Esophageal Granular Cell Tumor in the Setting of Eosinophilic Esophagitis: A Case Series

Benjamin Kuhn1, Grant Morris2* and Amitpal Johal3

1Department of Pediatrics, Section of Gastroenterology, Geisinger Medical Center
2Department of Pediatrics, Geisinger Medical Center
3Department of Internal Medicine, Section of Gastroenterology

Abstract

Granular cell tumors are generally benign neoplasms derived from Schwann cells most commonly found in subcutaneous tissues [1]. Eight percent of all GCT involve the gastrointestinal (GI) tract, two percent of which are esophageal [2,3]. The rate of malignant transformation is 2% [1]. There are eight reported gastrointestinal cases of GCT in children: esophageal (n=4) [4-6], appendiceal (n=2) [7], and cecal (n=2) [7,8]. There are eight reported cases of GCT in individuals with eosinophilic esophagitis (EoE), age ranging from 14 to 41 years [5,6,9]. Typically, esophageal GCTs are incidentally found on upper endoscopy.

Eosinophilic esophagitis is a clinicopathological disease with predominant esophageal symptoms, characteristic endoscopic findings, and histological criteria with esophageal eosinophilia. EoE presents with a variety of upper GI symptoms characterized by age of onset [10] with a mean age of 8 years. Seventy-five percent of cases are males [11]. Previously reported esophageal GCTs have presented with dysphagia, as can EoE. We present two pediatric patients with eosophageal GCT discovered while undergoing surveillance endoscopy for eosinophilic esophagitis.

Methods

A retrospective chart review was performed using the electronic medical record system on pediatric patients with the diagnosis of eosinophilic esophagitis and esophageal granular cell tumor.

Case 1

A 9-year-old boy with autism spectrum disorder, asthma, allergic rhinitis, and EoE underwent esophagogastroduodenoscopy (EGD) for EoE surveillance. He was diagnosed with EoE at age 2 years and was treated with 6-food elimination diet and lansoprazole. At 9 years of age, he was asymptomatic and undergoing follow-up surveillance EGD on a stable diet. A 2 mm by 4 mm firm nodule was found in the middle third of the esophagus (Figure 1). Biopsy showed squamous mucosa containing submucosal granular cell tumor, which was positive for S100, CD68 and inhibin-alpha immunostaining (Figures 2-5). Previous EGD one year earlier was without lesion. He subsequently underwent removal of GCT via EGD with endoscopic mucosal resection (Figure 6). Endosonographic findings were a single oval intramural (subepithelial) hypoechoic lesion in the middle third of the esophagus within the submucosa (Layer 3) and measured up to...
3 mm in thickness with well-defined borders. For removal, 2 mL of saline were injected to raise the lesion. Band ligator was applied to capture the tumor. Hot snare mucosal resection with Roth Net retrieval was performed. A follow-up EGD 3 month later showed a grossly normal esophagus and biopsies without evidence of GCT. All EoE surveillance esophageal biopsies obtained at discovery and at removal were negative for active eosinophilia or inflammation.

**Case 2**

A 16-year-old boy with asthma, allergic rhinitis, and EoE underwent follow-up EGD. He was initially diagnosed with EoE at age 14 years after a work-up for dysphagia, GERD-like symptoms, and vomiting refractory to acid suppression. His EoE failed 6-food elimination, swallowed fluticasone, and now relies on an elemental diet with isolated single food reintroductions. At age 16 years, surveillance EGD revealed a 2 mm by 4 mm hard, firm nodule in the middle third of the esophagus (Figure 7). Biopsies of the nodule revealed S-100 positivity, consistent with granular cell tumor. Prior endoscopy 3 months earlier was without lesion. He underwent removal of GCT via EGD with endoscopic ultrasound and endoscopic mucosal resection (Figure 8). Endosonographic findings revealed a single small nodule hypoechoic lesion within the submucosa (Layer 3). The mass measured up to 4 mm in thickness with well-defined borders. Resection was performed after 2 mL saline injection to raise the lesion, followed by band ligator to capture the tumor, and hot snare mucosal resection with Roth net retrieval. Follow-up EGD 3 months later showed a grossly normal appearing esophagus and biopsies without evidence of GCT. All EoE surveillance esophageal biopsies obtained at discovery and at removal were negative for active eosinophilia or inflammation.

**Discussion**

The first GCT in the esophagus was reported in 1931 [12] and since then there have been hundreds of GCTs found throughout the GI tract, with most cases found in adults. The rate of malignant transformation is 2% [1]. The first esophageal GCT in a pediatric patient was reported in 2003 [4].

The typical endoscopic appearance of GCT is a polypoid, yellow, firm submucosal mass. The definitive diagnosis is made...
both asymptomatic and without active eosinophilia or inflammation. Esophageal GCTs are reactionary given their findings of active EoE [6]. This same report notes that perhaps by incidental discovery. A recent retrospective report identified 18 cases are similar to other GCT cases in the literature characterized for eosinophilic esophagitis when esophageal GCTs were found. These identified with esophageal GCT.

19-9. Alone from this report, there are no specific serum markers. Immunohistochemical staining was interestingly negative for CA 19-9. Patient’s serum CA 19-9 level normalized post-operatively. The final pathologic diagnosis was a benign GCT. The carbohydrate antigen 19-9, raising concern for malignant potential with an esophageal GCT who had an elevated preoperative serum positivity of the S-100 protein is useful to support the diagnosis [13].

Recently in 2015, Yanoma and colleagues reported an adult with an esophageal GCT who had an elevated preoperative serum carbohydrate antigen 19-9, raising concern for malignant potential [16]. The final pathologic diagnosis was a benign GCT. The patient's serum CA 19-9 level normalized post-operatively. The immunohistochemical staining was interestingly negative for CA 19-9. Alone from this report, there are no specific serum markers identified with esophageal GCT.

The children in our case series were undergoing surveillance EGD for eosinophilic esophagitis when esophageal GCTs were found. These cases are similar to other GCT cases in the literature characterized by incidental discovery. A recent retrospective report identified 18 esophageal GCT, with two occurring in pediatric patients that were symptomatic from their EoE [6]. This same report notes that perhaps esophageal GCTs are reactionary given their findings of active EoE inflammation. However, this is contrary to our cases, which were both asymptomatic and without active eosinophilia or inflammation at time of discovery and removal. What is unique in this report is the strengthened recognition of additional esophageal GCT cases in the setting of EoE and only three prior in pediatric patients [5,6].

In summary, GCTs are rare in children. The relationship between GCT and EoE is unclear, with two possibilities being a coincidental finding versus long-term complications of chronic inflammation in EoE. The prevalence of EoE is certainly increasing, and with a potential increasing incidence [17], it is important for clinicians to be attentive of this possible association, which may shed insight into alterations in disease pathophysiology.

References