Persistently Altered Visceral Perception after Resection of an Esophageal Granular-Cell Myoblastoma: A Therapeutic Concept Revisited

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Anhaltende Störung der viszeralen Perzeption trotz Resektion: Ist die chirurgische Therapie von ösophagealen Granularzell-Tumoren ohne Alternative?

Abstract

Granular cell tumors (GCTs) are rare and usually benign gastrointestinal tumors. Their most frequent symptoms are dysphagia and epigastric or retrosternal discomfort. We here report a case of esophageal GCT with continued symptoms of retrosternal discomfort, postprandial feeling of fullness, and early satiety despite complete thoracoscopic resection of the tumor. In contrast, all functional tests were in the normal range. We thus suggest that, due to their neuroectodermal origin, GCTs may affect neuronal alterations leading to a persistently disturbed visceral mechanosensory perception. Consequently, this case also cautions the therapeutic concept to solely relieve GCT symptoms by resection if the tumor is less than 20 mm in diameter.

Key words
Granular-cell tumor · Abrikosov's tumor · myeloblastic myoma · visceral mechanosensory perception · functional gastrointestinal disorders · endosonography

Zusammenfassung


Schlüsselwörter
Granularzell-Tumor · Abrikosov-Tumor · Myeloblastom · viszeral-mechanosensorische Perzeption · funktionelle Verdauungsstörungen · Endosonographie
**Introduction**

Esophageal granular cell tumor (GCT) was first described in 1931 by Abrikosov [1]. However, while the number of cases reported has increased steadily with the advent of endoscopy [2], the disease is still poorly manageable.

In 1991, Cappell et al. suggested that the GCT-associated symptoms of dysmotility and dysphagia may result from the tumor’s tendency to infiltrate and replace the neural supply of the viscera [3, 4]. Our own findings support this hypothesis and suggest that the patients’ functional dyspepsia likewise relates to tumor-dependent neural alterations. Indeed, future confirmation of these conclusions may imply different approaches for the therapy of altered visceral perception after surgical removal of a granular-cell tumor.

**Case report**

A Caucasian female outpatient, 30 years of age, was referred to us for further evaluation of an esophageal lesion. She reported of occasional epigastric and retrosternal pain and discomfort throughout a period of six months. General physical examination as well as hematological and reference laboratory parameters were within normal ranges.

Upper gastrointestinal radiography did not show any alterations and demonstrated regular peristalsis. However, endoscopy revealed a small non-exophytic lesion approx. 30 cm afar her incisives. The white-yellowish mass was covered with normal mucosa, had a firm consistency, and measured about 25 mm in diameter (Figure 1). Several biopsies were consistent with the diagnosis of a granular-cell tumor (Figure 2). Endoscopic ultrasound showed a homogenous hypoechoic mass confined to the submucosal margins. We detected no evidence of lymph-node metastasis (Figure 3).

Motility testing by esophageal manometry utilizing a Dent-sleeve Catheter demonstrated regular contractions with a mean amplitude of 60 mm Hg (reference range: 35–120 mm Hg). Lower and upper esophageal sphincter baseline pressures were normal with 15 mm Hg (ref.: 9–32 mm Hg) or 80 mm Hg (normal range: 35–120 mm Hg), respectively, with complete relaxation after swallowing. Manometry and 24-h gastric pH measurement (Gastrograph Mark II, Ingold M6) excluded a case of reflux disease.

The tumor was resected by minimal invasive thoracoscopic surgery. Histology revealed large polygonal cells with eosinophilic cytoplasm and high numbers of periodic acid Schiff reaction-positive granules. Immunohistochemistry demonstrated the expression of S-100 protein. These findings confirmed the diagnosis of a granular cell tumor (a.k.a. Abrikosov’s tumor or myeloblastic myoma).

The patient was discharged without any perioperative complications. However, on follow-up after three months, she reported of the same degree of symptoms as before surgery, i.e. epigastric and retrosternal pain, early satiety, and a postprandial feeling of fullness. Yet, successive endoscopy, EGG and echocardiography excluded reflux disease or cardiac disease.

**Discussion**

Granular-cell tumors may occur at any age, but they reveal two peaks during the third and fifth decades, and a higher incidence in women [4, 5]. They are a rare class of tumors which may, however, develop in all tissue types. Most frequently, GCTs involve mucosal tissues such as of the gastrointestinal tract (including the tongue as a major location) and the female breast, the skin, and the central nervous system [4, 6].

In the G.I. tract, such tumors predominate in esophageal location, with approx. 30% of all cases [1, 7, 8]. While GCTs may be found in any part of the oesophagus, they mainly (60%) occur in its lower portion [5, 9, 10].

Tumoral lesions are of whitish or pale yellowish color if fat is incorporated, as seen in the case reported herein. The consistency

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**Figure 1** Endoscopy revealed a minimal protruding CCT located 30 cm afar the incisor teeth. The lesion had a slightly irregular surface, and a white-yellowish colour.
of GCTs varies from moderately firm and rubbery to hard and dense [4]. GCTs of the esophagus are typically located in the mucosal and/or submucosal layers [7]. Most GCTs are benign and small (with diameters of < 20 mm), but their malignant potential increases when exceeding 50 mm in diameter [11]. Malignant forms occur in less than 1–2% of all cases and may metastasize to the local draining lymph nodes [4, 5, 8, 9, 11].

The occurrence of symptoms such as discomfort in patients with Abrikosov-type tumors depends on their location, and characterize about 50% of all cases. Also, usually symptoms are only noticed when a GCT's diameter exceeds 20 mm [2, 4, 9]. The most common symptom caused by esophageal GCTs is dysphagia (43% of all cases), followed by epigastric and retrosternal sensations of discomfort (16%) [2, 4]. Yet, there are exceptions to the rule, such as with the patient presented herein, who suffered from pain before developing dysphagia.

Earlier histological and immunohistochemical studies have supported the concept of a neural origin of granular-cell tumors [6, 12]. Also, the frequent multicentricity of GCT lesions is reminiscent of neural tumors. A neural origin is further supported by the occurrence of GCTs in cranial, autonomic, and peripheral nerves [4]. Finally, expression of S-100 protein –like in the case presented – and neuron-specific enolase (NSE) by GCT cells suggest a Schwann-cell origin [4, 11].

As in pseudoachalasia [13], some granular-cell tumors cause esophageal or intestinal dysmotility by destroying enteric nerves. Indeed, GCTs have the general propensity to infiltrate and disrupt nerves [3]. These observations indicate that GCTs may likewise affect visceral perception which may, even after resection of the tumor, provoke persistent sensations of discomfort, postprandial fullness, and early satiety. This would imply a sustained reconstruction of the visceral autonomous innervation as well as mechanosensory function [3, 14]. The case presented herein obviously supports such a pathophysiologic scenario.

The likelihood of numerous similar cases cautions the therapeutic concept to surgically remove GCTs of less than 20 mm in diameter, if the sole objective is to relieve symptoms of discomfort [15, 16]. The case presented herein revealed normal motility of
the upper gastrointestinal tract. Functional dyspepsia in patients with GCTs may thus rather trace back to a visceral neural spreading of the tumor, which would advise a different therapeutic strategy. One possible therapeutic approach might be the use of anti-depressants, although solid prospective evidence is missing. Indeed, the quest for more suitable therapies might spare future patients with small granular-cell tumors the avoidable risk of surgical intervention. Alternatively, GCTs located within the mucosal layer can be resected by endoscopic mucosal resection, which may result in better outcome in regard to potentially persistent symptoms.

References
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