Journal of
Medical Case Reports

CASE REPORT

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Malignant gastric glomus tumor with heterochronous liver metastases: a case report and review of the literature

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Abstract

Background Glomus tumors are mesenchymal tumors originating from the neuromuscular arterial canal or vascular lumen. While most gastric glomus tumors are benign and solitary, rare cases can be malignant and have a poor prognosis. Definitive treatment options remain limited for multifocal metastases, often necessitating salvage therapy.

Case presentation A 36-year-old Han Chinese female patient presented with hematemesis, melena, and syncope persisting for four days. Diagnostic evaluations revealed a malignant gastric glomus tumor, prompting radical resection. During follow-up, radiological imaging identified liver metastases. Subsequent management included radiofrequency ablation and laparoscopic resection of select lesions.

Conclusions Gastric glomus tumors pose diagnostic challenges owing to radiological and pathological features that overlap with gastrointestinal stromal tumors. Immunohistochemistry remains critical for definitive diagnosis. While Folpe's criteria for malignant gastric glomus tumors have limitations, they provide a practical framework. Our findings suggest that surgical resection followed by radiofrequency ablation may offer effective local control for recurrent or metastatic gastric glomus tumors. Further research is warranted to explore targeted therapies based on molecular profiling.

Keywords Glomus tumor, Liver metastasis, Radiofrequency ablation, Laparoscopic resection, Case report

Introduction

Glomus tumors are mesenchymal tumors that originate from the neuromuscular arterial canal or vascular lumen. Although typically located in the dermis or subcutaneous tissues of the extremities, rare cases involve visceral organs, including the stomach [1–3].

Gastric glomus tumors (GGTs) are exceptionally rare, accounting for approximately 1% of gastric mesenchymal tumors, being 100-fold less frequent than gastrointestinal stromal tumors (GISTs) [4]. Most GGTs are benign and solitary, but rarely, they can be malignant. Few reported cases of malignant GGT with distal metastasis have shown poor prognosis despite their low morbidity [5, 6], and there is no definite treatment except salvage therapy.

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This report describes a case of malignant GGT with liver metastases and discusses therapeutic strategies through a literature review.

Case report

A 36-year-old Han Chinese female patient was admitted on 11 December 2021, with 4-day history of hematemesis, melena, and syncope. Initial gastroscopy at a local hospital identified a 2-cm submucosal tumor with ulceration on the greater curvature of the stomach, suspected to be a GIST (Fig. 1). Endoscopic biopsies confirmed a mesenchymal tumor requiring surgical intervention.

Preoperative blood tests revealed moderate anemia, while tumor markers [carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9), and alpha-fetoprotein (AFP)] were within normal limits. Contrast-enhanced abdominal computed tomography (CT) demonstrated a 2-cm lobulated gastric mass with heterogeneous enhancement and central necrosis (Fig. 2A, B). No distant metastases were observed. The patient underwent wedge resection of the gastric lesion.

Pathological findings of the gastric specimen showed a multinodular tumor with a solid growth pattern, characterized by significantly ectatic and staghorn-like vessels (Fig. 3). The tumor comprised nests of rounded epithelioid cells surrounding capillary-sized vessels, with marked nuclear atypia (Fig. 4A) and numerous mitoses (> 5/5 mm [2]) along with atypical mitotic figures (Fig. 4B). Immunohistochemistry revealed strong positivity for smooth muscle actin (SMA) and vimentin (Fig. 5A, B), moderate pericellular type IV collagen expression (Fig. 5C), and diffuse synaptophysin reactivity (Fig. 5D). Ki-67 was positive in up to 40% of tumor cells (Fig. 5E). Tumor cells were negative for Chromogranin A (CgA), Cluster of Differentiation 56 (CD56), Cytokeratin 7 (CK7), Cluster of Differentiation 117 (CD117), Discovered on GIST-1 (DOG-1), Cluster of Differentiation 34 (CD34), Somatostatin Receptor 2A (SSTR2A), Leukocyte

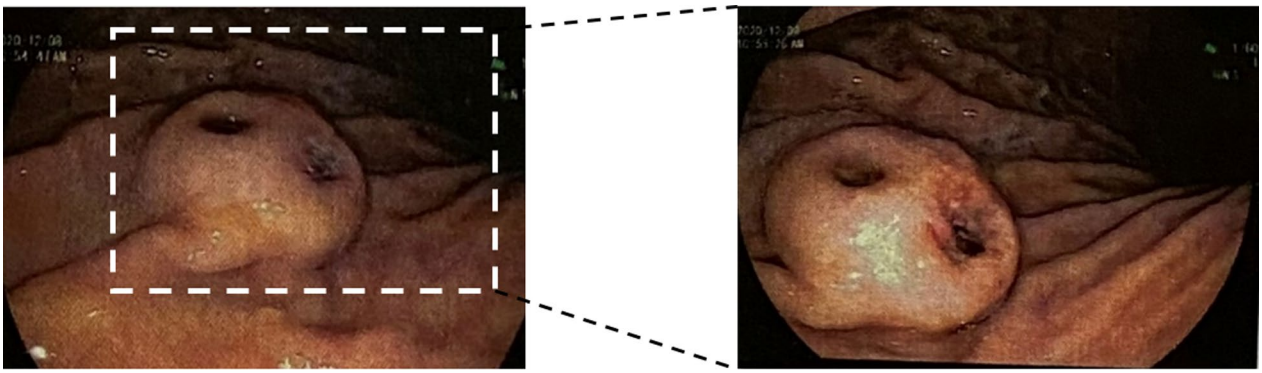

Fig. 1 Gastroscopy showing a submucosal tumor with bleeding ulcers, about 2 cm in diameter, on the side of the greater curvature of the stomach

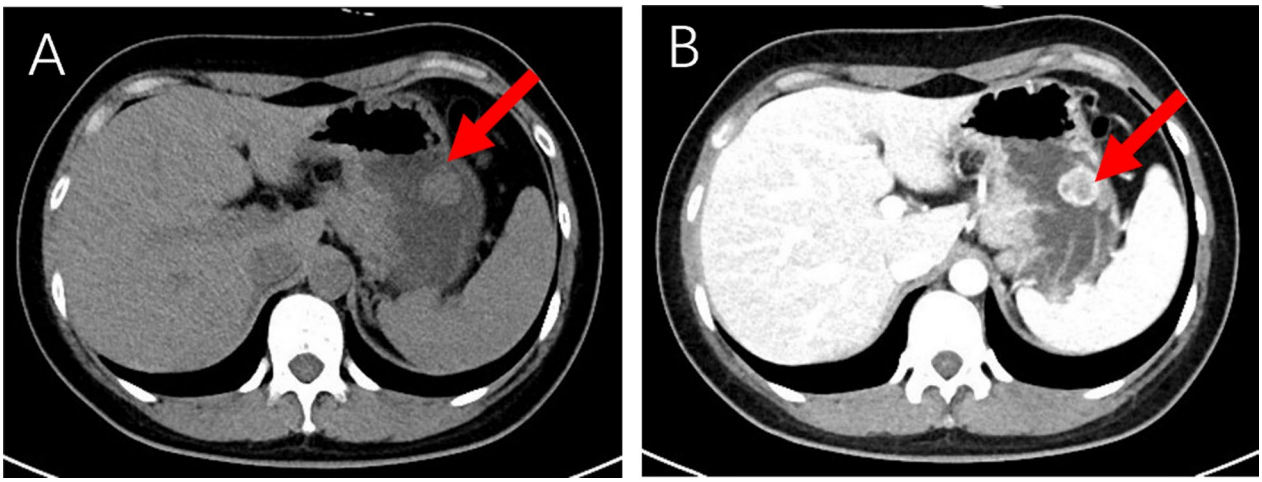

Fig. 2 Unenhanced images showing a lobulated mass (pointed by the red arrow) of about 2 cm with homogeneous low density in the greater curvature of the stomach (**A**). Contrast-enhanced computed tomography in the portal venous phase showed a heterogeneous and gradually enhancing mass (pointed to by the red arrow) with a low attenuating necrotic portion (**B**)

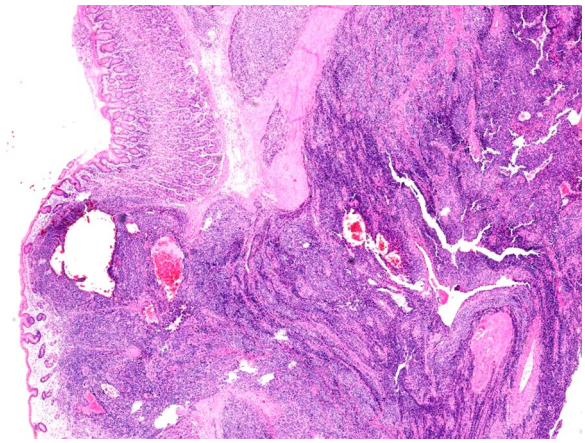

Fig. 3 A multinodular tumor with a solid growth pattern and characterized by significantly dilatated vessels (hematoxylin and eosin stain, ×20)

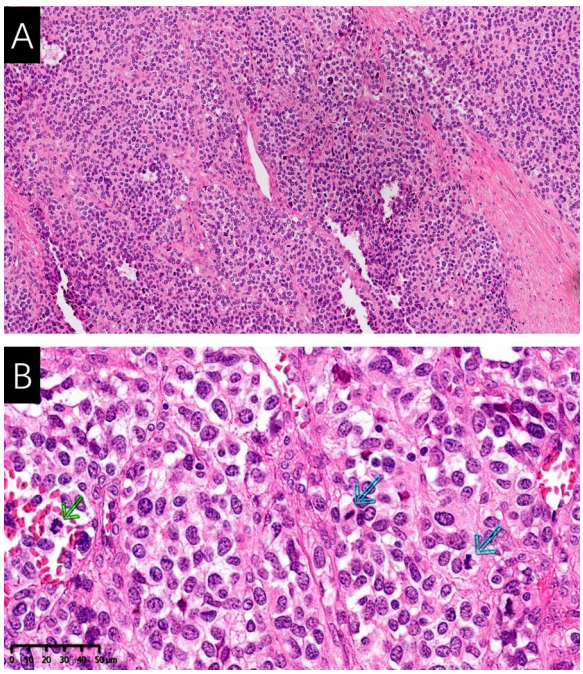

Fig. 4 Nests of rounded epithelioid tumoral cells with marked nuclear atypia surround capillary-sized vessels (hematoxylin and eosin stain, ×200) (**A**). The tumor shows marked nuclear atypia and high grade of mitotic activity (pointed to by the blue arrow)and atypical mitotic figures (pointed to by the green arrow) (hematoxylin and eosin stain, ×400) (**B**)

Common Antigen (LCA), Cluster of Differentiation 99 (CD99), S-100, and epithelial membrane antigen.

At 1 year postoperatively, surveillance imaging revealed two hypodense hepatic lesions in segments II and IV, suggestive of metastases. On magnetic resonance imaging (MRI), two abnormal signal masses were seen in the liver parenchyma, the large one being about 18 mm in length, with low signal in T1WI, high signal in T2WI and diffusion-weighted imaging (DWI), and slightly reduced signal in apparent diffusion coefficient (ADC) map, with circumferential enhancement in the late arterial phase and persistent enhancement in the portal venous phase after enhancement, and unenhanced necrotic liquefaction areas were seen within them (Fig. 6). After consultation with the oncology and interventional departments, a liver puncture biopsy and radiofrequency ablation (RFA) of three lesions were performed. Postoperative specimen pathology combined with immunohistochemistry was considered consistent with metastasis of GGT.

At 1 month later, MRI was performed on a 3.0-T MR machine. On MRI, multiple metastatic lesions were seen in segment III, IV, and VII. The metastasis mass showed T1 low, T2 high, and DWI high signal, with circumferential enhancement in the arterial phase and persistent enhancement in the portal vein phase after enhancement (Fig. 7).

As the previous time, these metastatic lesions were destroyed by RFA, except for one lesion in segment IV that was removed laparoscopically 2 months later because of its proximity to the transverse colon. Postoperative pathology reconfirmed metastasis of GGT.

From December 2021 to date, it has been 30 months since the initial diagnosis and the patient remains alive and in good health after a series of treatments (Fig. 8).

Discussion

GGTs are rare gastrointestinal lesions originating from the neuromuscular arterial canal or vascular lumen. These lesions are more commonly present in the peripheral soft tissue, but can rarely be found in the gastrointestinal tract [7]. Owing to their rarity and nonspecific clinical presentation, diagnosing GGTs is challenging. Imaging studies, including CT, MRI, endoscopic ultrasonography, and endoscopy, yield nonspecific results. Preoperative cytology may also provide inconclusive or misleading findings.

GGTs share overlapping features with other stromal lesions such as GISTs and carcinoid tumors. While ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) has been attempted for differential diagnosis, glomus tumors do not show any particular imaging characteristics [8]. In our case, initially, GGT was also misdiagnosed as GIST, and PET/CT proved useless in our subsequent evaluation of systemic metastases. Meanwhile, given that "bite-on-bite" punch biopsies have low diagnostic yield, endoscopy ultrasound (EUS)-guided biopsy via fine needle aspiration (FNA) or fine-needle biopsy (FNB) is recommended by several studies for more accurate preoperative diagnosis [9, 10].

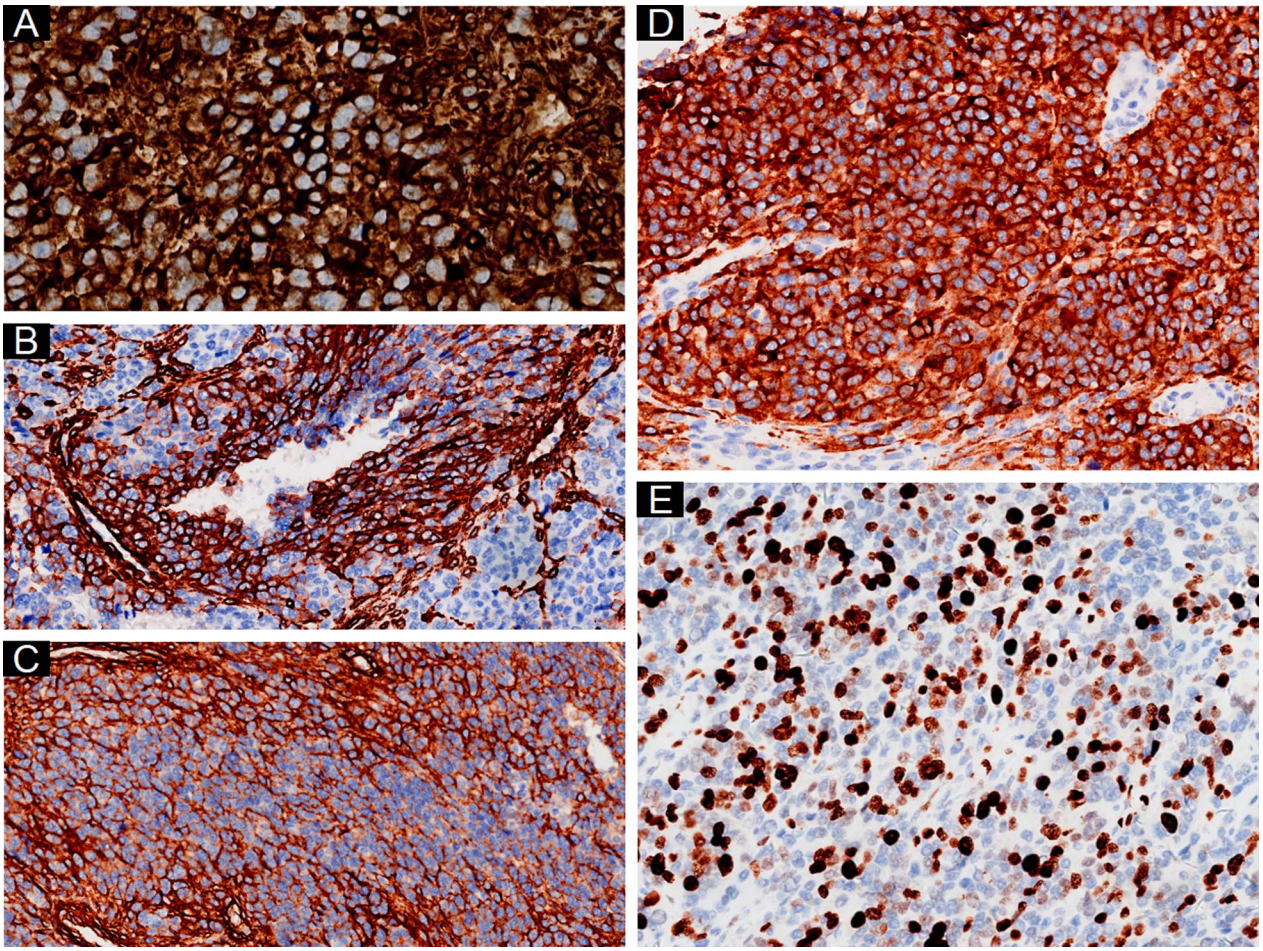

Fig. 5 **A**–**E** Immunohistochemical stains (×400). Tumoral cells show strong immunoreactivity for vimentin (**A**) and partial positivity for smooth muscle actin (**B**), prominent expression of pericellular type IV collagen (**C**), and abnormally diffuse positivity for synaptophysin (**D**). Ki67 was positive in up to 40% of tumor cells (**E**)

Immunohistochemistry is crucial for diagnosing glomus tumors, often revealing positivity for SMA and vimentin but lacking markers indicative of an epithelioid GIST, such as CD117, CD34, Desmin, S-100, and DOG1 [7].

Assessing prognosis for GGT is challenging owing to the lack of reliable histological features predictive of tumor behavior. Folpe *et al.* [11] proposed a classification scheme for glomus tumors with atypical features, categorizing a malignant glomus tumor as having at least one of the following criteria: (1) a deep location and size of more than 2 cm, (2) the presence of atypical mitotic figures, or (3) a combination of moderate to high nuclear grade and mitotic figures (five mitoses/50 high-power fields (HPF)). Atypical and malignant glomus tumors are not frequently encountered, and recurrence or metastasis is reported to be extremely rare [6] because malignant glomus tumors are low-grade malignancies that are locally aggressive and rarely metastasize [12]. According to the known reported literature, almost all metastatic or locally recurrent malignant GGTs basically meet this criterion, including the patient reported in our case. However, we found one exception case reported by Davis *et al.* [13] in which a 10-mm-diameter GGT and a 1.1-mm-diameter simultaneous liver metastasis were reported while no mitotic figures or necrosis were found. This small metastasis in the liver was discovered accidentally during biopsy and led to the identification of a small primary tumor in the stomach. This finding challenges the criteria summarized by Folpe and suggests that even small glomus tumors have metastatic potential. Considering the above, a surveillance strategy is not recommended and all GGT should be completely excised and followed up postoperatively.

Treatment modalities for GGTs vary. Small or benign tumors are often treated with gastric wedge resection or endoscopic resection [14, 15], while larger and malignant tumors may require subtotal or total gastrectomy [16]. Malignant GGTs are rarely reported to

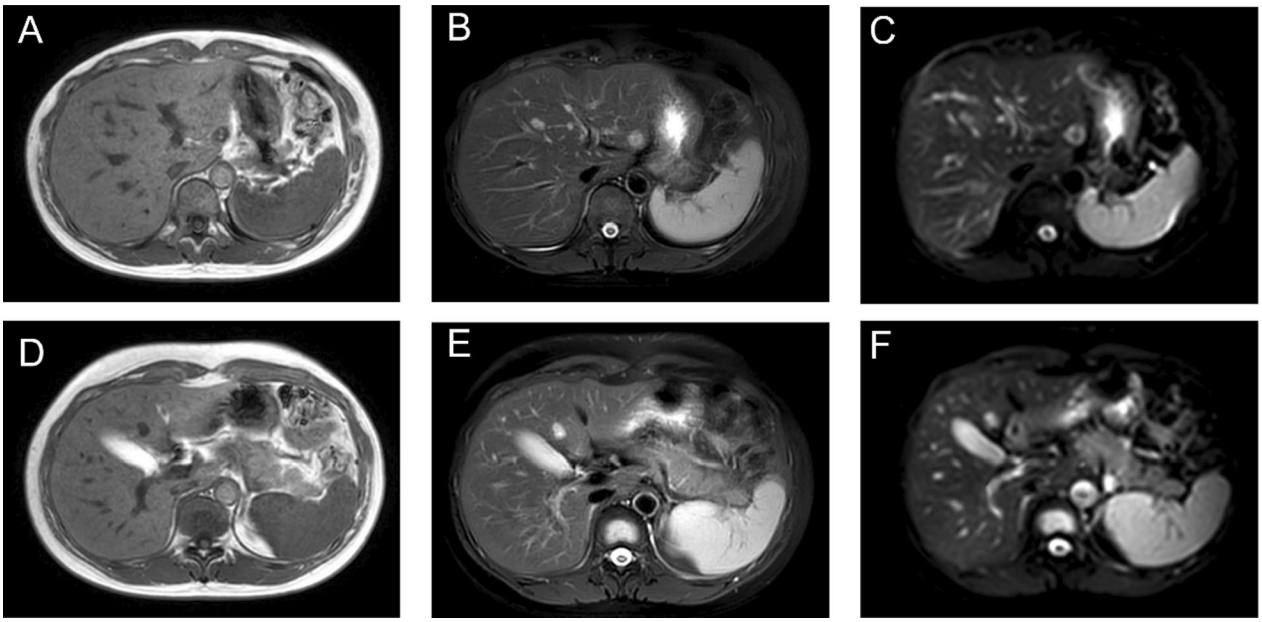

Fig. 6 Two abnormal signal masses were seen in the liver parenchyma on magnetic resonance imaging. **A**–**C** An abnormal signal mass was located in segment II of the liver on MRI with low signal in T1WI (**A**) and high signal in T2WI (**B**) and diffusion-weighted imaging (**C**). **D**–**E** An abnormal signal mass was located in segment IV of the liver on magnetic resonance imaging with low signal in T1WI (**D**) and high signal in T2WI (**E**) and diffusion-weighted imaging (**F**)

show lymph node metastasis, and wedge resection is believed to achieve radical treatment. However, cases of metastasis through both lymph and blood have been observed [6, 17]. Negahi *et al.* [6] reported a patient with a GGT in the lesser sac and simultaneous liver and lymph node metastasis. Zhang *et al.* [17] reported a malignant glomus tumor of the esophagus with mediastinal lymph node metastases. These two cases indicate that an appropriate range of lymph node dissection may be necessary.

For patients with widespread metastasis, prognosis may become rather poor and may eventually lead to death (Table 1). Often, in these kinds of cases, owing to the poor general condition of the patient, chemotherapy is not possible. Besides, in cases in which radiotherapy was conducted, there were no satisfactory results. However, there is another case introduced by Negahi *et al.* [6] of a 50-year-old patient with a mass in the lesser sac and simultaneous liver and lymph node metastasis. In this case, during a 4-year follow-up period, the patient's general condition was good and there was no evidence of mass recurrence. The progression of liver and lung metastases was halted as the result of a combination of chemotherapy with liposomal doxorubicin/ paclitaxel and bevacizumab. However, it is worth noting that, for those GGTs with high volume, preoperative neoadjuvant chemotherapy or palliative chemotherapy may cause massive bleeding from the tumor and result in rapid patient death because of the special characteristics of glomus tumor [18, 19].

In recent years, molecular studies have been carried out to investigate the genetic phenotype of glomus tumors. Mosquera *et al.* [20] revealed that overall *NOTCH2* gene rearrangements were identified in 52% of 33 glomus tumors, including all malignant cases. Karamzadeh Dashti *et al.* [21] reported that *BRAF* V600E mutation was detected in 6% of 102 glomus tumors, all of which were malignant glomus tumors or of uncertain malignant potential. These findings indicate that, in patients with progressive disease, *NOTCH2* gene and BRAF could be promising therapeutic targets.

This is the second report of liver metastasis treated with RFA, and the patient is still in good health with regular follow-up, which suggests that RFA may be an effective and minimally invasive tool to control liver metastases of malignant GGT. Our next step will be to perform gene sequencing for targeted drug therapy if new metastases are detected during follow-up, and we will continue to report on the effectiveness of the treatment.

Conclusion

At present, the diagnosis of GGT is difficult to distinguish from GIST on imaging and pathological examination, and accurate diagnosis still depends on immunohistochemistry. Folpe's criteria, while imperfect, aid in malignancy assessment. As a rare malignant tumor of the

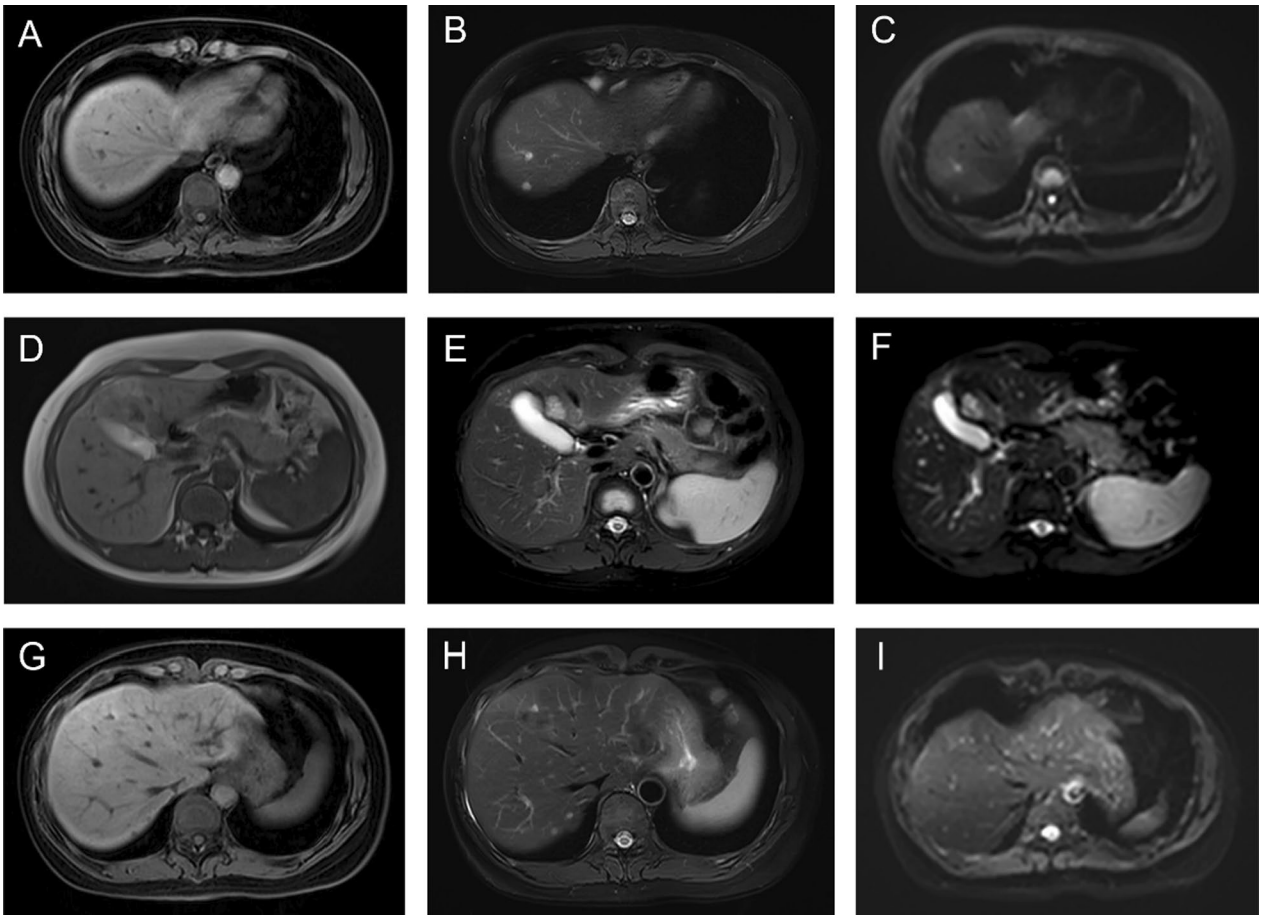

Fig. 7 On magnetic resonance imaging, multiple metastatic lesions were seen in segment VII (**A**–**C**), IV (**D**–**F**), and III (**G**–**I**). **A**–**C** Metastasis masses in segment VII with T1 low (**A**), T2 high (**B**), and diffusion-weighted imaging high (**C**) signal. **D**–**F** A metastasis mass in segment IV with T1 low (**D**), T2 high (**E**), and diffusion-weighted imaging high (**F**) signal. **G**–**I** A metastasis mass in segment III with T1 low (**G**), T2 high (**H**), and diffusion-weighted imaging high (**I**) signal

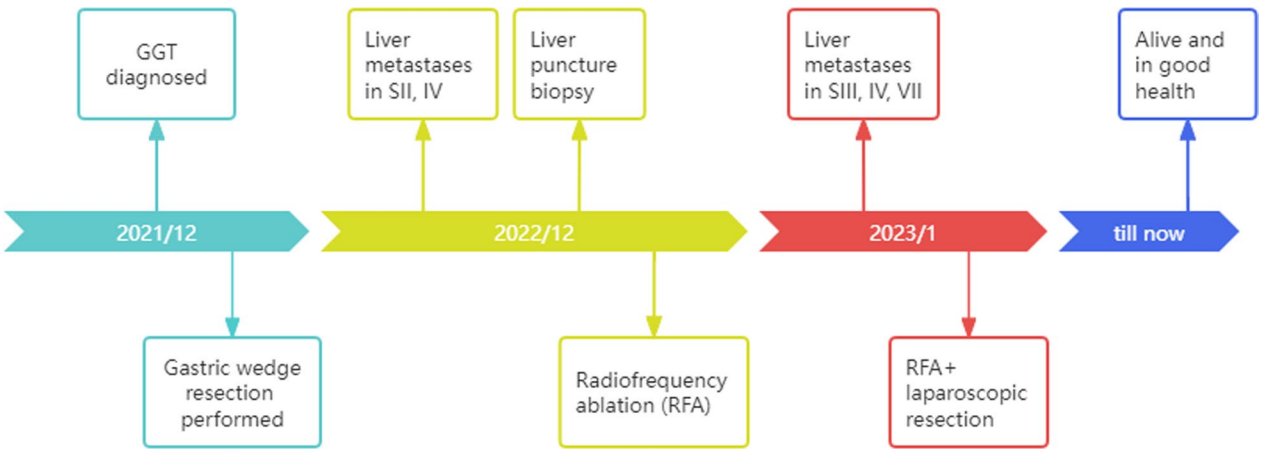

Fig. 8 Main timeline

Table 1 Review of published case reports of gastric malignant glomus tumors with metastases

Case no.	Ref.	Sex	Age (years)	Tumor location	Tumor size (cm)	Metastatic site	Treatment	Diagnosis to death
1	Bray	M	58	Stomach	11	Skin, lung, brain, liver	Subtotal gastrectomy + palliative radiotherapy	Soon
2	Negahi	F	57	Less sac	16	Liver, LN	Surgical resection + chemotherapy	Alive at the time of submitting
3	Song	F	65	Fundus	3	kidney, brain	Wedge resection + palliative radiotherapy	7 months
4	Folpe	M	69	Stomach	8.5	Liver	Unknown	36 months
5	Mettinen	M	69	Antrum	6.5	Liver	Unknown	50 months
6	Lee	F	65	Fundus	3	Kidney, brain	Surgical resection + radiotherapy	8 months
7	Lee	M	63	Antrum	9	Liver	Chemotherapy	Soon
8	Toti	M	72	Greater curvature	6	Liver	Surgical resection + RFA	Alive at the time of submitting
9	Davis	F	46	Body	1	Liver	Surgical resection	Unknown

gastrointestinal tract, there is no recognized standard treatment for GGT with distant metastasis. We suggest that RFA and laparoscopic resection, when necessary, may be effective and minimally invasive tools to control liver metastases of malignant GGT. Targeted therapies based on molecular profiling represent a future direction, necessitating further research.

Acknowledgements
We acknowledge Dr. Vivian Sung for her revision of the language in the article and the support of all personnel in the Department of General Surgery of Ruijin Hospital.

Author contributions
Shining Xu and Teng Xu wrote the main manuscript and contributed equally to this manuscript as first author and co-first author. Yihao Zhi, Chao Wu, and Feng Dong followed the patient and collected the clinical data. Minhua Zheng, Chao Wu, and Feng Dong reviewed the manuscript and are the corresponding authors. All authors contributed to the article and approved the submitted version.

Funding
This study was supported by the National Natural Science Foundation of China (82103356, 82072614) and Hubei Chen Xiaoping Science and Technology Development Foundation (CXPJJH12000001-2020329).

Data availability
The raw data of this article will be made available upon request, without undue reservation.

Declarations

Ethics approval and consent to participate
The study does not need specialized ethic approval. All treatment of this case was followed routine clinical practice and multidisciplinary consultation advice. Written informed consent was obtained before treatment.

Consent for publication
Written informed consent was obtained from the patient's legal guardian for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests
The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Received: 9 May 2024 Accepted: 19 February 2025
Published online: 01 May 2025

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