From Dyspepsia to Diagnosis: A Rare Gastric Subepithelial Lesion Definitively Diagnosed via Endoscopic Submucosal Dissection and Immunohistochemistry

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ABSTRACT

Introduction: Peripheral nerve sheath tumors, known as perineuriomas, are typically found on the trunk and extremities. They are less commonly described in the gastrointestinal tract (GI), and extremely rarely are described in the stomach.

Case Presentation: We present a case of a 2-cm gastric perineurioma in a 42-year-old patient with nonspecific GI complaints of chronic dyspepsia and epigastric discomfort. Esophagogastroduodenoscopy, followed by endoscopic ultrasound, revealed a 2-cm umbilicated lesion in the stomach, which was subsequently removed with endoscopic submucosal dissection and sent for pathology. Immunohistochemical staining revealed a rare entity known as a gastric perineurioma.

Conclusion: Since the first case of gastric perineurioma was first described in 2004, there have only been 4 reported cases in the English literature. This case highlights the crucial interdisciplinary multidisciplinary effort between pathologists and GI specialists required to reach this diagnosis and showcases endoscopic diagnosis using endoscopic dissection, which allows for complete lesion resection and complete resolution of the patient’s symptoms.

INTRODUCTION

Perineuriomas are peripheral nerve sheath proliferation tumors of mesenchymal and spindle cells. These are typically found in the trunk and extremities, and classified into intraneural and extraneural variants. The intraneural variant often involves the sciatic nerve or branches.1 Although most perineuriomas follow a benign course, because of their rare malignant potential, these tumors are usually resected for cure.1 They are less commonly seen in the gastrointestinal (GI) tract, with a predilection for the rectosigmoid colon (75%) in 1 small study of 8 intestinal perineuriomas.2 For unclear reasons, gastric perineuriomas are very rare, with only 4 reported cases since the first description in 2004.3 Here, we present a 2-cm gastric perineurioma in a 42-year-old female with chronic dyspepsia and epigastric discomfort.

Case Report

A 42-year-old female was referred to the gastroenterology department with chronic dyspepsia and epigastric discomfort for 4 years that persisted despite daily omeprazole and sucralfate. Because of the duration of symptoms, an esophagogastroduodenoscopy was performed, which revealed a 2-cm umbilicated mass in the gastric body. Endoscopic biopsies were nondiagnostic; thus, the patient was referred for an endoscopic ultrasound for further characterization. The lesion was hypoechoic and contiguous with the second echolayer (muscularis mucosa) (Figure 1). To confirm the clinical suspicion for gastrointestinal stromal tumor (GIST), a fine needle aspiration was performed, during which “gelatinous” material was aspirated. However, immunohistochemical (IHC) stains of the sample showed no definitive pattern of staining. Given the patient’s favorable health status and her desire for definitive diagnosis, the patient was referred to our center for a repeat endoscopic ultrasound and consideration of en bloc removal via endoscopic submucosal dissection (ESD). The lesion was again confirmed to involve the second and third echolayers (muscularis mucosa/submucosa). The fourth echolayer (muscularis propria) was intact. Despite the central ulceration and intense submucosal fibrosis, the lesion was successfully removed en bloc via hybrid ESD.

The microscopic examination showed a polyloid spindle cell lesion with prominent mucosal and submucosal involvement as well as ulceration of the overlying gastric mucosa. Histologic sections demonstrated a cellular proliferation of elongated spindle cells arranged in short interlacing fascicles within loose collagenous and myxoid stroma (Figure 2). IHC stains for CD117, DOG1, and CD34 were negative, thus arguing against a GIST. Additional stains for smooth muscle antigen, desmin, and pancytokeratin were negative, excluding a smooth muscle tumor and carcinoma. Last, S100 was negative, helping to exclude a neural tumor such as gastric schwannoma.

Because of the initial difficulty in rendering a pathologic diagnosis, this was sent to our regional bone and soft tissue pathology expert for consultation and additional IHC stains. Positive stains included NKIC3, CD56, epithelial

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membrane antigen (EMA), and glucose transporter protein (GLUT-1) (Figures 3, 4). This pattern of IHC staining most definitively classifies the lesion as gastric perineurioma.

Three months after removal of the perineurioma, the patient reported complete resolution of her dyspepsia and epigastric discomfort.

CONCLUSION
Mesenchymal/spindle cell proliferations comprise a class of gastrointestinal tumors, including GIST, neural tumors, and schwannomas. Because of the variety of clinical presentations associated with these tumors, diagnosis is challenging. Perineuriomas,
From Dyspepsia to Diagnosis: A Rare Gastric Subepithelial Lesion Definitely Diagnosed via Endoscopic Submucosal Dissection and Immunohistochemistry

<table>
<thead>
<tr>
<th>Date</th>
<th>Summaries from initial and follow-up visit</th>
<th>Diagnostic testing (including dates)</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/15/2015</td>
<td>Patient complained of epigastric pain, waxing and waning, worse after eating at times. Sometimes worse at night. Took Tums and Prilosec with minimal relief.</td>
<td>CBC, electrolytes, BUN, creatinine, UA, UCx, pregnancy test, liver function panel, lipase, <em>Helicobacter pylori</em> (1/15/2015): No significant findings.</td>
<td>Patient told to increased omeprazole to twice daily; added Carafate daily; ciprofloxacin prescribed.</td>
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<tr>
<td>2/6/2019</td>
<td>Patient reported stomach pain with severe flare up despite Carafate and Prilosec.</td>
<td>None</td>
<td>Referral to gastroenterology for EGD.</td>
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<tr>
<td>2/13/2019</td>
<td>Patient presented for EGD.</td>
<td>EGD findings: 8-mm nodule in antrum; 2-cm gastric body mass Pathology: negative. (2/13/2019)</td>
<td>Patient instructed to hold NSAIDs, aspirin. Continue Carafate and omeprazole twice daily. Referred for EUS of subepithelial gastric lesion.</td>
</tr>
<tr>
<td>2/19/2019</td>
<td>Patient presented for EUS.</td>
<td>EUS findings: Subepithelial distal gastric lesion measuring 12 × 15 mm arising from the muscularis mucosa going into the submucosa. Fine needle aspiration of lesion performed and sent for cytology. Fine needle aspiration cytology: spindle and epithelioid cell lesion (2/19/2019)</td>
<td>Referred for endoscopic resection via endoscopic mucosal resection or ESD.</td>
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<tr>
<td>3/9/2019</td>
<td>Patient presented with flare up of abdominal pain at night. Had been off Prilosec for 8-9 days because it was not helping.</td>
<td>None</td>
<td>Continue Prilosec and Carafate.</td>
</tr>
<tr>
<td>3/18/2019</td>
<td>Patient presented for official gastrointestinal consultation. Describes reflux sensation with partial relief with omeprazole twice daily and Carafate. Symptoms both during the day and night.</td>
<td>None</td>
<td>Patient told pathology came back inconclusive. Patient already referred for EUS with ESD. Patient instructed to continue Prilosec, Carafate. Avoid late night eating.</td>
</tr>
<tr>
<td>5/6/2019</td>
<td>Patient presented for EUS with ESD.</td>
<td>EUS findings: gastric body subepithelial lesion of 2 × 0.7 cm in 1 echoplane, contiguous with second echolayer. Antral subepithelial lesion of 0.7 × 0.5 cm in 1 echoplane, contiguous with second layer. ESD: 2 cm gastric body lesion resected via challenging ESD due to intense submucosal fibrosis.</td>
<td>Patient admitted for overnight observation. Start clear liquid diet. Intravenous proton pump inhibitor prescribed for 14 days. Pathology sent immediately.</td>
</tr>
<tr>
<td>8/12/2019</td>
<td>Patient reports resolution of symptoms via telephone appointment.</td>
<td>None</td>
<td>Patient instructed to wean off omeprazole completely.</td>
</tr>
</tbody>
</table>

Table 1. From dyspepsia to diagnosis: a rare gastric subepithelial lesion definitely diagnosed via endoscopic submucosal dissection and immunohistochemistry

Relevant medical history and interventions (migraines, obesity, acne, gastroesophageal reflux disease)

- a rare subset of mesenchymal cell proliferations, can be found both intra- and extraneurally. When found extra-neurally, they are more often painless, soft-tissue lesions found the in the trunk and extremities, though some cases have been noted in the head and neck area, retroperitoneum, brain, kidney, and intestines. In the English literature, a total of 4 patients with gastric perineuriomas have been described. Because of the paucity of reported cases, gastric perineuriomas are underrecognized culprits for nonspecific gastrointestinal symptoms, and have occasionally even been misdiagnosed as a GIST. In the 4 previously reported cases, patients experienced protean complaints either singly or in combination, including epigastric pain, nausea, gastroesophageal reflux, or upper gastrointestinal bleeding. For unclear reasons, gastric perineuriomas have been described more often in women (4/5 cases including present case), with a wide range in size (0.5-1.5 cm) and age of diagnosis (25-58 years). IHC stains are critical to the proper diagnosis of perineuriomas. Typically, at least 1 perineural marker will stain positive, such as EMA, GLUT-1, and claudin-1. Expression of these markers ranged from variable and weak, to strong and diffuse. EMA was positive in 50% of gastric perineuriomas. More prominent expression was noted in those specimens stained for GLUT-1 (n = 2). Claudin-1 was positive in 15/17 intestinal perineuriomas and 1 gastric perineurioma stained for this marker. CD34 expressivity was widely variable. Adequate tissue sampling is often mandatory for proper pathologic and IHC diagnosis. In this case, an en bloc ESD removal not only secured a diagnosis (where fine needle aspiration could not), but also it allowed for confirmation of complete removal (negative lateral and deep margins) and
offered the patient a definitive cure (complete resolution of symptoms after removal).

As with previously reported cases, our female patient also experienced protean GI complaints including epigastric pain and gastroesophageal reflux disease. Our present case appears to describe the largest described gastric perineurioma (2 cm).

This case highlights the value of an esophagogastroduodenoscopy to evaluate patients with persistent upper GI symptoms. We not only highlight the crucial multidisciplinary effort between pathologists and GI specialists required to reach this diagnosis, but also showcase endoscopic diagnosis using ESD, which allows for complete lesion resection and, in this case, complete resolution of symptoms.

BUN = blood urea nitrogen; CBC = complete blood count; EGD = esophagogastroduodenoscopy; ESD = endoscopic submucosal dissection; EUS = endoscopic ultrasound; NSAID = nonsteroidal anti-inflammatory drug; UA = urinalysis; UCx = urine culture.

### Disclosure Statement

The author(s) have no conflicts of interest to disclose.

### How to Cite this Article


### References