Multifocal Synchronous Granular Cell Tumors of the Gastrointestinal Tract

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Abstract
Granular cell tumors (GCT) are rare and unusual tumors, which are usually benign and asymptomatic. Only 5–10% of cases involve the gastrointestinal tract, most commonly as singular, non-cancerous lesions in the esophagus. We report a rare case of symptomatic, multifocal, synchronous GCT involving the esophagus, stomach, and cecum.

Introduction
Granular cell tumors (GCT) are rare and unusual tumors, which are usually benign and asymptomatic. They were first described by Abrikossoff in 1926 as a lesion on the tongue.¹ Although GCT can occur virtually anywhere in the body, nearly half of reported cases involve the head and neck, and approximately 5–10% involve the gastrointestinal (GI) tract,²,³ most commonly as singular lesions found incidentally in the esophagus.⁴,⁵ In unusual cases where symptoms do occur, dysphagia and chest pain are the most commonly described complaints. GCTs are typically non-cancerous, but have malignant potential, and typically recur due to incomplete excision. Recurrence is uncommon in other parts of the GI tract.

Case Report
A 55-year-old male was referred for evaluation of an incidental computed tomography (CT) finding of thickening of the distal esophagus. The study was obtained for evaluation of a lung nodule seen on a chest x-ray indicated for shortness of breath evaluated in the emergency department. The patient noted intermittent, progressive dysphagia for solids but not to liquids, without significant weight loss. A double-contrast upper GI series demonstrated a well-circumscribed submucosal mass lesion of the distal esophagus (Figure 1). An upper endoscopy and subsequent endoscopic ultrasound (EUS) showed 3 large submucosal lesions bulging into the distal esophageal lumen with an additional nodule of the gastric fundus (Figure 2). Core biopsies showed evidence of large tumor cells with granular eosinophilic cytoplasm, consistent with GCT. Immunohistochemistry confirmed the diagnosis (S-100 positive and smooth muscle actin negative).

The patient developed progressively severe dysphagia with enlargement of the lesions nearly occluding the esophageal lumen. He underwent a transhiatal esophagectomy and wedge excision of the gastric nodule. There was no gross evidence of metastatic disease. Pathologic evaluation demonstrated 4 esophageal nodules, which ranged in size from 1 to 2.2 cm, and a 1-cm gastric nodule. All had a uniform tan/yellow cut surface and microscopically demonstrated features of GCT on hematoxylin and eosin (H&E) examination. Some showed minimal atypia (Figure 3). One tumor extended into the muscularis propria and another extended into the subserosa, showing an infiltr-
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Tive growth pattern. All were completely excised with negative margins and lymph nodes. The patient did well postoperatively, with resolution of his dysphagia.

Two years later, the patient underwent a screening colonoscopy and 2 cecal nodules were removed by snare cautery (Figure 4). They measured 8 mm and 7 mm; one nodule extended to the deep margin of resection. These tumor cells had the same morphology as the prior esophageal and gastric tumors, but one had dense collagen deposition and the other had calcifications (Figure 5). The patient has had no additional symptoms and there have been no additional GCT noted on subsequent follow-up upper and lower endoscopies.

Discussion

The exact histiogenesis of GCT lesions remains uncertain, but immunohistochemical studies identifying the presence of S-100 protein and neuron-specific enolase support a neural cell origin theory, with GCT likely originating from Schwann
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Cells. GCT are generally benign tumors, and often remain stable or very slowly increase in size. Malignancy is rare, occurring in less than 1–2% of lesions. Management includes monitoring the lesion for stability or resection. However, as these lesions are submucosal, there is a potentially increased risk of perforation with removal. Although some physicians may prefer surveillance rather than resection, there is no consensus on the appropriate interval to survey. If completely resected, recurrence is unlikely. However, patients should be followed up after resection, as there is a 2–10% risk of recurrence.

Multifocal lesions, either synchronous or metachronous, are distinctly uncommon. Fried et al reported a case with multiple synchronous gastrointestinal GCT of the esophagus, stomach, appendix, and cecum. In a study of 74 cases of GCT of the GI tract and perianal region, only 3 of 74 patients had multiplicity of tumors; only one case showed involvement in more than one segment of the GI tract. If multiple lesions are found, they are typically grouped in one area, especially the esophagus or stomach. The occurrence of multiple lesions does not appear to increase the risk of malignancy. None of our patient’s 7 tumors were malignant.

Our case illustrates the unusual combination of multifocal symptomatic GCT arising synchronously in multiple segments of the GI tract. Although rare, physicians should be aware of the potential for multiple symptomatic lesions throughout the GI tract.

Disclosures
Author contributions: Z. Lipkin-Moore performed the literature review and wrote the manuscript. R. Thomas was involved in patient care, revised the manuscript, and provided pathology slides. R. Rothstein was involved in patient care, reviewed and revised the manuscript, and is the article guarantor.

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References
1. Abrikossoff A. Ueber Myome ausgehend von quergestreifter willkiirlicher Muskulatur. Virchow Arch Path Anat. 1926;260:214–33.
2. Fried KS, Arden JL, Gouge TH, et al. Multifocal granular cell tumors of the gastrointestinal tract. Am J Gastroenterol. 1984;79(10):751–5.
3. Lack EE, Worsham GF, Callihan MD, et al. Granular cell tumor: A clinicopathologic study of 110 patients. J Surg Oncol. 1980;13(4):301–16.
4. Johnston J, Helwig EB. Granular cell tumors of the gastrointestinal tract and perianal region: A study of 74 cases. Dig Dis Sci. 1981;26(9):807–16.
5. Giacobbe A, Facciorusso D, Conoscitore P, et al. Granular cell tumor of the esophagus. Am J Gastroenterol. 1988;83(12):1398–400.
6. Ordóñez, NG. Granular cell tumor: A review and update. Adv Anat Pathol. 1999;6(4):186–203.
7. Nathrath WB, Remberger K. Immunohistochemical study of granular cell tumors: Demonstration of neurone specific enolase, S-100 protein, laminin and alpha-1-antichymotrypsin. Virchows Arch A Pathol Anat Histopathol. 1986;408(4):421–34.
8. Orlowska J, Pachlewski J, Gugulski A, et al. A conservative approach to granular cell tumors of the esophagus: Four case reports and literature review. Am J Gastroenterol. 1993;88(2):311–15.
9. Mitomi H, Matsumoto Y, Mori A, et al. Multifocal granular cell tumors of the gastrointestinal tract: Immunohistochemical findings compared with those of solitary tumors. Pathol Int. 2004;54(1):47–51.
10. Maekawa H, Maekawa T, Yabuki K, et al. Multiple esophagogastric granular cell tumors. J Gastroenterol. 2003;38(8):776–80.
11. David O, Jakate S. Multifocal granular cell tumor of the esophagus and proximal stomach with infiltrative pattern: A case report and review of the literature. Arch Pathol Lab Med. 1999;123(10):967–73.