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Granular cell tumor of the appendix: a case report and literature review

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Abstract

A granular cell tumor (GCT) is an unusual benign soft tissue tumor that can occur at any age and in any part of the body. GCTs are mostly found in the skin and subcutaneous tissues, bronchi, esophagus, breast tissue, and tongue. A GCT originating in the digestive tract, particularly in the appendix, is relatively rare and usually diagnosed as an incidental finding. We herein describe the first case of abdominal distension and occasional pain secondary to a GCT of the appendix in our hospital. The findings from this case suggest that a GCT of the appendix is a rare entity for which surgical resection is an efficient therapy.

Keywords

Granular cell tumor, ileocecal appendix, laparoscopic appendectomy, oncologic management, therapy, case report

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Introduction

A granular cell tumor (GCT) is a rare benign soft tissue tumor that was first reported by Abrikossoff in 1926.[1,2] GCTs are generally believed to originate from neural/schwannian cells.[3] These tumors can occur at any age and in any part of the body.[4,5] The peak incidence of GCTs is between 40 and 60 years of age, and they most often occur in women and Black people.[6,7] The tumors are mostly

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found in the skin and subcutaneous tissues, bronchi, esophagus, breast tissue, and tongue. GCTs originating in the digestive tract are relatively rare, accounting for 5% to 10% of all clinical cases, and GCTs in the appendix are found in only 1% of diagnosed patients.[8,9] Our review of the literature revealed only 16 documented cases of appendiceal GCT (Table 1).[3,6,10–20]

We herein describe the first case of a GCT of the appendix in our hospital. This case indicates that surgical resection is an efficient therapy and should be performed in the early stages of the disease.

Case report

A 60-year-old man was found to have an ileocecal mass and chronic colitis during a physical examination and was referred to our hospital for surgical excision. The patient had an almost 1-year history of persistent abdominal distension and occasional pain in the right lower quadrant. Colonoscopy revealed a smooth protuberance of about 1.0×0.8 cm in size at the base of the appendix, where it was at risk of damage from reactive changes and local inflammation. Endoscopic ultrasonography showed a hypoechoic mass located in the mucosal muscularis and partially protruding to the submucosal layer; the mass was continuous and intact with clear boundaries (Figure 1(a), (b)). A neuroendocrine tumor was considered, and the patient was admitted to our hospital for further diagnosis and treatment. The patient had undergone surgery for glaucoma 18 years previously, denied smoking and alcohol addiction, and had no medical or family history of malignancy. He reported a 3-year history of hepatitis B that was well controlled by oral antivirals. Physical examination and laboratory tests showed no abnormalities. Chest computed tomography (CT) examination showed stable pulmonary tuberculosis and bronchitis in the upper lobe of the right lung. Abdominal CT examination revealed liver occupation, which was considered to be abnormal perfusion and cholecystitis. Intraoperative exploration revealed an appendiceal mass that was slightly adherent to the ileocecal part; therefore, laparoscopic appendectomy was very carefully performed by separating the appendix from the intestine and removing a small piece of it for rapid pathology during the surgery. Rapid pathology suggested a mesenchymal neoplasm with benign tendency. Postoperative pathological examination of the tumor revealed mild morphology; the specimen was composed of nests and sheets of round, oval, polygonal, or spindle-shaped cells with abundant granular eosinophilic cytoplasm (Figure 2(a)). The cells had small and consistent nuclei but no signs of mitosis or necrosis, confirming the diagnosis of a GCT. The patient tolerated the surgical procedure well with full recovery. Immunohistochemical staining showed the following results: S-100 protein (+), smooth muscle actin (−), desmin (−), Ki-67 protein (<1%+), CD117 (−), CD34 (−), CD68 (−), neuron-specific enolase (+), and SOX10 (+) (Figure 2(b)–(d)). The histopathologic diagnosis of the biopsy specimen was a GCT.

The reporting of this study conforms to the CARE guidelines.[21]

Discussion

GCTs generally grow slowly and are usually confined to the mucosal and submucosal layers of the gastrointestinal tract.[22] Their diameter varies from 0.5 to 2.0 cm; GCTs with a diameter of <1.0 cm are called micro-GCTs and are characterized by the lack of specific symptoms.[23] Patients are often referred to the hospital for common gastrointestinal symptoms or a mass in the alimentary tract found during physical examination.[24] Endoscopy shows that the epidermis of the GCT is covered by

Table 1. Previous reports of appendiceal granular cell tumors.

Reference	Title	Journal, year published	Number of cases
Johnston and Helwig[9]	Granular cell tumors of the gastrointestinal tract and perianal region: a study of 74 cases	*Dig Dis Sci* 1981	4
Fried et al.[10]	Multifocal granular cell tumors of the gastrointestinal tract	*Am J Gastroenterol* 1984	1
Apisarnthanarax[11]	Granular cell tumor. An analysis of 16 cases and review of the literature	*J Am Acad Dermatol* 1981	1
Sarma et al.[12]	Granular cell tumor of the appendix	*J Surg Oncol* 1984	1
Pipeleers-Marichal et al.[13]	Granular cell tumour of the appendix in a patient irradiated for a rectal carcinoma	*Virchows Arch A Pathol Anat Histopathol* 1990	1
Kaltschmidt et al.[14]	[Granular cell tumor of the vermiform appendix. Case presentation with discussion of histogenesis]	*Zentralbl Pathol* 1992	1
Gavelli et al.[15]	[Granular cell tumor involving the appendix]	*Gastroenterol Clin Biol* 2005	1
Saleh et al.[16]	Multiple synchronous granular cell tumors involving the colon, appendix and mesentery: a case report and review of the literature	*J Gastrointestin Liver Dis* 2009	1
Moreno Gijon et al.[17]	[Granular cell tumor of the appendix]	*Rev Esp Enferm Dig* 2009	1
Zoccali et al.[5]	Acute appendicitis secondary to a granular cell tumor of the appendix in a 19-year-old male	*J Gastrointest Surg* 2011	1
Roncati et al.[2]	Granular cell tumor of the appendix: a new case and review of the literature	*Springerplus* 2013	1
Ye et al.[18]	[Granular cell tumor of appendix: report of a case]	*Zhonghua Bing Li Xue Za Zhi* 2014	1
Allison and Rao[19]	Granular cell tumor confined to the muscularis propria of the appendix: a case report	*Am J Clin Pathol* 2020	1

multiple layers of epithelial cells,[25] and the lesion presents as a sharp "submucosal eminence" with a flat or depressed surface; this is also known as a "molar eminence."[26] Endoscopic ultrasonography is used to determine the origin level and the boundaries of the lesions, which are generally described as hypoechoic masses with clear boundaries, and their properties are therefore difficult to distinguish.[27,28] General imaging examinations of GCTs, such as CT examination, lack specificity, making it difficult for physicians to accurately evaluate the case.[29,30] The diagnosis of such cases is mainly based on pathologic morphology and immunohistochemistry.[31,32] The gold standard for the diagnosis of GCT is histopathology, which reveals at least one of the following characteristics: (i) the tumor is mainly composed of large tumor cells that contain eosinophilic cytoplasmic granules and are densely

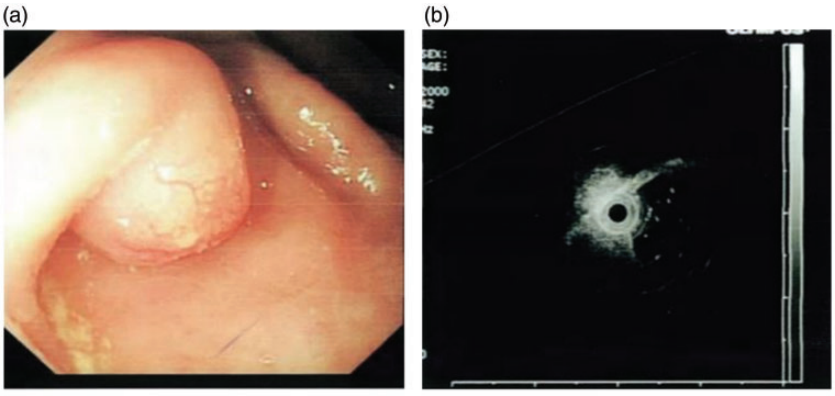

Figure 1. Endoscopic and ultrasonographic findings. (a) Endoscopic appearance of appendiceal granular cell tumor: smooth protuberance of about 1.0 × 0.8 cm in size and (b) Endoscopic ultrasound findings of granular cell tumor: hypoechoic, smooth, homogenous mass.

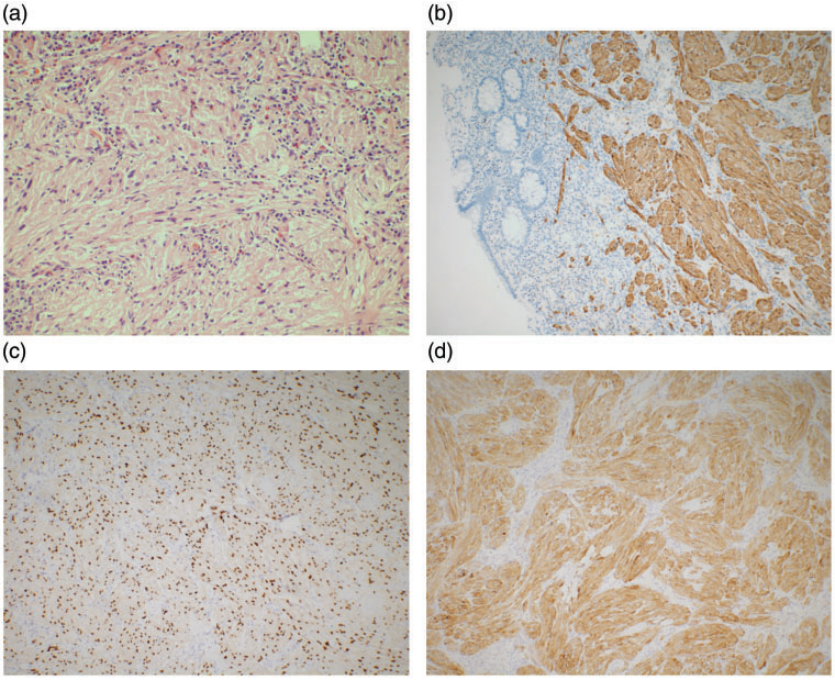

Figure 2. Histopathologic and immunohistochemical findings. (a) Histopathologic findings of the appendiceal mass. Clusters of large cells were present within the lamina propria, and they contained abundant eosinophilic granular cytoplasm and small round to oval nuclei (hematoxylin and eosin, ×100). The cells were (b) strongly immunoreactive for S-100 protein (×100), (c) positive for SOX10 immunostain (×100), and (d) positive for neuron-specific enolase immunostain (×100).

distributed in nests or cords; (ii) the tumor cells are filled with cytoplasmic granules positive for periodic acid-Schiff with diastase; or (iii) the tumor cells express S-100 protein, SOX10, neuron-specific enolase, HMB-45, cytokeratin, CD34, and CD68. Because of the relatively special histologic morphology of GCTs, the diagnosis is relatively simple. Notably, however, a GCT is a rare and sporadic disease, with few cases following a malignant course. Fanburg-Smith et al.[33] reported that the microscopic criteria by which to predict the malignant potential of GCTs include necrosis, spindling, vesicular nuclei with large nucleoli, nuclear pleomorphism, a high nuclear-to-cytoplasmic ratio, and more than 2 mitoses in 10 high-power fields (200× fields). GCTs that meet at least three of these criteria are classified as malignant GCTs (MGCTs), and those that meet one or two criteria are classified as atypical GCTs. A few retrospective studies have suggested that some metastatic MGCTs still have histological morphologies indistinguishable from those of benign GCTs. In 2007, Kapur et al.[34] regarded metastasis as the sole criterion for malignancy. Importantly, no widely accepted histological criteria with which to differentiate benign GCT, MGCT, and atypical GCT have yet been established.[30,35]

The pathogenesis of GCTs remains unclear, but the possibility that they are secondary to chronic inflammation/trauma has been proposed.[3,24] There are no major findings of MGCT occurrence in the appendix, but MGCTs may show an invasive growth pattern in some cases. Nuclear necrosis and mitotic activity appear to be the most effective histological criteria with which to detect aggressive tumors.[33] In 2011, Nasser et al.[36] proposed a simpler diagnostic approach that depends only on necrosis and/or mitosis as the most reproducible criteria. Their method classifies tumors with neither of these two features as benign and tumors with at least one of these characteristics as GCTs with uncertain potential, thus facilitating separation of the different diagnostic subgroups of GCT. They also emphasized that Ki-67 immunostaining is still helpful for diagnosis of difficult cases. Enzinger and Weiss[37] showed that true malignancy, as affirmed by metastasis of GCT, is found in almost 2% of the cases. Thus, the presence of metastasis remains the most accepted and definitive criterion for the diagnosis of MGCT.[38]

For benign GCTs in the gastrointestinal tract, surgical resection is still recognized as the best treatment, with a low odds of recurrence or malignant transformation after complete resection.[39] Patients with negative surgical margins always have a better prognosis. In addition, previously reported data are in concordance with these findings; no patients described in previous reports developed tumor progression or recurrence after a long follow-up, despite incomplete surgical removal in some cases.[40,41]

Conclusions

A GCT of the appendix is a rare entity that generally presented with symptoms of acute appendicitis. In the present case, the patient developed symptoms of chronic appendicitis such as persistent abdominal distension and occasional pain in the right lower quadrant, and the postoperative histopathological morphology was consistent with a GCT without necrosis or mitosis. These findings combined with the immunohistochemistry results led to a diagnosis of a benign GCT with a good prognosis.

Declaration of conflicting interest

The authors declare no conflict of interest in preparing this article.

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Ethics approval and consent to participate

The study protocol was approved by the ethics committee of The First Hospital of Jilin University, China (no. 2022-248). Written consent was obtained from the patient for publication of this case report.

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