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Gastric Schwannoma: A Retrospective Analysis Of 21 Cases At A Single Hospital In China

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2. Keywords

Mesenchymal tumor; Schwannoma; Stomach; GIST; Endosonography

1. Abstract

1.1. Background/Objective: Gastric schwannoma is rare benign mesenchymal tumor that is difficult to differentiate from other mesenchymal tumors with malignant potential, such as gastrointestinal stromal tumors (GIST). The aim of this study is to explore the clinicopathologic characteristics and surgical outcomes of gastric schwannomas.

1.2. Methods: The clinical data and follow-up information of 21 gastric schwannoma cases were retrospectively reviewed.

1.3. Results: The 21 patients comprise 12 men and 9 women, with a mean age of 52.0 years (range, 23 to 74). Fourteen patients (66.7%) had no symptoms, and the remaining 7 (33.3%) were symptomatic. The tumor location was the fundus in 3 cases, the body in 14, and the antrum in 4. The mean tumor diameter was 3.6cm, ranging from 2.0cm to 7.5cm, and mucosal ulceration was observed in 1 case (4.8%). The correct preoperative diagnosis was only in one case (4.8%), and the others were preoperatively misdiagnosed as gastric GIST in 13 cases, gastric submucosal mass in 4, gastric neoplasm in 3 and gastric leiomyoma in 1, respectively. All the tumor cells were strongly positive for S-100 protein.

All patients underwent surgical treatment, and the procedures included local excision or wedge resection in 14 cases, and partial gastrectomy in 5, and subtotal gastrectomy in 2. At a median follow-up time of 56 months (range, 6-132 months), all patients were disease free without recurrence or metastases.

1.4. Conclusion: Gastric Schwannoma is often misdiagnosed as gastric GIST before operation, and the long-term outcome is excellent after complete resection.

3. Introduction

Gastric schwannoma is a benign slow-growing neoplasm originating from the nerve plexus of gastric wall [1]. Although it is usually benign, but some gastric schwannoma cases may have malignant potential [1-4]. Gastric schwannoma represents 0.2% of all gastric neoplasms, and it is one of the gastric mesenchymal tumors (mainly spindle cell tumors), which include gastrointestinal stromal tumors (GIST), leiomyoma and leiomyosarcoma [5-9]. Among these tumors, GIST is the most commonly (60-70%) occurring in the stomach [7-9].

To explore the clinicopathologic characteristics, diagnosis, treatment, and prognosis of gastric schwannoma, the data of 21 patients diagnosed with gastric schwannoma were retrospectively collected and analyzed.

4. Methods

4.1. Patient's selection

Twenty-one patients with gastric schwannoma treated at the First Hospital of Wenzhou Medical University between January 1995 and December 2016 were recruited for this study. The admis-

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sion criterion was schwannoma of the stomach confirmed by pathologic examination at our institution. Patient data, including patient demographics, clinical presentation, preoperative imaging evaluation results, histopathology, postoperative complications, and follow-up results, were retrospectively analyzed.

All patients provided written informed consent. The institutional review board and the ethics committee of Wenzhou Medical University deemed that an ethical review was not required for this retrospective analysis.

4.2. Diagnosis of gastric schwannoma

Immunohistochemical study for S-100 protein, CD117, CD34, glial fibrillary acidic protein(GFAP), smooth muscle, actin, neurofilament, desmin, nestin, platelet derived growth factor-alpha (PDGFR-α) and vimentin was carried out.

3.3. Statistical Analysis

Statistical analysis was performed using SPSS version 20.0 software (SPSS Inc., Chicago, IL). Significant differences were evaluated using Fisher exact test for categorical data and Student's t-test for quantitative data. A $P<0.05$ was considered to indicate a statistically significant difference.

5. Results

5.1. Clinical characteristics of patients with gastric schwannoma

The clinical data for the 21 patients with gastric schwannoma are summarized in Table 1. The 21 patients comprise 12 men and 9 women, with a mean age of 52.0 years (range, 23 to 74). Fourteen patients (66.7%) had no symptoms, and their gastric tumors were incidentally detected by routine physical examination and endoscopy in 12 patients and 2 patients discovered during surgery for concomitant diseases. Among the 7 remaining symptomatic patients (33.3%), one patient (4.8%) presented with gastrointestinal bleeding (including melena and hematemesis), other complaints included poor appetite in 2 patients (9.5%) and epigastric pain or discomfort in 4 patients (19.0%). Three patients had concomitant diseases, including gallbladder polyp in one case and giant hepatic cyst in another **(Table 1)**.

Table 1: The clinical data of 21 patients with gastric Schwannoma.

No	Gender/age	Chief presentation	Size(cm)	Location	Preoperative diagnosis	Surgical procedure
1	M/23	asymptomatic	2.5	body	GIST	local excision
2	M/34	asymptomatic	3	fundus	GIST	wedge resection
3	F/44	asymptomatic	3.5	antrum	GIST	local excision
4	M/74	melana	4	body	GIST	local excision
5	F/56	poor appetite	5	body	schwannoma	local excision
6	M/67	asymptomatic	6	body	GIST	partial gastrectomy
7	F/31	epigastric pain	4.5	fundus	GIST	partial gastrectomy
8	F/55	epigastric pain	7.5	body	GIST	subtotal gastrectomy
9	M/48	asymptomatic	7	antrum	GIST	subtotal gastrectomy
10	M/62	epigastric pain	4	body	submucosal mass	wedge resection
11	M/66	asymptomatic	5	antrum	GIST	partial gastrectomy
12	M/72	epigastric pain	3.5	body	submucosal mass	local excision
13	F/73	asymptomatic	2.5	body	GIST	wedge resection
14	F/59	asymptomatic	3	antrum	GIST	local excision
15	M/51	asymptomatic	4	body	GIST	local excision
16	M/32	asymptomatic	3	body	GIST	wedge resection
17	F/44	asymptomatic	5.5	body	GIST	partial gastrectomy
18	F/47	poor appetite	5	body	GIST	partial gastrectomy
19	M/48	asymptomatic	4	fundus	GIST	local excision
20	M/52	asymptomatic	3	body	GIST	local excision
21	F/55	asymptomatic	3. 0	body	GIST	local excision

5.2. Preoperative correct diagnosis

The rate of correct preoperative diagnosis was only in one case (4.8%), and all of the remaining was preoperatively misdiagnosed as gastric gastrointestinal stromal tumor (GIST) or other diseases. Among these patients, the preoperative diagnoses were gastric GIST in 13 cases, gastric submucosal mass in 4 cases, gastric neoplasm in 3 cases and gastric leiomyoma in 1 case.

Endoscopy was performed on all patients at our hospital, with submucosal mass as the main finding. Mucosal ulceration was observed in 1 patient (4.8%). Nineteen patients (90.5%) underwent endoscopic ultrasonography, and typical features were hypoechoic, submucosal masses arising from the proper muscle layer. Moreover, endoscopic biopsy was performed on all patients, but no patient obtained correct diagnosis with normal gastric mucosa before surgery. Only 2 patients underwent endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) biopsy, and one of them was diagnosed as gastric schwannoma.

Computed tomography (CT) was performed for all patients, presented with a homogeneous enhancement pattern, and they included endoluminal type in 10 cases, exogastric type in 8 cases, and intramural type in 3 cases. Tumor markers were examined in 17 patients, and all were negative.

5.3. Histopathological and immunochemical findings

The tumors were located at the fundus in 3 cases, at the body in 14 cases, and at the antrum of the stomach in 4 cases. The mean diameter of the tumor was 4.6cm, ranging from 2.0cm to 7.5cm. Ulceration of the mucosa was observed in 1 case (4.8%).No necrosis, cystic changes, or calcification were detected in any of these tumors.

Histologically, tumors were homogeneous, firm, yellow or gray-white in cut surface without true fibrous capsule on gross examination. Microscopically, the tumors were composed of spindle cells with microtrabecular architecture and focal nuclear atypia, and peritumoral lymphoid cuff. Some of them showed somewhat degenerative changes including cyst formation, calcification, hemorrhage, necrosis and hyalinization. The mitotic rate was <5 mitoses per 50 high power fields in all tumors.

Immunohistochemically, all the tumor cells were strongly positive for S-100 protein. All examined tumors were negative for CD117, DOG-1, smooth muscle actin (SMA), desmin and HMB-45. The Ki-67 index was less than 2% in all patients, indicating a low proliferation rate.

5.4. Surgical treatment

All patients underwent surgical treatment, including laparoscopic resection for 3 patients and open resection for 18. The surgical procedures included local excision or wedge resection in 14 cases, and partial gastrectomy in 5 cases, and subtotal gastrectomy in 2 cases. Four patients underwent additional procedures during the treatment for gastric schwannoma, including laparoscopic and open cholecystectomy in one case each, open fenestration of giant hepatic cyst in 1 case, and laparoscopic appendectomy in 1 case. No postoperative complication occurred after surgery.

5.5. Surgical outcomes

At a median follow-up time of 56 months (range, 6-132 months), all patients had a complete follow-up data, and they were disease free, without recurrence or metastases.

6. Discussion

The mesenchymal tumors of stomach mainly consist of a spectrum of spindle cell tumors, which include gastrointestinal stromal tumors (GISTs), leiomyomas or leiomyosarcomas, and schwannomas[1,5,7,10].Among these neoplasms, GISTs are the most common tumors and account for 60-70% of gastric mesenchymal tumors[6,8,10]. Gastric schwannomas account for only 0.2% of all gastric tumors and 4% of all benign gastric neoplasms [1-4]. It was first described by Daimaru et al. [11] in 1988, also known as neurinoma or neurilemmoma, and is a generally benign, slow-growing, encapsulated nerve-sheath tumor arising from the nerve plexus of gastric wall. Gastric schwannoma can occur at any age but are most frequently noted in fifth and sixth decades with female predominance[2-5].Voltaggio et al. [5] reported gastric schwannomas predominantly occurred in older adults with a marked female predominance (40 women and 11 men; median and mean ages, 60 and 58 years). In this study, there were 12 men and 9 women, with a mean age of 51.3 years (range, 23 to 74). Hou et al. [12] analyzed 33 cases of gastrointestinal schwannomas to elucidate their peculiar clinicopathological, immunohistochemical and ultrastructural features. The patients were 16 men and 17 women, whose ages ranged from 27 to 81 years (median 52.6 years).

Gastric schwannomas variably present with epigastric discomfort and upper gastrointestinal bleeding because of ulceration secondary to the fast growth of submucosal mass, or rarely gastric outlet obstruction secondary to submucosal intra-luminal mass near the pylorus; many are often asymptomatic and discovered incidentally through upper GI endoscopy or imaging study or during laparotomy. If the tumor shows exophytic growth, then the patient may present with a palpable epigastric mass [5-9]. Tao et al. [4] reported that the main complaint of gastric schwannoma patients was epigastric pain or discomfort. Voltaggio et al [5] analyzed clinicopathologically 51 gastric schwannomas, and the symptoms were gastric discomfort, bleeding, or rarely gastric outlet obstruction; many were incidental findings during other medical procedures. In this study, 14 patients (66.7%) had no symptoms, and their gastric tumors were incidentally detected incidentally by routine physical examination and endoscopy in 12 and discovered during surgery for concomitant diseases in 2. The remaining 7 patients (33.3%) were symptomatic, presenting gastrointestinal bleeding in one patient (4.8%), poor appetite in 2 (9.5%) and epigastric pain or discomfort in 4 (19.0%).

6.1. The diagnosis and differential diagnosis

Owing to their typical presentation as submucosal neoplasms, gastric schwannomas and GISTs appear grossly similar[1-4,9,10]. In this study, the rate of correct preoperative diagnosis was seen in only one case (4.8%), and the remaining were misdiagnosed as gastric GIST in 13 cases, gastric submucosal mass in 4 cases, gastric neoplasm in 3 cases and gastric leiomyoma in 1 case. It is similar to the report from Tao K et al [4], whereas the rate of correct preoperative diagnosis was only 3.3%.

The definitive diagnosis of gastric schwannoma is determined by pathologic and immunohistochemical examination of surgical specimens, for example, schwannoma shows strong positive staining for S-100 protein and negative staining for CD117, CD34, desmin, and SMA [1-2,12]. Hou et al. [12] reported that in the immunohistochemical study of gastrointestinal schwannomas, the tumors were strongly positive for S100 protein and vimentin, variably positive for nestin (78.8%, 26/33) and glial fibrillary acidic protein (63.6%, 21/33), but all were negative for CD117, alpha-smooth muscle actin and desmin. In this study, all the tumor cells were strongly positive for S-100 protein, and negative for CD117, DOG-1, smooth muscle actin (SMA), desmin and HMB-45. Moreover, the Ki-67 index was less than 2% in all patients, indicating a low proliferation rate. However, the preoperative differential diagnosis is still challenging. Endoscopy and endoscopic ultrasonography (EUS) are the principal tools used for diagnosis of gastric schwannoma, but it is difficult to make pathologic differential diagnosis of schwannoma from GIST only based on biopsy examination. Recently, endoscopic needle biopsy has been reported to be useful to establish a precise preoperative diagnosis [13]. The others diagnostic modalities include computed tomography (CT) scan, magnetic resonance imaging (MRI), upper gastro intestinal barium study, and positron emission tomography (PET) [14-16]. The features of EUS may be helpful for differentiating gastric schwannomas from other mesenchymal tumors, demonstrated as heterogeneously hypoechoic lesions with decreased echogenicity compared to the normal proper muscle layer [17]. On CT scanning, gastric schwannomas typically manifest as ovoid, well-defined, exophytic, or mixed growth pattern masses, and strong homogeneous enhancement on dynamic CT. On T1 weighted images of MRI, gastric shwannoma have low to medium signal intensity whereas high signal intensity on T2 weighted Images [15-16]. The Definite diagnosis of gastric schwannoma is often established by pathological and immunohistochemical examination of surgically resected specimens. In this study, CT presented with endoluminal type in 10 cases, exogastric type in 8 cases, and intramural type in 3 cases. Kamiyama et al [17] have reported that fluorodeoxyglucose (FDG) uptake and the malignant potential of gastric GIST are strongly correlated. However, increased FDG uptake has also been reported in 3 patients of gastric schwannoma [18-20].The actual mechanism of high F-18 FDG uptake in gastric schwannoma has not yet been clarified in detail and may be related to intracellular glycolytic activity [20]. In this study, no patient underwent PET/CT scan.

Gastric schwannomas are most commonly intramural lesion (65%), followed by intraluminal or subserosal. The tumors arise most commonly from the body of the stomach (50%) followed by the antrum (32%) and the fundus (18%) [7-9]. The typical histologic features of gastric schwannoma are proliferated spindle cells usually arranged in microtrabecular architecture and curling bundles and presence of peritumoral lymphoid cuff. Some of them showed somewhat degenerative changes such as cyst formation, calcification, hemorrhage, necrosis and vascular hyalinization [1-2].

6.2. Treatment and survival

Surgical resection is the first choice of treatment in patients with gastric schwannoma, and the surgical procedures include tumor local extirpation, wedge resection, partial, subtotal or even total gastrectomy, which is decided based on the tumor size, tumor location and adjacent tissues involvement[3-8]. In this study, all patients underwent surgical treatment, including local excision or wedge resection in 14 cases, and partial gastrectomy in 5 cases, and subtotal gastrectomy in 2 cases.

Nowadays laparoscopic techniques have been reported to be feasible and safe treatment with a low recurrence rate [4,21].Voltaggio et al. [13] reported that in 51 cases of gastric schwannoma no malignant variants and recurrences or metastases by long-term follow-up were found. Recently, Cai et al [22] reported that endoscopic resection is safe and effective in treating gastric schwannoma with excellent long-term outcomes. Tao et al.[4] reported that laparoscopic surgery for gastric schwannoma was associated with less blood loss and a shorter postoperative hospital stay than open surgery ($P<0.01$). In this study, 3 patients underwent laparoscopic resection.

Gastric Schwannoma usually carries good prognosis, and rarely recurs after complete surgical resection [1-5]. In this study, all patients were disease free without recurrence or metastases at a median follow-up time of 56 months (range, 6-132 months). Although some gastric schwannomas exceed 10 cm in size, and a minority has mitotic rate >5/50 HPFs, none of these tumors showed evidence for aggressive behavior. However, isolated cases of “malignant schwannomas” have been reported [19-20]. Whether these malignant tumors arising de novo or from be-

nign schwannomas remain controversial. Currently, such malignant tumors with neural differentiation are regarded by most pathologists as distinct from gastrointestinal schwannomas and are termed gastrointestinal autonomic nerve tumors. Hong et al. [3] reviewed 8 studies (total 137 patients) with follow-up data (median follow-up time ranging from 22-132 months across different studies), and no recurrence had been recorded during the follow-up period. Tao et al [4] reported that a total of 28 patients with gastric Schwannoma were disease free without recurrence or metastasis at a median follow-up time of 50 months. Choi et al [22] calculated the growth rate of benign Schwannoma based on CT images of gastric Schwannoma patients with a series of follow-ups. The mean doubling time of Schwannoma was nearly 5 years. Hou et al. [12] reported the follow-up of 23 cases of gastrointestinal schwannomas from 6 months to 13 years showed no recurrences or metastases.

7. Conclusion

gastric schwannoma is often misdiagnosed as gastric GIST before operation, and the long-term outcome is excellent after complete resection.

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