



# Gastrointestinal schwannomas: A case series of 9 patients and literature review

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## ABSTRACT

Gastrointestinal schwannomas are benign, slow-growing, rare tumors comprising 2-6% of all mesenchymal tumors of the gastrointestinal tract and 0.2% of all gastric neoplasms. In the gastrointestinal system, schwannomas are mostly observed in the stomach, followed by the colon and rectum. In this case series, we present the clinicopathological results of 9 cases, along with a literature review. A retrospective analysis was conducted on nine patients diagnosed with gastrointestinal schwannoma in a single institution. Tumors were located in the small intestine and stomach, with an average tumor size of 4.6 cm (range: 1.8-8.5 cm). Diagnoses were incidental in most cases, with only four patients presenting symptoms such as epigastric pain and changes in bowel habits. Histopathological characteristics of tumors were studied. Surgical resection with negative margins was performed in 8 cases. Histopathological analysis confirmed schwannomas characterized by solid, homogeneous, spindle-cell structures without cystic changes or necrosis. Immunohistochemically, all tumors were S-100 positive, with variable expression of other markers. Desmin was negative in seven samples. One gastric schwannoma showed focal smooth muscle actin positivity, while others were negative. The Ki-67 index ranged from 0% to 6%, and c-Kit was negative in all cases. DOG-1 expression was examined in four cases, showing focal positivity in small bowel schwannoma and negativity in three gastric schwannomas. Gastrointestinal schwannomas are predominantly benign tumors, more common in women, and typically occur in the sixth decade of life. While imaging and endoscopic techniques help in diagnosis, definitive diagnosis relies on histopathological analysis. Surgical resection remains the gold standard for treatment.

**Keywords:** Gastric schwannoma, intestinal schwannoma, mesenchymal tumor

## INTRODUCTION

Schwannomas were first described by Verocay in 1910 and examined pathologically by Stout in 1935 (1,2). Gastrointestinal system schwannomas were first described by Daimaru in 1988 as generally benign tumoral structures, different from central nervous system schwannomas (3).

Schwannomas are slow-growing, generally benign tumors arising from Schwann cells in the nerve sheath. The majority of cases are seen in the cranial nerves, with the 8<sup>th</sup> cranial nerve, being the most common. They can also be seen in the peripheral nerves in extremities, the spinal cord, and the central nervous system (4,5). Schwannomas are rarely seen in the gastrointestinal system and constitute about 2-6% of all mesenchymal tumors, including gastric tumors. It constitutes 0.2% of neoplasias and 4% of gastric benign neoplasias (6). In the gastrointestinal system, schwannomas are mostly observed in the stomach at 60%, followed by the colon and rectum at 3% (7,8). Their occurrence within the small intestine and rectum is very rare. Although gastric schwannomas are generally asymptomatic, they can present with epigastric pain, swelling, hemorrhage, changes in bowel habit, or perforation (9-11).

Gastrointestinal tract schwannomas are generally asymptomatic, submucosal structures detected incidentally during laparoscopy, laparotomies, or imaging (6,12). Although computerized tomography (CT) imaging, endoscopy, endoscopic ultrasonography (EUS), colonoscopy, and endoscopic fine needle aspiration biopsy (FNAB) are helpful in the diagnosis of schwannomas, they can be confused with other mesenchymal tumors such as gastrointestinal stromal tumors (GIST), gastrointestinal autonomic nerve tumors (GANT), and leiomyosarcoma, and the

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differential diagnosis is made by postoperative pathological and immunohistochemical examination of the specimen (13).

Gastrointestinal schwannomas are nerve sheath-differentiated tumors that show S100 and glial fibrillary acidic protein (GFAP) positivity (14,15). Gastrointestinal schwannomas are considered largely benign tumoral structures, and the most commonly performed treatment is surgical resection. Cases of local recurrence due to inadequate resection have been reported in the literature (16). Our aim in this study is to examine the clinical, histopathological, and immunohistochemical features of gastrointestinal tract schwannomas in 9 cases observed at our clinic.

### MATERIAL and METHODS

The study included 9 patients who were diagnosed with gastrointestinal schwannoma at a single institution between January 2017 and August 2022. Patient information was collected regarding clinicopathological parameters. Tumor locations were confirmed through an endoscopic examination, chart review. Histologically, tumors were confirmed using parameters like smooth muscle actin (SMA) and desmin. The Ki-67 index was obtained for all patients. The positivity with S100 and c-Kit was also noted.

The study was performed in accordance with the ethics guidelines of the Helsinki Declaration and was approved by the Local Ethics Committee of İstanbul University-Cerrahpaşa (approval number: E-83045809-604.01-978438, date: 03.05.2024). All patients provided written informed consent prior to their inclusion in the study.

### Statistical Analysis

We did not perform any statistical analysis in this study.

### RESULTS

In this study, five male and four female patients were diagnosed with gastrointestinal tract schwannoma. The average age was 63, the youngest patient was 30 years old, and the oldest patient was 88 years old. One tumor was seen in the small intestine (n=1), tumors and 8 tumors were observed in the stomach (n=8). The average tumor size was 4.6 cm, the smallest was 1.8 cm, and the largest was 8.5 cm. Among these 9 cases, 1 was detected in the duodenum, 3 in the gastric antrum, 3 in the gastric fundus, and 2 in the lesser curvature of the stomach.

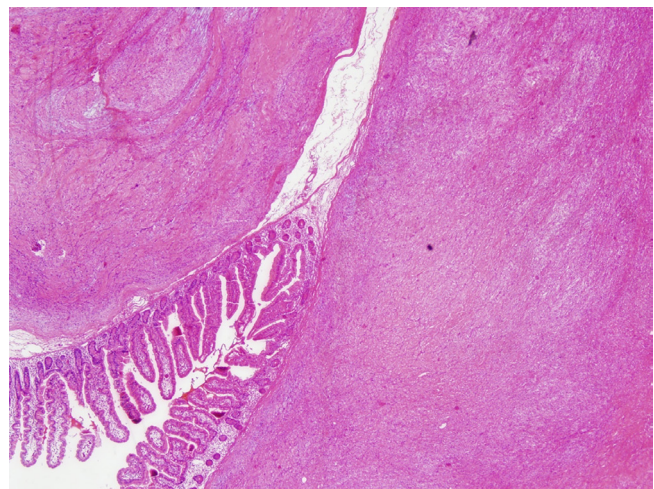
Only 4 of the patients were admitted to the hospital with complaints of epigastric pain radiating to the back, nausea, vomiting, change in bowel habits, and abdominal pain. Of the other five patients, the diagnosis was made incidentally during imaging, endoscopy, and surgery performed for other reasons.

In one of the cases where incidental diagnosis was made, this was achieved via subtotal gastrectomy during a Whipple procedure

for a pancreatic tumor. In another case, the diagnosis was made from a CT taken during the follow-up period for kidney stones. In the other seven cases, the diagnosis was made as a result of endoscopic evaluations performed for follow-up purposes. On CT imaging, schwannomas were observed as round, homogeneous, exophytic lesions with contrast enhancement in the stomach. Upper gastrointestinal endoscopy was performed in 4 of the patients, revealing a submucosal smooth-surfaced exophytic lesion on the stomach wall. For further evaluation, EUS and contrast-enhanced abdominal CT were performed in the cases that revealed hypoechoic heterogeneous submucosal tumors originating from the gastric muscularis propria. Preoperative diagnosis of schwannoma was not made by biopsy in any of the cases.

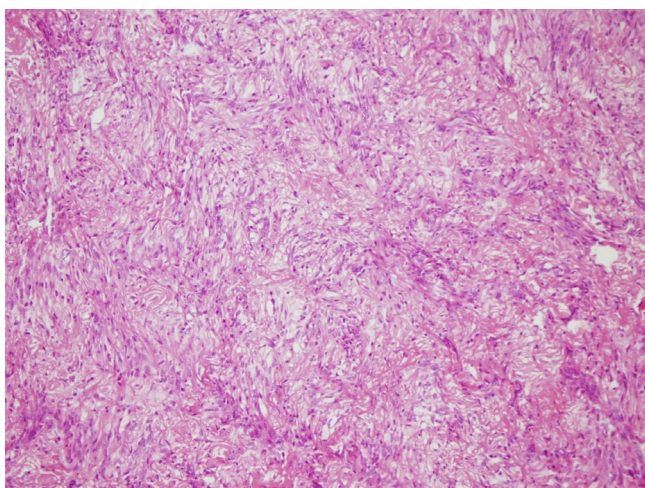
Resection with negative surgical margins was performed in 8 of the cases, and the tumor was found adjacent to the surgical margin in only 1 case. The preliminary diagnosis was pancreatic tumor in 1 patient, GIST in 5 patients, gastrointestinal sarcoma in 1 patient, and desmoid tumor in 1 patient. The Whipple procedure was performed on the patient who was operated on for a pancreatic tumor, and incidental gastric schwannoma was detected in the postoperative subtotal gastrectomy material. Of the remaining gastric schwannoma cases, 5 underwent subtotal gastrectomy, 1 underwent wedge resection, and 1 underwent total gastrectomy. The open technique was used in all cases. In the case of small bowel schwannoma, segmental small bowel resection was performed (Figures 1-4).

While no morbidity or mortality was observed in any case during the first 5 years of postoperative follow-up, 1 patient died in the 7<sup>th</sup> postoperative year. In all cases, the diagnosis of schwannoma was confirmed histopathologically. As a result of pathological examinations, gastrointestinal schwannoma tumors were reported to be solid, homogeneous, dense, and spindle cell

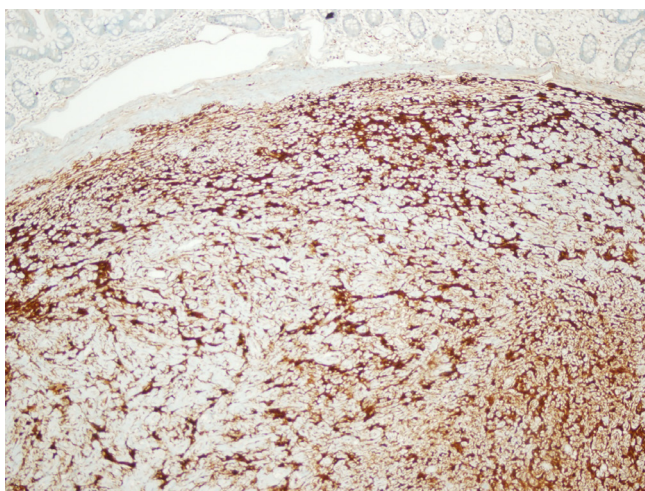


**Figure 1.** Well circumscribed nodular lesion in submucosa of the intestine (hematoxylin and eosin, X40).

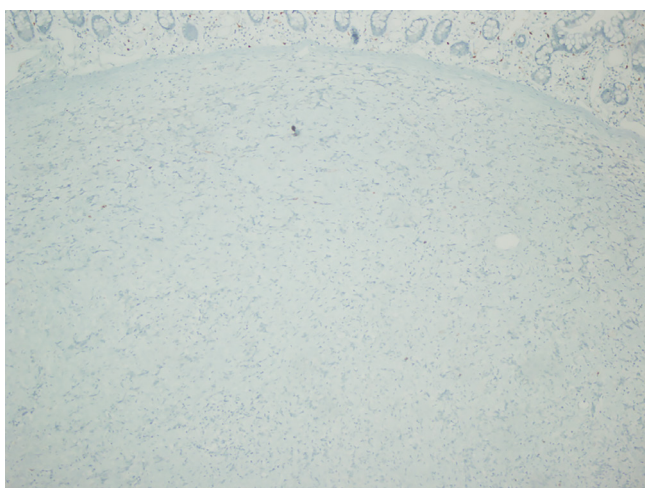




**Figure 2.** Hypercellular areas in schwannoma (Antoni A type) (hematoxylin and eosin, X200).



**Figure 3.** S100 shows strong and diffuse positivity for schwannoma.



**Figure 4.** Tumor cells show negative c-Kit immunohistochemistry (ABC method, X100).

tumors. Cystic change and areas of necrosis were not seen in any of the cases.

The mitotic rate was found to be less than 5/50 in all gastric schwannoma cases. In pathological examination, all samples were found to be positive for S-100 (n=4 samples positive and n=5 samples strongly positive) (Table 1). Desmin was found to be negative in 7 of the samples, and SMA were not observed in both a gastric case nor in the small intestine tumor. While only one gastric schwannoma showed SMA focal positivity, SMA expression was found to be negative in the remaining gastric schwannomas. Ki-67 and c-Kit were studied in all patients except the pancreatic tumor patient who had a Whipple procedure. While the Ki-67 rate of the cases was between 0-6%, c-Kit was reported as negative in all cases. In the study, DOG-1 expression was analyzed in only 4 cases, and was focally positive in small bowel schwannoma and negative in the other 3 gastric schwannoma cases. During the 5-year postoperative follow-up period, no gastrointestinal side effects such as recurrence, weight loss, bloating, and dyspepsia were observed in any patient.

## DISCUSSION

Gastrointestinal schwannomas are slow-growing, mostly asymptomatic gastrointestinal mesenchymal tumors, first identified by Daimaru with S-100 immunohistochemical staining (2). These structures, which have characteristics different from central nervous system schwannomas, constitute 2-6% of mesenchymal tumors of the gastrointestinal tract (16-18). Gastric schwannomas constitute 0.2% of all gastric tumors, 6.3% of gastric mesenchymal tumors and 4% of gastric benign tumors (19,20).

Gastrointestinal schwannomas are a group of non-epithelial tumors that differ from leiomyomas, leiomyosarcomas, GANTs, and GISTs. Although they can originate from different parts of the gastrointestinal system, they are most commonly found in the stomach (60-70%), followed by the colon and are rarely in the small intestine and esophagus (21,22). Gastric schwannomas most commonly arise from the stomach corpus (50%) followed by the gastric antrum (32%) and the gastric fundus (18%). In our study, three of the gastric schwannomas originated from the gastric antrum, three from the fundus, and two from the lesser curvature.

Our study included four male and five female patients who were diagnosed with gastrointestinal tract schwannoma according to the results of postoperative pathological examination. The average age of the patients was determined to be 58.8 years and ranged from 30 to 89 years. These findings correlate with other studies showing that gastrointestinal tract schwannomas are most common in the 5<sup>th</sup> and 6<sup>th</sup> decades of life and are more common in women (11). There are studies in the literature showing that the incidence of intestinal schwannomas is almost

Table 1. Immunohistochemical examinations of all specimens involved						
Patient	Location	SMA	Desmin	Ki-67	S100	c-Kit
1	Duodenum	Negative	-	-	Positive	Negative
2	Antrum	Negative	Negative	3%	Strongly positive	Negative
3	Antrum	Negative	-	0-1%	Positive	Negative
4	Fundus	Negative	Negative	1-3%	Strongly positive	Negative
5	Fundus	Negative	Negative	5%	Strongly positive	Negative
6	Lesser curvature	Negative	Negative	2-3%	Positive	Negative
7	Fundus	Focally positive	Negative	2-3%	Strongly positive	Negative
8	Lesser curvature	Negative	Negative	5%	Strongly positive	Negative
9	Antrum	Negative	Negative	1-2%	Positive	Negative

SMA: Smooth muscle actin.

equal in men and women, and the average patient age is 60-65 years (23).

On CT images, schwannomas are generally seen as hypodense, well-circumscribed, solid structures adjacent to the stomach wall, without cystic change necrosis, calcification, and with homogeneous exophytic or intramural extension as well as spherical, oval, or multilobulated contours. CT scans are helpful in visualizing the location and invasion of the tumor and distinguishing it from GIST. On CT imaging, schwannomas, unlike GISTs, are homogeneous, strong enhancing lesions that do not show hemorrhage, necrosis, cystic change, or calcification (24). Also, since the preoperative differential diagnosis often includes GIST, biopsy is sometimes contraindicated in suspected GIST due to risks such as capsular rupture or peritoneal seeding.

During endoscopy, they are generally seen as elevated submucosal lesions, and a central ulcer is observed in about 25-50% of the cases (25). In 4 of the 9 in our series, a submucosal smooth-surfaced, exophytic lesion was observed on the stomach wall during endoscopy. While EUS-guided FNAB is helpful in the diagnosis of submucosal schwannomas in the upper gastrointestinal tract, it is not definitive in the diagnosis of deeper-seated lesions.

Gastrointestinal schwannoma cells usually show S-100 protein and GFAP positivity. They originate from the submucosally located myenteric plexus (Auerbach's plexus) of the gastrointestinal tract and, to a lesser extent, from the Meissner plexus (26). Macroscopically, schwannomas are round, fusiform, grey-white structures with well-defined borders. Although microscopically gastrointestinal schwannomas are generally well-circumscribed, unlike other schwannomas, they are not encapsulated or surrounded by epineurium. Nuclear palisading, xanthoma cells, vascular hyalinization, and dilatation seen in other soft tissue schwannomas are not observed in gastric schwannomas (27). In our study, the histopathological diagnosis of schwannoma was accepted in all cases, and similar to previous studies, microscopic

pathological examination revealed that the schwannomas had a solid, homogeneous structure, and a structure consisting of spindle cells. While no area of necrosis was observed in any of the specimens, the submucosa, the muscularis propria, and subserosal involvement were generally observed. While cytological atypia was observed in 3 cases, ulceration, bleeding, or perforation was not observed in any of them. Since gastric schwannomas rarely exhibit malignant properties, tumor size and mitotic activity are not of great importance in terms of prognosis. In our study, the average tumor size was determined to be 4.6 cm, with a range of (range 2.5 cm-8.5 cm).

The immunohistochemical pattern of schwannomas is important in distinguishing them from other GI mesenchymal neoplasias. Vimentin, GFAP, and S100 proteins are known to be expressed by gastrointestinal schwannoma cells. In various studies, S100 positivity and CD34 positivity were observed in gastric schwannomas, whereas CD117, SMA, actin, HHF35, melan A, HMB45 and desmin were typically negative (27-29). GIST is typically positive for CD34 and CD117 (30,31). In our study, while immunohistochemical examinations of all specimens showed strong positivity for S100, no immune reactivity was detected for DOG1, c-Kit (CD117), CD34, desmin, and SMA.

The incidence rate of gastrointestinal schwannomas is approximately one per 45 in comparison to GISTs (27). While GISTs, appear heterogeneous on CT due to the presence of necrosis, hemorrhage, and cystic degenerative changes, schwannomas appear homogeneous on CT. In these cases, immunohistochemistry is extremely important for differential diagnosis. GISTs are macroscopically distinguished from the yellow and white structure of gastric schwannomas by their pink-hemorrhagic structure.

Another differential diagnosis of gastrointestinal schwannoma is primary and secondary lymphomas due to the similarity in CT images. The presence of adenopathy in the surrounding tissue on imaging distinguishes lymphoma from gastrointestinal

schwannoma. Other entities in the differential diagnosis are sarcomas, metastatic melanomas, and gastrointestinal adenocarcinomas.

Studies have shown that most gastrointestinal schwannomas are benign. In this respect, it is important to distinguish them from GISTs, which show malignant features in 10-30%, and GANTs, which have a recurrence and metastasis rate of more than 55% (32-34). There are also a few very rare cases of malignant schwannoma in children reported in the literature (35). Studies have shown that the standard treatment for benign schwannomas is surgical resection with negative margins and that there is no need for radical surgeries or extended resections. Radical surgery is typically the management of choice for malignant schwannomas, and the role of chemoradiotherapy in treatment is unclear (36). No malignancy was observed in our study. Total resection was considered the primary treatment method in these cases due to the > uncertainty of the preoperative diagnosis, and long-term results were favorable.

## CONCLUSION

Gastric schwannomas, different from soft tissue and central nervous system schwannomas, are rare, slow-growing, usually asymptomatic, originate from neuronal Schwann cells, and are tumors that are generally benign, more common in women, and in the 6<sup>th</sup> decade. Radiological imaging, EUS, and endoscopic FNAB help in the diagnosis, and the definitive diagnosis can be made after postoperative immunohistochemistry and histopathological examinations. The treatment of choice is complete surgical resection, since it is mostly benign except for a few reported cases.

## Ethics

**Informed Consent:** All patients provided written informed consent prior to their inclusion in the study.

## Footnotes

### Author Contributions

Concept - S.S.U., E.E.; Design - S.S.U., E.E.; Data Collection or Processing - S.S.U., E.E., N.G.; Analysis or Interpretation - S.S.U., E.E., Ş.B.; Literature Search - E.E., N.G., Z.Ö., N.K., Ş.B.; Writing - E.E., N.G., Z.Ö., N.K., Ş.B.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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