Upper Gastrointestinal Tract Schwannomas- Report of Three Cases and Literature Review

Kamran Mushtaq*, Manik Sharma, Muhammad ElBadri, Arsalan Ahmad and Saad Al Kaabi

Department of Gastroenterology, Hamad General Hospital, Doha, Qatar

*Corresponding Author: Kamran Mushtaq, Department of Gastroenterology, Hamad Medical Corporation, Doha, Qatar.

Received: March 23, 2021; Published: April 15, 2021

DOI: 10.31080/ecgds.2021.08.00750

Abstract

Background: Schwannoma is a benign mesenchymal tumor arising from peripheral nerve sheath. Schwannoma can occur sporadically or as a part of hereditary syndromes like Neurofibromatosis. Schwannomas are rare tumors in the gastrointestinal tract, the stomach being the most common site. Esophageal Schwannoma is even rarer, with fewer than 90 cases reported.

Methods: We report 3 cases of upper GI schwannomas (Gastric-2 Esophageal-1). The average age of detection was 36 years, and two of them were males. The average size of the tumor at detection was about 2.5 cm. Two of them required laparoscopic resection, and one of them was treated endoscopically. Histopathology revealed strong S-100 positivity on immunohistochemistry, and all of them were of benign nature.

Conclusion: Schwannomas are clinically, endoscopically and radiologically difficult to distinguish from gastrointestinal stromal tumors (GIST). Distinguishing Schwannoma from GIST is important as the latter has malignant potential. Schwannomas have a good prognosis with an extremely low recurrence rate.

Keywords: Gastric Schwannoma; Esophageal Schwannoma; GIST; Submucosal Tumors; Endoscopic Ultrasound

Introduction

Schwannoma is a type of mesenchymal tumor arising from the peripheral nerve sheath. It can occur as a solitary lesion or multiple lesions as a part of a syndrome like Neurofibromatosis [1]. They are rare in the gastrointestinal tract, with the stomach being the most common site, followed by the colon and rectum [2]. Schwannomas arise from the submucosa and comprise less than 1 percent of the stomach’s submucosal tumors and 0.2% of all the Gastric tumors [3]. Esophageal schwannomas are extremely rare benign tumors of the esophagus, with fewer than 90 cases reported. We report clinical and pathologic characteristics of three cases of schwannomas, two in the stomach and one in the esophagus, along with a relevant literature review.

Case Reports

Case 1

A 38-year-old female presented with complaints of generalized fatigability, epigastric pain for one month, and melena for eight days. Physical examination was remarkable only for mild epigastric tenderness. Initial labs revealed microcytic hypochromic anemia with
hemoglobin of 11 g/L. The abdomen’s ultrasound scan revealed an epigastric cystic structure with solid components measuring 37 X 33 mm with no clear connection to the adjacent left lobe of the liver. A contrast-enhanced Computed tomography (CT) of the abdomen revealed a well-defined rounded hypoechoic mass attached to the stomach wall's lesser curvature (exophytic) measuring 3.1 x 3.5 cm with a density of 35 HU and showing faint post-contrast enhancement. Gastroscopy revealed submucosal mass lesion over lesser curvature with otherwise normal endoscopy until the Second part of the duodenum (Figure 1A). Endosonography (EUS) revealed a 3.6 x 3.4 cm predominantly hypoechoic mass with central areas of necrosis on the lesser curvature in the body of the stomach. The mass was submucosal and had a large exophytic component. The mass did not breach the muscularis propria, and no adjacent lymph nodes were seen (Figure 1B). The patient underwent laparoscopic wedge resection of the submucosal gastric lesion with clear margins.

Histopathologic examination showed a partially encapsulated submucosal neoplasm of spindle cells with benign nuclear features and focal areas of mild nuclear hyperchromasia and mild nuclear enlargement arranged in short fascicles in a collagenous stroma reminiscent of Antoni A areas. Focal short, tongue-shaped extensions into the superficial muscularis propria were noted. Mitotic figures were 0-1 per high-power field (Figure 1C). The neoplasm was strongly positive for S100 with non-neural cell positivity for SMA while negative for CD 117, DOG1, and CD34 with a Ki-67 index of 3 - 5%. A final diagnosis of Benign Peripheral nerve sheath tumor, consistent with schwannoma, was made (Figure 1D). At 12 months follow-up, the patient is asymptomatic with no disease recurrence.

**Case 2**

A 36-year-old male patient with a past medical history significant for Squamous cell cancer of the Tongue (T1N0M0) who underwent wide local excision and sentinel lymph node dissection was on regular follow-up with Oncologist. The six-month later patient had a follow-up PET CT scan which revealed an intense uptake near the gastric wall (Figure 2, SUV max 8.9) and was referred for gastroscopy.

---

The patient underwent gastroscopy and a linear EUS examination. Endoscopy revealed a submucosal bulge at the incisura (Figure 3A). EUS revealed a 3 x 3 cm hypoechoic lesion wedged between the lesser curvature of the stomach and liver. The lesion was well circumscribed and was in proximity to the liver (Figure 3B). EUS guided FNA of the lesion was done, and histopathology revealed spindle cells’ presence (Figure 3C). The patient underwent laparoscopic resection of the gastric mass. Immunohistochemistry revealed strong S-100 positivity (Figure 3D). The remaining stains, including DOG1, CD117, CD34, SMA, Desmin, HMB45, were all negative. Ki 67 index was < 1%. At 18 months of follow up patient has no evidence of recurrent disease.

**Figure 2:** PET CT scan with a coronal plan showing increased uptake in the stomach next to the left lobe of the liver (white arrow).

**Figure 3:** 3A: Gastroscopy showing submucosal bulge at the antrum of the stomach. 3B: Endoscopic Ultrasound showing hypoechoic lesion (white arrow). 3C: Hematoxylin and Eosin stained Photomicrograph showing the hypercellular area (Antoni A); occasional Palisading Verocay bodies can be identified. 3D: S-100 stain showing strong positivity.
Case 3

A 33-year-old male presented with symptoms of epigastric pain and dyspepsia for more than six months with no dysphagia or any other alarm symptoms. Upper GI endoscopy revealed a large polypoidal structure in the distal esophagus 3 cm above GE junction (Figure 4A). EUS revealed one x1.3 cm sized lesion without any deeper invasion into the submucosa with a large hiatal hernia (Figure 4B). Polypectomy was performed using the hot snare cautery technique.

Histopathological revealed a polypoid fragment of esophageal mucosa containing a non-encapsulated well-defined multinodular submucosal spindle cell neoplasm comprising spindle cells with abundant eosinophilic cytoplasm and vesicular nuclei with myxoid areas. Some of the nodules contain epithelioid cells with pseudo glandular and signet ring-like microcystic appearances (Figure 4C). No necrosis or significant mitotic activity is seen. The spindle cells were diffusely positive with S-100, CD34, CD56, and NSE (Figure 4D). There was no expression of CD117, DOG1, SMA, Desmin. The proliferation fraction (Ki67) was less than 1%. He was diagnosed with a microcystic variant of esophageal schwannoma. The patient is asymptomatic with no evidence of recurrent disease at 22 months follow-up. Summary of the clinical characteristics and immunohistochemistry markers of three cases are presented in table 1 and 2, respectively.

Figure 5: 4A: Endoscopic view showing esophageal polyp. 4B: Endoscopic ultrasound showing a small hypoechoic lesion (white arrow). 4C: Hematoxylin and Eosin stained Photomicrograph showing proliferative whorls. 4D: S-100 stain again showing very strong positivity.
Discussion

Schwannomas are rare mesenchymal tumors that arise from the Schwann cells of the peripheral nerve sheath of the Auerbach plexus or Myenteric plexus in the muscularis propria layer of the esophagus and stomach. The prevalence estimate is less than 0.4% of all gastric and 3% of mesenchymal tumors of the stomach [4]. The esophageal schwannomas are even rarer with few case reports.

The most common site of schwannoma in the gastrointestinal tract is the stomach. Gastric schwannomas (GS) are generally submucosal, discovered as an incidental finding, and are asymptomatic during diagnostic workup for something else [6]. When symptomatic, they commonly present with Epigastric pain, upper GI bleeding, or epigastric mass [7]. Gastric schwannomas are tumors with female predominance, and the ratio described in the biggest case series is 1:4 but is variable in other series. It predominantly occurs in the fourth to sixth decade of life [7].

Esophageal schwannoma comprises a very small percentage of benign tumors of the esophagus. Most cases reported are from Asia. They are also predominantly seen in females of the middle age group. The most common site for esophageal schwannoma is the upper and middle esophagus. The commonest presentation is dysphagia and occasionally is longstanding before further investigations are taken. Other presentations include dyspnea, cough, chest pain, neck mass, polyp or large mediastinal mass on radiologic imaging [8].

The sporadic schwannoma’s exact pathogenesis is still not clear; but there is evidence suggesting that loss of expression of a tumor suppressor protein merlin, also called neurofibromin or schwannomin, plays a key role in pathogenesis [9]. The characteristic histopathologic findings of schwannoma include a well-formed collagenous capsule and hyalinized vessels. The cells may be arranged in Antoni A tissue area, which is highly cellular and shows nuclear palisading along with Verocay bodies, and Antoni B tissue area, which is loosely arranged cystic myxomatous changes representing Degenerated Antoni A area [1,10]. The exact diagnosis, however, is made by the diffuse and strong expression of S100 on immunohistochemistry. Vimentin is positive in most cases. A subset of Schwannoma also expresses Glial

### Table 1: Clinical summary of the three cases of upper GI Schwannomas.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age/Gender</th>
<th>Clinical Presentation</th>
<th>Site and size (cm)</th>
<th>Diagnostics</th>
<th>Treatment</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>38-year-old Female</td>
<td>Epigastric pain, fatigue.</td>
<td>Lesser curvature stomach 4.2 x 4 x 2.3</td>
<td>EUS, CT Abdomen, Biopsy.</td>
<td>Laparoscopic partial wedge resection.</td>
<td>30 months</td>
</tr>
<tr>
<td>2</td>
<td>36-year-old Male</td>
<td>Asymptomatic, Whole-body PET-CT scan showing high uptake in the stomach.</td>
<td>Stomach lesser curvature, 2.8 x 2.5 x 2.3</td>
<td>PET-CT, EUS, Biopsy.</td>
<td>Laparoscopic resection</td>
<td>24 months</td>
</tr>
<tr>
<td>3</td>
<td>33-year-old Male</td>
<td>Epigastric pain.</td>
<td>Lower esophagus 1.5 x 1.3 x 0.8</td>
<td>EUS. Biopsy.</td>
<td>Endoscopic polypectomy</td>
<td>22 months</td>
</tr>
</tbody>
</table>

### Table 2: Immunohistochemistry characteristics of the 3 cases.

<table>
<thead>
<tr>
<th>Stain</th>
<th>S-100</th>
<th>Desmin</th>
<th>DOG-1</th>
<th>SMA</th>
<th>CD 117</th>
<th>CD 34</th>
<th>KI-67</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>3 - 5%</td>
</tr>
<tr>
<td>Case 2</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>&lt; 1%</td>
</tr>
<tr>
<td>Case 3</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>&lt; 1%</td>
</tr>
</tbody>
</table>

fibrillary acid protein (GFAP). The markers for other mesenchymal tumors are negative. The smooth muscle actin SMA, Desmin are markers for leiomyoma and leiomyosarcoma, while CD117, DOG-1 are the markers for GIST [11]. These findings were consistent in our cases. The characteristic microcystic pattern seen in our case of esophageal schwannoma is extremely rare, with only one more case reported [12].

The major differential diagnosis of the upper GI tract's schwannoma is GIST, which comprises 80 percent of all the mesenchymal tumors of GIT. Identification of GIST is important due to the potential of malignancy in these tumors. GIST comprises 2.2% of all the malignant gastric tumors, and the benign GISTs with high-risk features are the reason also need to be treated in time [13].

Multiple modalities play an important role in the diagnosis of submucosal lesions of the Upper GI tract like EUS, CT, MRI and PET-CT scan. But none of these investigations can clearly diagnose a schwannoma. Confirmation of the diagnosis is only achieved by histopathology with immunohistochemistry. PET-CT has a limited diagnostic value pre-operatively in differentiating GS and GIST but can distinguish reliably between benign and malignant peripheral nerve sheath tumors as studied by Benz., et al. [14]. Our second case demonstrated that FDG uptake on PET CT scan could precede a clinical presentation of a schwannoma that signifies a PET CT scan’s good sensitivity. The most important diagnostic tool for submucosal tumors is Endoscopic ultrasound (EUS). Though no EUS feature is specific to Gastric or esophageal Schwannoma, the echogenicity compared to the muscularis propria layer can help differentiate Schwannoma and GIST [15,16].

As preoperative diagnosis of schwannoma is often difficult to achieve, the most common approach is to remove the lesion completely with a free margin. The treatment of choice is complete surgical resection with organ preservation as much as possible [8]. For gastric schwannomas, various approaches can be used, including Laparoscopic or open surgery. When compared to open surgery, the Laparoscopic approach was associated with short postoperative hospital stay and less blood loss [17]. Surgical resection depends on the site and size of the lesions and various case series showed that partial or complete wedge resection and partial gastrectomy have all been effective.

or large esophageal schwannoma, an open surgical approach is often employed, but with smaller size tumors, a minimally invasive or endoscopic approach can be used. The endoscopic approach will depend on the type of lesion and the experience of the operator. In our case patient had a medium-sized polyp with stalk; hence endoscopic approach was used without any complications. Endoscopic resection of esophageal schwannoma has been attempted before in a similar scenario [18]. In cases of very large esophageal schwannomas, esophagectomy may be required. The chances of recurrence after complete resection is very low, and the prognosis is good.

The potential for malignant transformation of benign esophageal or gastric schwannoma is extremely low, and no case has been reported to date [19]. The prognosis post-surgical resection is excellent, and to date, we haven’t encountered any case in the literature of recurrence of benign gastric schwannoma after complete margin-free resection [17]. Patients had been disease-free in this case series of mean follow up of 56 months. Malignant Gastric schwannoma itself is extremely rare, and very few cases have been reported. Most of them presented with Upper GI bleeding [20]. There are no characteristic features of malignant schwannoma, and differentiation from benign Schwannoma is primarily based on histology. The most reliable feature suggestive of malignant schwannoma is mitotic features of more than 5 on 50 high power fields [21].

Conclusion

Schwannomas are one of the rare mesenchymal tumors of the gastrointestinal tract. They are difficult to diagnose on clinical characteristics and radiologic imaging. It is important to differentiate them from GISTs as the latter has malignant potential. There are several features on EUS which may differentiate between GIST and schwannomas, but ultimate differentiation and diagnosis are based on histopathology and subsequent immunohistochemistry. The treatment is complete resection surgically or endoscopically. Prognosis of schwannomas overall is excellent, with a very low risk of recurrence.
Upper Gastrointestinal Tract Schwannomas- Report of Three Cases and Literature Review

Bibliography


