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Rectal Granular Cell Tumors are Rare and Difficult to Diagnose Preoperatively

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Abstract

Granular cell tumors (GCTs), likely derived from Schwann cells can occur in any organ, including the gastrointestinal tract. Among gastrointestinal GCTs, esophageal GCTs are the most common; however, GCTs can also occur in the large intestine, especially the right-sided colon. Rectal GCTs are extremely rare. Here, we describe a case of rectal GCT detected incidentally during a colonoscopy. A submucosal tumor (SMT) with a smooth, yellow surface, approximately 5 mm in diameter, was observed in the rectum. Endoscopic ultrasonography showed a well-demarcated, homogenous hypoechoic mass in the third layer. Although a rectal neuroendocrine tumor (NET) was suspected, histopathological examination of multiple endoscopic biopsies of the lesion did not successfully reveal the tumor type. Therefore, we performed an endoscopic mucosal resection with ligand (EMRL).Based on histopathological analysis and immunohistochemical studies, this SMT was diagnosed as a GCT. The endoscopic features of colorectal GCTs closely resemble those of colorectal NETs. Colorectal GCTs have a reported diagnosis rate of only 50% on endoscopic biopsy and are difficult to diagnose preoperatively. When endoscopic biopsy does not provide a reliable diagnosis, GCTs should be included within the differential diagnosis; without malignant signs, endoscopic resection for diagnosis and treatment may be recommended.

Keywords: *Colonoscopy; Endoscopic Ultrasonography; Granular Cell Tumor of Rectum; Neuroendocrine Tumor of Rectum; Submucosal Tumor*

Introduction

Granular cell tumors (GCTs) are tumors derived from Schwann cells. GCTs can occur in any organ, but gastrointestinal GCTs are most often detected in the esophagus[1]. Several reports have shown that GCTs can also occur in the large intestine, especially the right-sided colon[1], but are rarely identified in the rectum. Preoperative diagnosis of colorectal GCT, especially small GCT, is difficult; additionally, endoscopic findings resemble colorectal neuroendocrine tumor (NET). Here we report the case of a 61-year-old man with a rectal GCT, which could not be diagnosed with a preoperative endoscopic biopsy. In this report, we discuss the appropriate approach for cases similar to ours based on the case and a study of the related literature.

Case Report

A 61-year-old man was referred to our department from another hospital for a detailed examination of a rectal submucosal tumor (SMT). The patient had a history of colon cancer in the ascending colon for which he had undergone surgical treatment. He had also been prescribed an anticoagulant (rivaroxaban 10mg/day) to treat a trial fibrillation. This SMT was incidentally detected during a colonoscopy to investigate the origin of bloody stool. It was suspected

that the bloody stool was caused by a diverticulum. The patient was asymptomatic on first examination. The initial laboratory evaluation showed mild anemia (10.4g/dl) and mildly elevated aspartate transaminase and alanine aminotransferase levels (AST/ALT 48/59 U/L). A colonoscopy was performed to examine the SMT in minute detail. A yellowish SMT in the rectum, approximately 5 mm in diameter, was identified (Figure 1a,1b). Endoscopic ultrasonography showed a well-demarcated, homogenous, hypoechoic mass located in the third layer (Figure 1c,1d). A rectal NET was initially suspected, but the histopathological examination of several endoscopic biopsies of this lesion proved inconclusive. Therefore, we performed an endoscopic mucosal resection with ligand (EMRL) of the SMT and submitted the entire specimen for histopathological analysis (Figure 2a).This indicated that the tumor cells formed a well-defined mass located in the submucosal layer and contained eosinophilic and granular cytoplasm (Figure 2b, 2c, 2d). Immunohistochemical analysis showed that the tumor cells were positive for neuron-specific enolase and S-100 protein (Figure 2e,2f). This SMT was diagnosed as a rectal GCT.

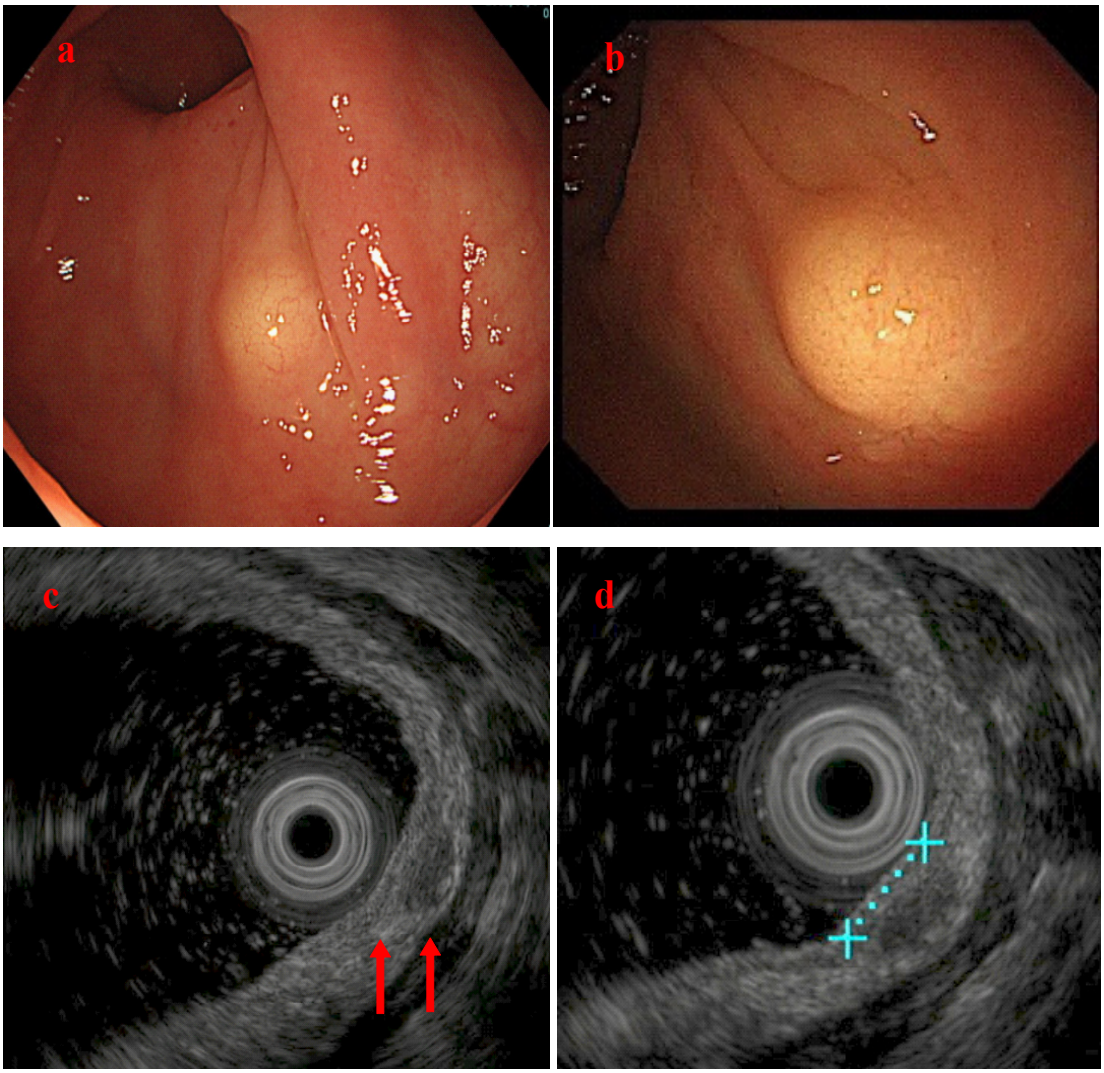

Fig 1. Endoscopic and endoscopic ultrasonography images

(a,b) Endoscopic image of the rectal tumor. A yellowish SMT approximately 5 mm in diameter is seen in the rectum.

(c,d) Endoscopic ultrasonography showing a well-demarcated, homogenous, hypoechoic mass located in the third layer (20MHz).

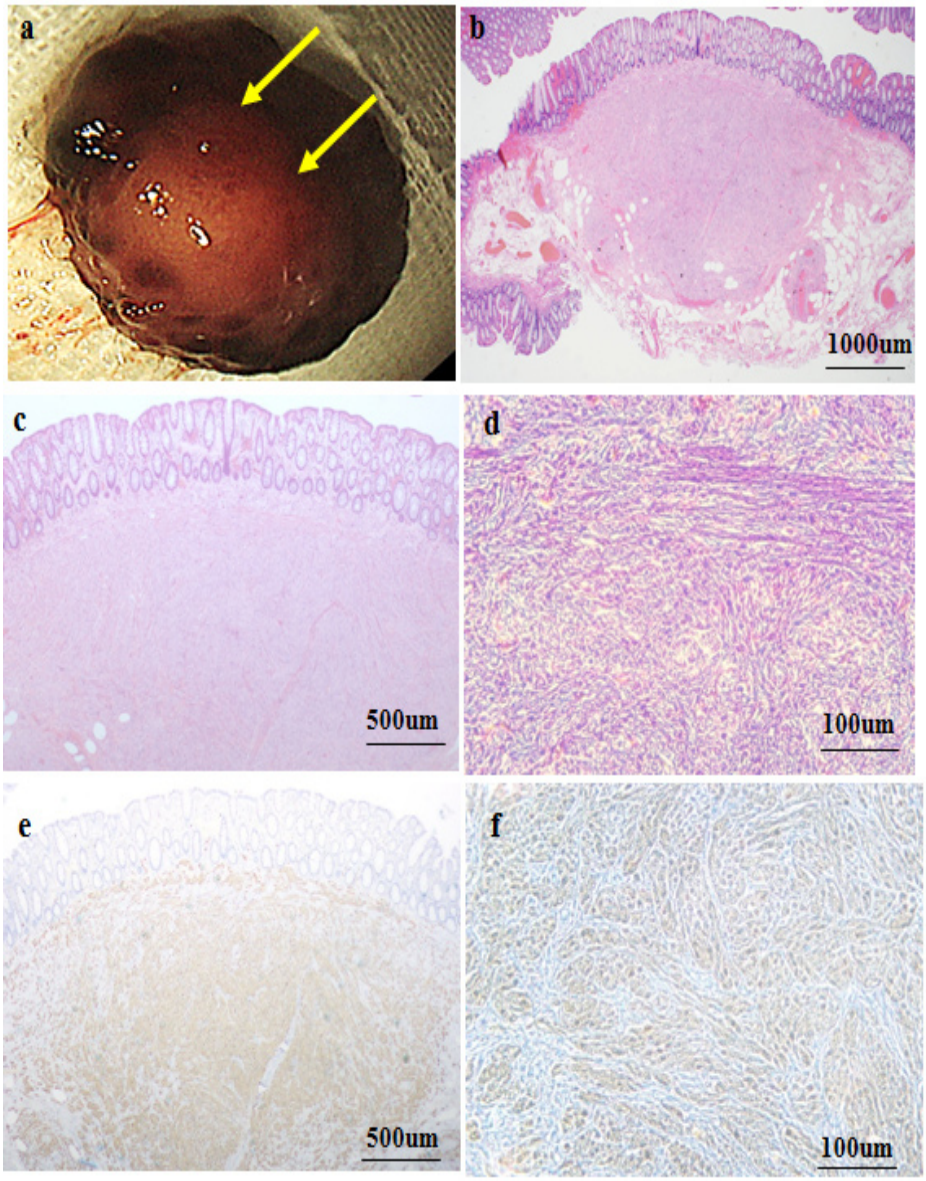

Fig 2. Gross specimen and histological findings of the resected tumor

(a) Gross specimen of the resected lesion

(b,c) Hematoxylin and eosin (H&E) staining showing a tumor in the submucosal lesion (b×20, c×40)

(d) Magnified image showing the tumor had eosinophilic and granular cytoplasm and formed a well-defined and non-uniform large cells with small round nuclei (×400).

(e,f) Immunohistochemical staining for S-100 protein was positive (e,×40, f,×400).

Discussion

GCTs are derived from Schwann cells. GCTs can occur in any organ, and while infrequently found in the gastrointestinal system, it is most often reported in the esophagus, the colon, and the stomach[1]. Approximately 28% of gastrointestinal GCTs occur in the colorectum. Colorectal GCTs occur more in men and is often seen in patients between the ages of 40 and 60 years. Colorectal GCTs are predominantly located on the right side of the colon[2-4]. Rectal GCTs are rare, in fact, Kawano et al. summarized the cases of colorectal GCTs in Japan and reported that only 2 cases[5] of the 37 colonic GCTs were found in the rectum.

Colorectal GCTs are reportedly identified during other procedures because they are usually small (<10mm) and asymptomatic. During the endoscopic examination, colorectal GCTs appear as a submucosal tumor that has a yellowish or white color[4,6]. Endoscopic ultrasound (EUS) can provide a qualitative description of gastrointestinal SMTs, such as tumor size and the invasion depth. EUS shows that gastrointestinal GCTs comprise a well-defined, solid, and homogenous hypoechoic mass that occurs deep in the submucosal layer[7].The endoscopic and EUS findings in our case are characteristic of gastrointestinal GCT. However, these features also extremely closely mimic the appearance of colorectal NETs, and distinguishing between these two tumor types using only endoscopic and EUS methods is very difficult.

Histopathological findings are useful for differentiating these tumors. The histopathological features of gastrointestinal GCTs include well-defined, relatively large cells with alveolar growth and eosinophilic and granular cytoplasm. Immunohistochemical analysis indicates that the cytoplasm of GCT cells is positive for the S-100 protein[8].

Though it is possible to diagnose gastrointestinal GCTs through biopsy, the diagnosis rate of colorectal GCTs on endoscopic biopsy is approximately 50% because GCTs can occur from the mucosal muscle layer to the submucosal layer and the main lesion exists under the mucosal epithelium[4]. Therefore, the preoperative diagnosis of colorectal GCTs is often difficult. Colorectal NETs are epithelial tumors that resemble an SMTform[4]and can be diagnosed using endoscopic biopsy with high probability. In our case, while several endoscopic biopsies were performed, diagnosis was not successful. This difficulty may point to a possible GCT.

While a GCT is a benign tumor, 2% undergo malignant transformation[9]. Signs of potential malignant transformation include a large tumor size (>3cm), rapid tumor growth, and ulceration. Malignant transformation of a colonic GCT has been documented[10]. However, Fanburg-Smith et al. reported six histologic criteria for malignant GCTs; necrosis, spindling, vesicular nuclei with large nucleoli, increased mitotic activity (>2 mitoses/10 high-power fields at ×200 magnification), high nuclear-to-cytoplasmic ratio, and pleomorphism when three or more of these items are defined as malignant[11].

The first treatment for a benign GCT is an endoscopic resection, such as endoscopic mucosal resection with ligand (EMRL) or endoscopic submucosal resection (ESD)[6]. When a diagnosis is difficult, the tumor has no signs of malignancy, and endoscopic resection is feasible, endoscopic resection for diagnosis and treatment may be recommended. In our case, EUS indicated that the tumor was located in the third layer and was small. Therefore, EMRL was performed for diagnosis and treatment. If the tumor cannot be resected using endoscopy, for example, if the tumor is large or potentially malignant, surgical resection is an option[2]. A report suggested that recurrence was extremely rare when complete resection was performed; therefore, the prognosis was good[3].The follow-up protocol is not clear. Chen et al. reported the following protocol: Patients with lesions <1 cm, and no histological malignancy signs were followed up annually. Patients with tumors >1 cm or possible histological malignancy signs were supervised every 6 months for the first 2 years and annually after that. They also reported all patients were monitored for recurrence using computed tomography scans, endoscopy, and EUS, and there were no patients with recurrence [3]. A follow-up after one year seems good for our case as well.

In conclusion, colorectal GCTs, and rectal GCTs, in particular, are rare. As the endoscopic features of colorectal GCTs and colorectal NETs are extremely difficult to distinguish, diagnosis of GCTs can be very challenging. When a colorectal lesion cannot be diagnosed, despite multiple endoscopic biopsies, GCT should be included in the differential diagnosis. Even without signs of malignancy, endoscopic resection for diagnosis and treatment may be recommended.

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