

A Large Esophageal Granular Cell Tumor with Review of Literature

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Abstract

Granular cell tumor (GCT) is an uncommon entity which occurs in all organs and tissues and is most frequently found in the tongue and skin. Within the gastrointestinal system, granular cell tumor occurs most frequently within the esophagus. The clinical presentation and imaging features of esophageal GCT overlap with leiomyoma in many aspects, making it difficult to separate these entities on a purely clinical basis. Therefore, the definitive diagnosis of granular cell tumor relies upon pathological examination. GCT of the esophagus is benign and surgical excision is usually curative. Here we report a case of a large, submucosal GCT of the distal esophagus, mimicking leiomyoma in clinical presentation and on esophagogastroduodenoscopy (EGD) imaging. Surgical resection resulted in apparent cure, with no recurrence after 3 years of follow-up. Pathologic examination of the lesion showed a typical granular cell tumor.

Keywords: Granular cell tumor; Esophagus; Leiomyoma

Introduction

Granular cell tumors (GCTs) were first described by Arbibosoff in 1926 as part of a series of five tumors of the tongue, which he collectively called myoblastoma [1]. They are infrequent lesions and have been described in every organ and body site, although they are most commonly found in the tongue and skin. GCTs are now determined to be of neural (Schwann cell) origin. GCTs originating in the esophagus account for 1% of all reported cases. Leiomyoma, in contrast to GCT, is a benign smooth muscle neoplasm and is the most common benign stromal tumor of the esophagus. The overlapping clinical and endoscopic appearances of these two entities make diagnosis on such grounds difficult without the aid of microscopic examination. Recently, esophageal ultrasound has been used to differentiate these stromal tumors according to their localization within the esophageal wall; GCTs usually involve the submucosal layer while leiomyomas arise from the muscular layer. Here we report a case of a granular cell tumor of the esophagus mimicking a leiomyoma on clinical and sonographic features, with emphasis on pathologic findings.

Case Report

A 66-year-old African American male presented with progressive solid food dysphagia of 2-3 years duration. There were no reported episodes of acute bolus obstruction or hematemesis. His past medical history was significant for chronic obstructive pulmonary disease (COPD) and a 25 packs-year history of smoking. An esophagogastroduodenoscopy (EGD) revealed a broad-based, submucosal mass of the distal esophagus (34 to 37 cm from incisors), without mucosal ulceration (Figure 1). The endoscopic ultrasound showed a well delineated mass in the posterior wall of the esophagus, possibly arising from the muscularis propria (Figure 2). A clinical and endosonographic diagnosis of leiomyoma was made.

Given the patient's history of progressively dysphagia, a right thorascopic excision was performed. The mass could readily be identified just below the pulmonary hilum and was enucleated. The patient was discharged on day 2 after surgery. Pathologic examination revealed a GCT. On three-year follow-up the patient was asymptomatic.

Gross examination of the surgical specimen revealed an

encapsulated, oval, tan-gray soft tissue nodule measuring 4.0 x 2.5 x 2.0 cm. The cut surfaces were white-tan, homogenous with granular appearance, and without hemorrhage or necrosis (Figure 3).

Microscopic examination showed an encapsulated (Figure 4A) mass composed of sheets of tumor cells with little stroma (Figure 4B). The composite cells were large and polyhedral, with abundant, granular eosinophilic cytoplasm and oval to spindle-shaped nuclei. Some cells demonstrated prominent basophilic nucleoli. No cellular or nuclear polymorphism and no mitoses were identified (Figure 4B). Immunohistochemical stains showed tumor cell positivity for S-100 protein (Figure 4C), but negativity for desmin, smooth muscle actin (SMA), CD117, and CD34 (not shown). Electric microscopy showed tumor cells to be surrounded by basal lamina and joined by primitive junctions; abundant cytoplasm was filled with large numbers

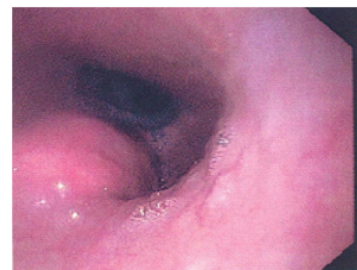


Figure 1: Esophagogastroduodenoscopy revealed a broad-base mass in the distal esophagus.

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of lysosomes, varying in size and containing dense granular material (Figure 5). The final diagnosis of granular cell tumor was made based on light and electron microscopic findings, which were confirmed upon immunohistochemical staining.

Discussion and Conclusion

Granular cell tumors commonly occur in the skin, tongue, and breast. The gastrointestinal (GI) tract is an uncommon site for GCTs, accounting for about 8% of all cases. Of all GI tract GCTs, the esophagus is the most common site [2], with a distal location the most common.

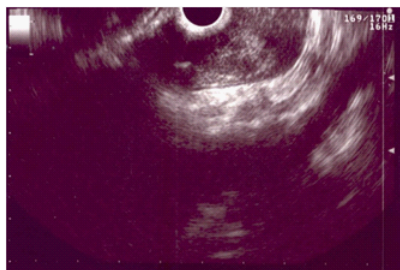


Figure 2: The endoscopic ultrasound showed the mass, opposite to the wall of the heart, was clearly well marginalized and well encapsulated. It also showed the lesion may be involved with esophageal muscular propria.

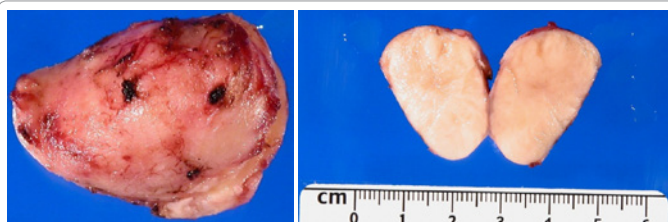


Figure 3: The sharply circumscribed tumor has a white-tan color and elastic consistency.

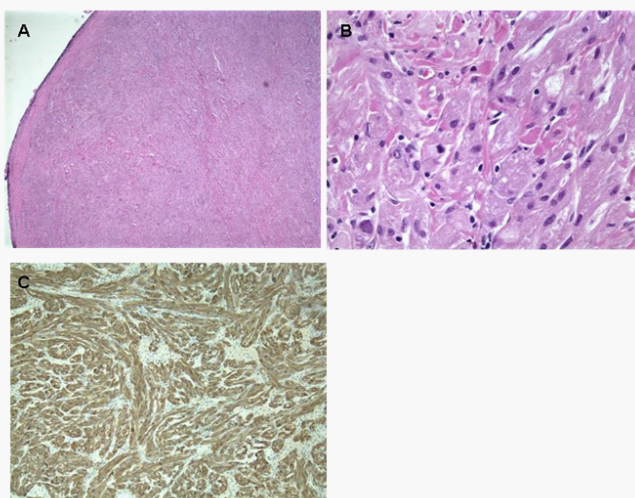


Figure 4: Light microscopic examination of the tumor. A, Lower magnification shows the tumor is well circumscribed. B, Higher magnification shows large polyhedral cells with abundant granular eosinophilic cytoplasm and oval or spindle nuclei. C, S-100 immunostain is diffusely and strongly positive for the tumor cells.

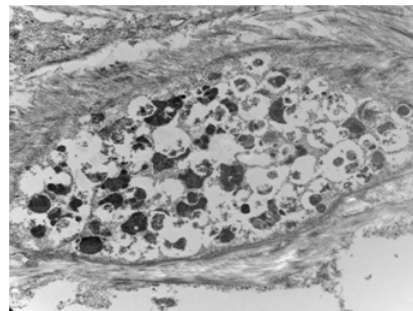


Figure 5: EM demonstrated that the lysosomes vary in size and contain dense granular material.

Since Abrikossoff first described esophageal granular cell tumors over 75 years ago, over 200 cases have been documented in the literature [3].

The pathogenesis of GCT was unknown for decades, with both neoplastic and degenerative origins postulated. The histogenesis of GCTs has been debated for a long period of time, but is now generally accepted to be of neurogenic (Schwann cell) origin based on immunohistochemical (S-100 positive) and ultrastructural findings [4]. The granular cytoplasm of tumor cells is attributed to accumulation of numerous lysosomes.

Esophageal granular cell tumors usually occur as a solitary nodule of the distal esophagus, but multiple tumors have also been reported [5]. Tumor measuring less than 1 cm are mostly asymptomatic, while larger tumors may present with dysphasia and chest pain mimicking acid reflux symptoms. In fact, GCTs of the distal esophagus may contribute to the development of reflux esophagitis. In the esophagus, GCTs are normally located within the submucosa, but may rarely involve the mucosa or muscularis propria. Those tumors that involve the muscularis propria may be particularly difficult to differentiate clinically from leiomyoma. In our patient, endoscopic examination revealed a medium-sized, single, sessile, submucosal firm nodule. The overlying mucosa was intact and smooth (Figure 1). Endoscopic ultrasonography (EUS) demonstrated a hypoechoic, well-demarcated, homogenous lesion involving the esophageal muscular propria, mimicking leiomyoma (Figure 2).

The diagnosis of esophageal GCT relies on patient presentation and endoscopic, ultrasonographic, and microscopic examination. Most cases are asymptomatic and are incidentally discovered during examination for other medical conditions. Tumors generally range from a few millimeters to 2 cm in size, with 75% measuring less than 2 cm in diameter. Endoscopically, GCT's appear as small, isolated, sessile, submucosal nodules, with a "morula-like" appearance. The overlying mucosa is usually intact.

EUS remains a principal technique for diagnosis and treatment of GCTs, since it is able to determine to which layer the tumors are localized. Palazzo [6], performed this procedure on 15 patients with 21 lesions microscopically diagnosed as esophageal GCTs and reported endosonographic features of: a) tumor size of less than 2 cm in 95% of cases; b) hypoechoic solid pattern in 100% of cases, and c) tumor arising in the inner layers (second echo-poor layer) in 95%. The authors concluded that: when a granular cell tumor of the esophagus is suspected, EUS can show the inner layer location of the tumor and thus

contribute to planning the endoscopic resection or follow up. When the tumor also invades the outer layers, EUS can contribute to planning the surgical resection.

The definitive diagnosis of GCT, however, is based on microscopic examination, either through cytology or surgical biopsy. For example, ultrasound-guided fine needle aspiration (FNA) has been used to diagnose GCTs with some degree of accuracy. Cytologic findings include single or clusters of cells with ill-defined cell borders containing abundant, basophilic, granular cytoplasm [7,8]. Microscopic examination of surgical biopsy material demonstrates a poorly circumscribed, infiltrative tumor composed of large polyhedral cells with abundant, granular cytoplasm and small, central nuclei. The overlying mucosal epithelium often shows pseudoepitheliomatous hyperplasia. Immunohistochemical shows tumor cells which stain positively for S100 protein, vimentin, neuron specific enolase, and PAS. One notorious pitfall in diagnosis is the presence of pseudoepitheliomatous hyperplasia in a superficial biopsy specimen, which might be mistaken for squamous cell carcinoma if the deep underlying granular cells are not identified.

The majority of GCTs are benign, although cases of malignant GCT have been reported. Proposed histologic criteria of malignancy in GCTs include tumor necrosis, tumor cell spindling, high nuclear to cytoplasmic ratio, nuclear pleomorphism, large nucleoli, and increased mitotic activity. Tumors fulfilling at least 3 of these criteria are classified as malignant according to Fanburg-Smith et al. [9]. Approximate 2% of the GCTs referred to in the literature proved to be malignant [9,10]. Clinical manifestations suggesting malignancy include a history of rapid and recent tumor growth, large tumor size, and local recurrence [11]. Local extension and invasion and infiltration growth pattern without metastasis are not considered to be malignant features, however [12,13].

Like esophageal GCTs, esophageal leiomyomas are rare, but represent the most common benign intramural tumor of the esophagus and account for 10% of all gastrointestinal leiomyomas. Esophageal leiomyomas usually occur in middle-aged to elderly patients, presenting with dysphagia and heartburn. The most common site is in the distal third of the esophagus. The tumor arises from the esophagus as a sessile or pedunculated, polypoid, exophytic intraluminal solid mass. Leiomyomas show a grayish-white, whorled cut surface. Focal calcification is sometimes noted and secondary ulceration may be present. The tumor rarely presents as a lobulated, extramural mediastinal mass.

The treatment for the granular cell tumors include various modalities, including Yttrium-aluminum-garnet laser ablation, dehydrated alcohol injection, endoscopic resection, and surgical treatment. In order to remove tumors adequately by endoscopy, it is suggested that they be limited to the submucosa and not extend into the muscularis propria [14]. Endoscopic resection with biopsy forceps may be effective only for tumors measuring < 2cm, as there is increased risk of an incomplete resection [15]. Transthoracic excision of GCTs is the most definitive treatment and is indicated for tumors amenable to endoscopic resection. Recent advances in minimally invasive surgery allows for decreased peri-operative morbidity and hospital stay. In this patient, a right thoracoscopic excision was performed. The patient had an unremarkable post-operative course and was discharged in 2 days following surgery. Follow-up 3 years later showed the patient to be free of symptoms and without recurrence.

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