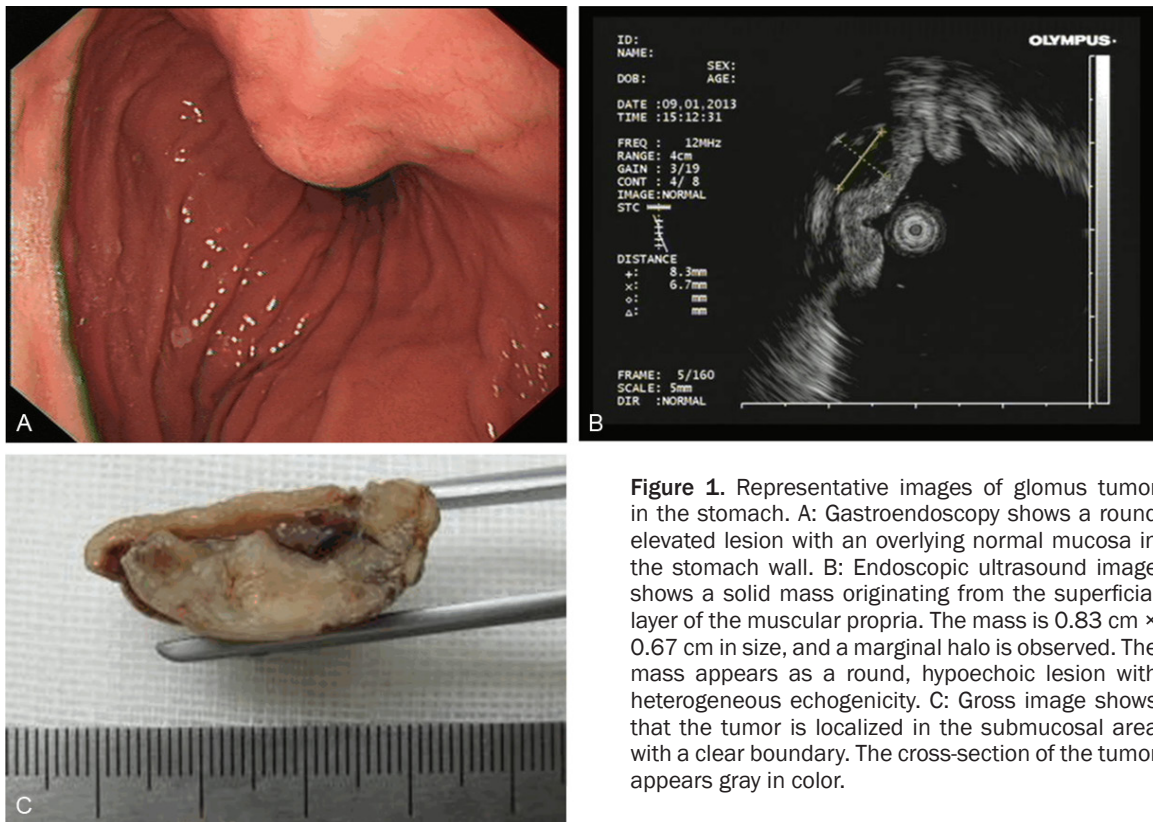
#### *Electron microscopy*

Tumor tissue was fixed in 2.5% glutaraldehyde, and washed twice with 0.1 mol/L two- dimethyl

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**Table 3.** Clinical characteristics of patients with gastric glomus tumor

No	Age	Gender	Symptom	Initial diagnosis	Gastric location	Site	size (cm)	Follow up (month)	Recurrence metastasis
1	56	M	Epigastric discomfort	Leiomyoma	Body	Submucosa	3×2×1.5	19	No
2	55	F	Upper GI bleeding	GIST	Antrum	Submucosa	2.5×2.5×2	34	No
3	50	F	Epigastric discomfort	GIST	Antrum	Muscularis	2.5×2×2	43	No
4	35	F	Epigastric discomfort	GIST	Antrum	Submucosa	2.7×2×2	144	No
5	47	M	None	Leiomyoma	Body	Submucosa	1.5×1.5×1	1	No
6	65	M	Upper GI bleeding	Cancer	Antrum	Muscularis	2.3×2×2	39	No
7	64	M	Diarrhea	GIST	Body	Submucosa	8×6×5	66	No
8	43	M	Epigastric discomfort	GIST	Antrum	Submucosa	2.5×2×1.2	55	No
9	52	F	Upper GI bleeding	Cancer	Antrum	Submucosa	2.0×2×1.5	44	No
10	62	M	Diarrhea	Leiomyoma	Body	Muscularis	1.5×1.5×1	60	No
11	45	M	None	GIST	Antrum	Submucosa	2.2×2×2	74	No



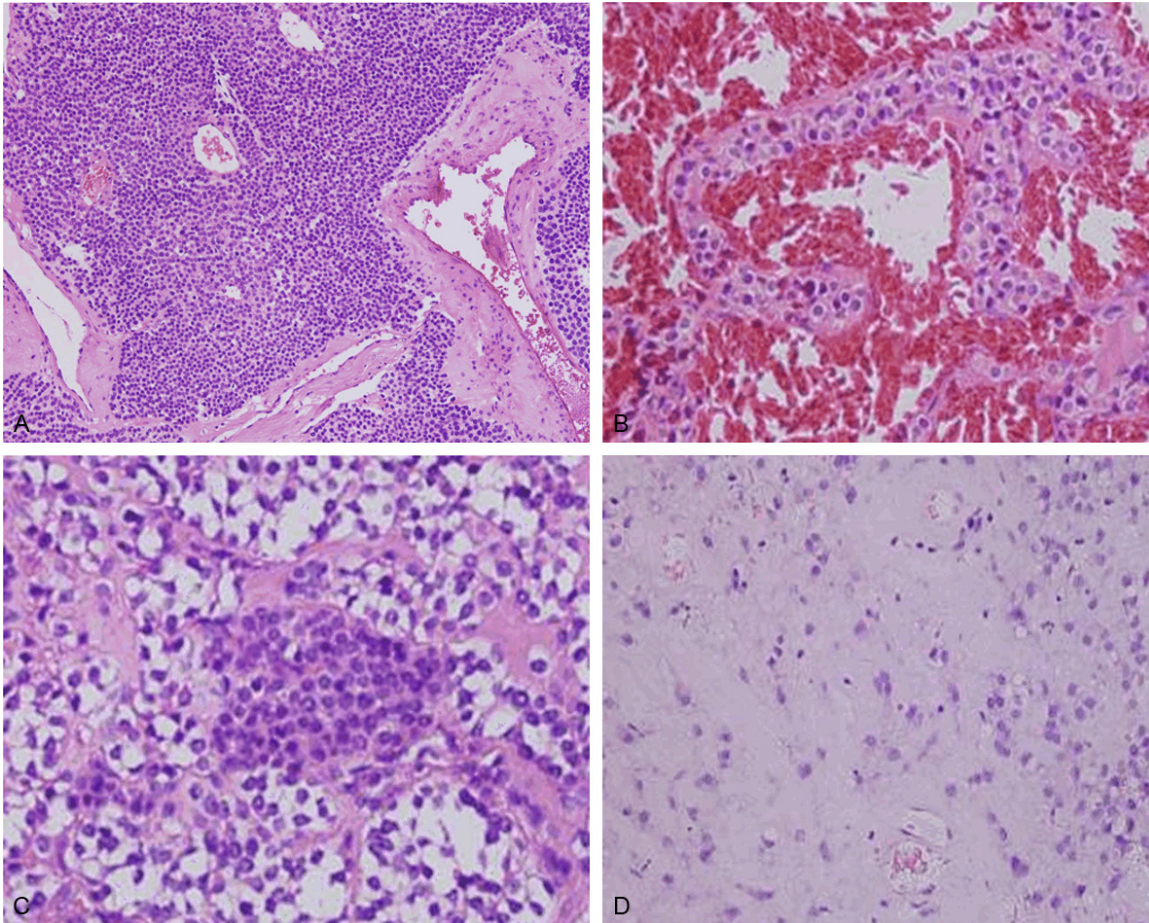
**Figure 1.** Representative images of glomus tumor in the stomach. A: Gastroendoscopy shows a round elevated lesion with an overlying normal mucosa in the stomach wall. B: Endoscopic ultrasound image shows a solid mass originating from the superficial layer of the muscular propria. The mass is 0.83 cm × 0.67 cm in size, and a marginal halo is observed. The mass appears as a round, hypoechoic lesion with heterogeneous echogenicity. C: Gross image shows that the tumor is localized in the submucosal area with a clear boundary. The cross-section of the tumor appears gray in color.

arsenate buffer, fixed with osmium tetroxide, washed with washing buffer, and dehydrated with acetone. The samples were then soaked in epoxy resin 815, embedded and sectioned. Double staining was performed using uranium acetate and lead citrate. The ultrastructure of tumor cells was examined using a transmission electron microscope (JEM-1011, Japan) at the First Affiliated Hospital of PLA General Hospital.

### Genetic analysis

C-kit and platelet-derived growth factor receptor (PDGFR)- $\alpha$  genetic mutations were analyzed in all patients. Human genomic DNA was extracted from paraffin embedded tissues using phenol/chloroform extraction methods. Exons 9, 11, 13 and 17 of the C-kit gene, and exons 12 and 18 of the PDGFR gene were eval-





**Figure 2.** Pathological examination revealed the nested growth of cells of a gastric glomus tumor. A: Microscopic examination shows numerous dilated, thin-walled vascular spaces surrounded by uniform glomus cells. The cells are round with sharp borders. (hematoxylin and eosin stain, magnification 200×). B: Prominent clear cell feature (hematoxylin and eosin stain, magnification 300×). C: Large hemangioma-like blood vessels inside the tumor. Tumor cells are clustered around the walls of blood vessels (hematoxylin and eosin stain, magnification 300×). D: The stroma shows diffuse mucoid degeneration (hematoxylin and eosin stain, magnification 300×).

uated for mutations by polymerase chain reaction amplification and direct sequencing, as previously described [15-17]. The amplification products were size fractionated on 2% agarose gels, purified from the gel, and directly sequenced. The sequences were analyzed using the Lasergene software and the data from the GeneBank database ([www.ncbi.nlm.nih.gov/Genbank/](http://www.ncbi.nlm.nih.gov/Genbank/)). The primers used in this study were summarized in **Table 2**.

#### *Comparisons of present and previous reports*

Literature searches with the keywords “stomach” and “GT” were performed in the Pubmed database in records from 1988 to 2013. Results from Miettinen et al. [2] and Kang et al. [13] groups were compared in parallel with results from our current study.

## **Results**

### *Clinical characteristics of patients*

The clinical characteristics of patients with gastric GT were summarized in **Table 3**. The gastric GTs account for 0.58% (11/1894) of gastric mesenchymal tumors. There were eleven cases of gastric GTs, including seven male (7/11) and four female (4/11) patients. The average age was 52.1 years (35-64 years old). Four patients complained of upper abdominal pain (4/11), three complained of upper gastrointestinal hemorrhage (3/11), two complained of diarrhea (2/11), and two had no complaints (2/11). Four had tumor on the gastric body (4/11), and seven had tumor on the gastric antrum (7/11). Tumors localized in submucosa were seen in

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**Table 4.** Comparisons among presently and previously reported cases of gastric glomus tumor

Features		Present study (n=11)	Kang et al. [13] (n=10)	Miettinen et al. [2] (n=31)
Demography	Age, y (median age)	35-64 (52.1)	37-72 (48)	19-90 (56)
	Male:female	7:4	8:2	9:22
Symptom	Ulceration	3/11 (27%)	1/10 (10%)	14/31 (45.2%)
	GI bleeding	3/11 (27%)	1/10 (10%)	11/31 (35.5%)
	Epigastric discomfort	4/11 (36%)	5/10 (50%)	9/31 (29.0%)
	Incidental	2/11 (18%)	4/10 (40%)	5/31 (16.1%)
Tumor	Size, mean (cm)	1.5-8.0 (2.7)	1.0-3.6 (2.0)	1.5-6.0 (3.0)
	Location			
	Antrum	7/11 (63%)	7/10 (70%)	22/31 (70.9%)
	Body	4/11 (37%)	3/10 (30%)	5/31 (16.1%)
	Unknown	0	0	4/31 (12.9%)
IHC	α-SMA	11/11 (100%)	10/10 (100%)	23/23 (100%)
	Vimentin	11/11 (100%)	10/10 (100%)	17/17 (100%)
	Laminin	11/11 (100%)	-	18/20 (90%)
	Collagen IV	11/11 (100%)	-	15/16 (94%)
	CD34	3/11 (27%)	0/10 (0%)	4/20 (20%)
	Synaptophysin	2/11 (18%)	-	3/17 (18%)
	Chromogranin	0/11 (0%)	-	0/13 (0%)
	Keratin 18	0/11 (0%)	-	0/14 (0%)
	CD56	0/11 (0%)	-	-
	CD117	0/11 (0%)	0/10 (0%)	0/18 (0%)
Surgery	Wedge or segmental resection	8/11(70%)	-	15/31 (48.4%)
	Hemigastrectomy or antrectomy	3/11 (30%)	-	10/31 (32.3%)
	Subtotal gastrectomy	0	-	4/31 (12.9%)
	Unknown	0	-	2/31 (6.4%)

eight cases, and tumors in muscularis in three cases. Four were initially considered as GIST (6/11) before surgery, three were leiomyoma (3/11), and two were gastric cancer (2/11). All patients underwent surgical resection and all tumors were solitary. Wedge or segmental resection was performed in eight cases and Hemigastrectomy was performed in three cases. None were confirmed as gastric cancer. None had relapse or metastasis after 1 to 144 months of follow-up (**Table 3**).

### *Imaging findings*

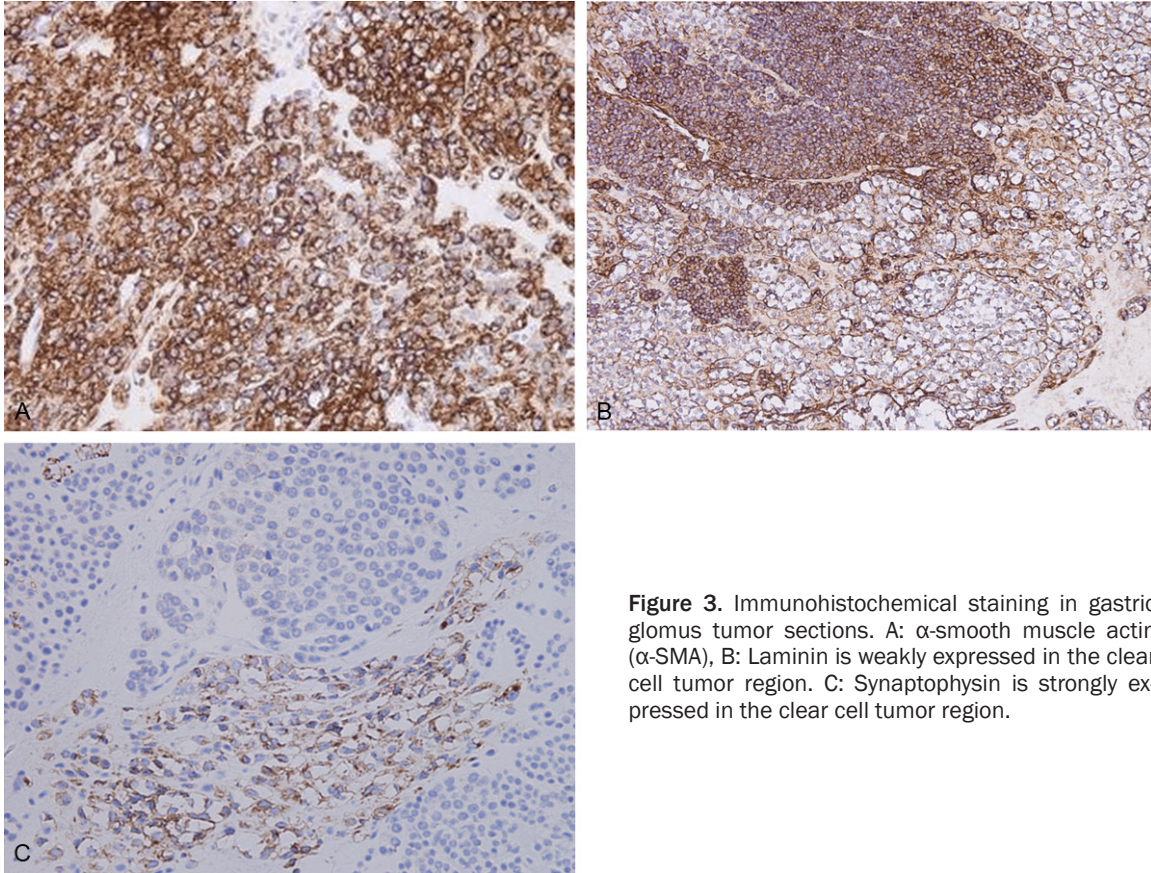
Before the surgery, all patients underwent upper gastrointestinal endoscopy and tissue biopsy. Endoscopy showed round or oval elevated lesions with smooth surfaces under the gastric mucosa of most patients (**Figure 1A**). One patient underwent endoscopic ultrasonography. Endoscopic ultrasonic showed a solid mass originating from the superficial layer of

the muscular propria. The hypoechoic lesion was prominent toward the cavity and had clear boundary (**Figure 1B**). One patient underwent MRI examination and all other patients were examined by CT scan. The tumors presented as masses located inside the gastric wall.

### *Gross findings*

The tumors were seen as circumscribed oval or spherical intramural masses and measured 1.5-8.0 cm in diameter. Two patients had a maximal tumor diameter less than 2 cm, eight patients had maximal diameter of 2-5 cm, and one was greater than 5 cm. Mucosal ulceration was seen in three patients. The tumors variably bulged to mucosal or serosal surface. The gross section of tumor appeared soft and/or rubbery and sometimes as spongy with a white to pink color, with or without hemorrhage. The tumors were single solid masses with sharp boundaries (**Figure 1C**).





**Figure 3.** Immunohistochemical staining in gastric glomus tumor sections. A:  $\alpha$ -smooth muscle actin ( $\alpha$ -SMA), B: Laminin is weakly expressed in the clear cell tumor region. C: Synaptophysin is strongly expressed in the clear cell tumor region.

#### *Histopathological findings*

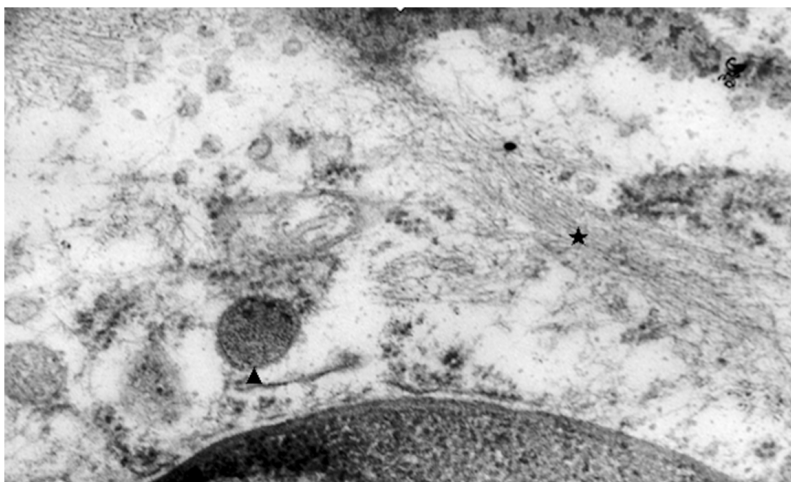
Histologically, GTs were well circumscribed and located in gastric submucosa or muscularis. Most GTs had solid nests of tumor cells with dilated blood vessels. The tumor nodules were separated by bundles of smooth muscle and fibrous tissue with hyalinization. (**Figure 2A**). Some tumors showed hemangiopericytoma-like vascular pattern and the tumor cells had well-defined cell borders. Large cavernous vessels were seen in some tumor sections (**Figure 2B**). Focal calcification was seen in one case. Most tumors showed sharply defined cell membranes and centrally located round or oval, uniform nuclei with delicate chromatin and inconspicuous nucleoli. The cytoplasm of tumor cells was red or translucent. Prominent clear cell features were observed in two cases and mild nuclear atypia was seen focally, but there was no necrosis in these areas (**Figure 2C**). Mitotic figures were seen, but were very scarce and numbered less than 3/50 HPFs. The stroma showed myxoid changes in some cases (**Figure 2D**).

#### *Immunohistochemical findings*

The immunohistochemical staining results are summarized in **Table 4**. Expression of  $\alpha$ -smooth muscle actin (ASMA), laminin, collagen type IV, and vimentin were positive in the tumor sections from all eleven patients (**Figure 3**). However, these antibodies were strongly positive in the classic tumor region, while weakly expressed in clear cells region (**Figure 3**). Interestingly, Syn was strongly positive in the clear cell-dominant areas (**Figure 3**). Other neuroendocrine cell markers, including CD56 and CgA, were negative in these areas. CD34 was positive in three cases, CD117, S-100, CD31, HMB45, Melan-A and CK were negative.

#### *Ultrastructural findings under electron microscopy*

The ultrastructure of the synaptophysin-positive tumors were examined by electron microscopy. The cytoplasmic membrane was surrounded by a thick basement membrane like material. Nuclei were round or oval in shape.



**Figure 4.** Ultrastructure of gastric glomus tumor under electron microscopy. Muscular actin structure (★) and neuroendocrine granules (▲) inside the tumor cells (magnification 20000×).

Pinocytotic vesicles and myofibrils were observed in most tumor cells and a few scattered electron-dense granules were seen inside the tumor cells. In addition, the granules were of uniform density and resembled neuroendocrine granules (**Figure 4**).

#### *C-kit and PDGFR- $\alpha$ mutation analysis*

All tumor samples from eleven patients were examined for mutations of the C-kit and PDGFR- $\alpha$  using the specific primers shown in **Table 2**. The sequencing results confirmed no mutations in either gene in all patients (**Figure 5**).

#### *Comparisons of present study with previous reports*

A literature search in the PubMed database showed that there were less than 200 cases of gastric GTs reported from 1988 to 2013. The majority of reports were single case reports. We compared our cases with 2 major series in the English literature (those of Miettinen et al [2] and Kang et al [13]). The detailed comparisons were summarized in **Table 4**.

#### **Discussion**

In present study, we screened 1894 cases of gastric mesenchymal tumors that underwent operation. Eleven patients were confirmed as gastric GT, including seven males and four females, indicating slightly more male patients

with GT than female patients. This observation is not consistent with the gender difference described in previous reports. Both Miettinen et al. [2] and Fang et al. [1] showed higher numbers of female patients with GT, while Kang et al. [13] reported higher numbers of males. The small amount of patients enrolled in each study likely accounts for this difference. The average age of the eleven patients was 52.1 years (35-64 years), indicating that gastric GT frequently occurred in elder individual. This finding is consistent with previous reports. However, most

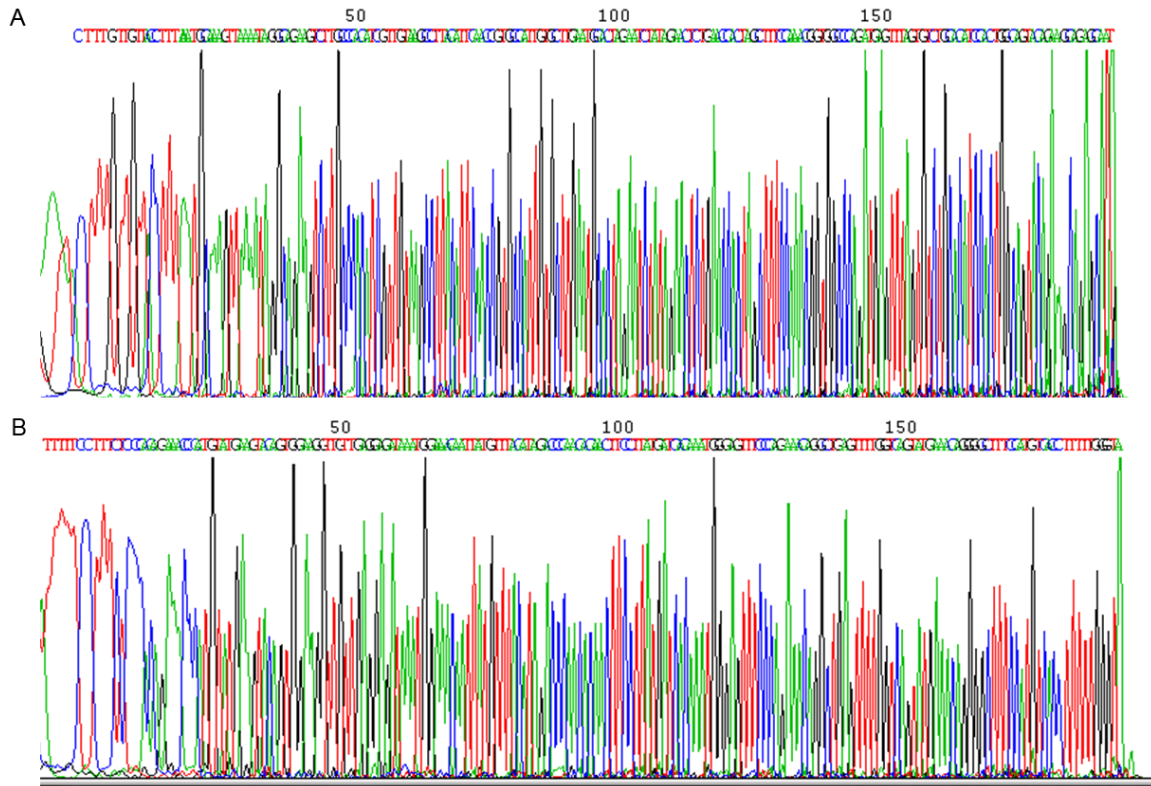
GTs occurred in soft tissues and were diagnosed in young adults [18].

Four patients had epigastric discomfort, three had upper gastrointestinal bleeding, and two had diarrhea. Hemorrhage in some patients is life threatening, as reported previously [2, 19]. Two patients in our study had no symptoms and were identified incidentally.

In our patient set, GTs were more common in gastric antrum than in the gastric body. All tumors in our study were solitary, with an average maximum diameter of 2.7 cm. These findings were in line with previous reports, which showed that most tumors were between 2-5 cm [2, 13], and the average diameter of gastric GT was 2-3 cm [13]. The reported tumor sizes of those with metastasis ranged from 6.5 cm to 17 cm [2, 18, 20]. Thus, some studies suggested tendency towards malignancy when the diameter of the tumor was greater than 5 cm [2, 14]. In our current report, one case had a tumor diameter of 8 cm, but no relapse or metastasis was found after 66 months follow-up. Warner et al. [21] also reported one case of gastric GT with a diameter of 30 cm without recurrence and metastasis after 20 years follow-up. This line of evidence indicated that tumor size is not an accurate predictor for malignancy.

The pathologic features of GT in the stomach are very similar to GT in soft tissue. Tumor tissue is comprised of nested glomus cells sur-

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**Figure 5.** Representative sequences of *C-Kit* genetic mutation analysis. No mutations were detected by sequencing using (A) exon 9 primers or (B) exon 11 primers.

rounding blood vessels. The stroma is composed of a small amount of fiber smooth muscle and unmyelinated nerve fiber. Based on components of glomus cells, vascular smooth muscle and mucus, GTs are divided into several subtypes. The most common type in stomach is the solid GT with large spherical cells surrounding the capillaries in a nested arrangement. Foci of hyaline and myxoid change were often observed [2]. Fang et al. [1] reported the incidence of this type was 94.7% (54/57). In our study, nine patients were identified with this subtype. The second subtype is glomangiomas. The vascular components are large veins with cavernous hemangioma-like structure. Two cases in our study were of this subtype. Other subtypes including glomangiomyomas and glomangiomas were scarce. No cases in our cohort showed these subtypes.

The interpretation of nuclear atypia (an indicator of malignancy) in gastric GT is somewhat subjective [13]. Even if the numbers of mitoses are less than 5/50 HPF, it is not possible to completely rule out the potential for malignancy.

The vascular invasion of GT in soft tissue usually predicts poor prognosis and metastasis [2]. However, That is not necessarily the case in gastric GT [22]. Some diagnostic criteria for malignant gastric GT remain controversial. Tumor location, mass, cellularity, nuclear atypia, spindle cell change, mitotic activities, atypical mitotic features, necrosis, and angiolymphatic invasions have been fundamentally recognized as probable factors that determine the propensity for malignancy. Malignant glomus tumors arising from the stomach with metastasis are rare, and therefore long-term follow-up is highly advised [23]. Further investigation and comparative studies are required to define the criteria.

The immunohistochemical features of gastric GT are similar to those of soft tissue GT [24] which express  $\alpha$ -SMA, vimentin, laminin, and collagen type IV. In particular,  $\alpha$ -SMA is strongly positive in nearly all tumor tissues, and thus  $\alpha$ -SMA is very useful marker in the diagnosis of GT [1]. The expression levels of  $\alpha$ -SMA, laminin, and type IV collagen are different between the



classic glomus cells and the clear cells. The levels are much higher in the classic tumor region. However, Syn was strongly positive in clear cells. Miettinen et al. also reported a large area of clear tumor cells in 10 cases that was accompanied with a certain degree of atypia. Focal synaptophysin positivity was an occasional finding in gastric glomus tumors, but no explanation was proposed [2]. In our study, both CD56 and CgA were negative in all patients. To further explore the possible reasons, we performed electron microscopy in the synaptophysin-positive tumors. Ultrastructurally, the tumor cells exhibited ultrastructural features of smooth muscle and myofibrils. Neuroendocrine granules were found in these tumor cells. Five decades ago, Kim et al. [25] reported endocrine granules were observed in gastric glomus tumors. They further identified that the morphology of these endocrine granules were similar to particles in paraganglioma and adrenal tumors. The authors postulated that partial gastric glomus tumors may exhibit endocrine function. However, they were unable to confirm this finding through immunohistochemistry. The present study confirmed the existence of neuroendocrine granules inside the glomus tumor cells and indicated that some gastric GTs exhibit certain neuroendocrine differentiation by immunohistochemical staining. It is unclear whether this type of tumor is present in soft tissue GT and whether it has different prognosis. Therefore, this will require additional studies for confirmation.

CD117 and CD34 expression is typically negative in this tumor type. In our study, three cases were CD34 positive. Miettinen et al. [2] also reported CD34-positive cases, and CD34-positive expression has also been seen in some GT in soft tissue [26].

The gastrointestinal stromal tumor (GIST) is the most common mesenchymal gastrointestinal tumor. The proportion of GIST in the study group was 84.6% (1604/1894). Moreover, diverse morphology is one of the characteristics of GISTs [15-17]. Therefore, genetic analysis is strongly recommended during the diagnosis of gastric mesenchymal-originating tumors.

The gastric GTs should be differentiated from those tumors with similar structures [27]. 1) Neuroendocrine tumor: The tumor is rich in blood sinus and the tumor cells are uniform. It

can be easily confused with GT. The nuclear chromatin in this type of tumor is relatively crude and strongly stained, and the cytoplasm is light red. Keratin markers (e.g., CK18) and multiple neuroendocrine markers are typically positive, but  $\alpha$ -SMA is negative; 2) Paraganglioma: It is frequently located in the retroperitoneal and mesenteric areas, and rarely seen in the gastrointestinal tract. It expresses neuroendocrine markers and S-100 but not  $\alpha$ -SMA; 3) Hemangiopericytoma: It is located in the retroperitoneal and mesenteric areas and rarely occurs in the gastrointestinal tract.  $\alpha$ -SMA is negative or weak focal positive; 4) Epithelioid gastrointestinal stromal tumors: Tumor cells are epithelioid, nested, or scattered in arrangement. The cytoplasm is eosinophilic or clear. CD117 and CD34 are usually positive, and  $\alpha$ -SMA can be weak focally positive. Laminin is negative. The C-kit gene mutation is helpful to confirm diagnosis; 5) Lymphoma: Immunohistochemical staining is very helpful in the differential diagnosis; 6) Tumors with perivascular epithelioid cell differentiation (PEComa): PEComa rarely occurs in the gastrointestinal tract. The cytoplasm is transparent or granular, light eosinophilic color, and surrounding thin wall vessels. Cells far from vessels are spindle-shaped smooth muscle cells that are  $\alpha$ -SMA-positive, and HMB45 and Melan-A positive [28].

Endoscopic ultrasonography (EUS) combined with CT is considered to be the most useful diagnostic tool for gastrointestinal submucosal tumors [29]. Both the location and category of tumors can be determined using this tool [29]. EUS combined with CT contributes to the early detection and identification of gastric GTs, particularly in terms of assessing the tumor blood supply. Endoscopic biopsies may fail to provide sufficient amounts of material or representative samples because the submucosal lesion and deeper submucosal lesions can not be reached adequately. Operative intervention is the major treatment for gastric GT. The majority of patients reported in this study underwent surgical resections, and the most commonly used methods were wedge or segmental resection.

### Conclusion

GT in the stomach is rare. The diagnosis for GT is mostly dependent on the histopathologic and

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immunohistochemical findings after operation. Neuroendocrine granules and neuroendocrine differentiation are found in some gastric GT cases. Immunohistochemical and molecular studies are essential in the differential diagnosis of gastric GTs from other gastric mesenchymal tumors.

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### Disclosure of conflict of interest

None.

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