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Case Report

Incidental granular cell tumor at the ileocecal junction mimicking a lymph node metastasis in a patient with history of neuroendocrine tumor of the right colon

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Abstract: Granular cell tumors are rare neoplasms originating from Schwann cells found in various organs. GCTs are seldom reported in the gastrointestinal tract. Pre-operative detection and diagnosis of colonic GCTs is challenging since the tumors are mainly asymptomatic, small, slow-growing, and submucosal. Most of these tumors are benign in histopathology and behavior. Recently, there has been greater insight into the varying presentations and behaviors of colonic GCTs with atypical histopathologic features. To contribute, we describe a GCT (2.3 cm) at the ileocecal junction found incidentally during follow-up for an excised ileal neuroendocrine tumor in a 65-year-old woman. Our GCT had an unusual focal atypia and infiltrative behavior into the pericolonic adipose tissue without metastasizing to the lymph nodes. These features are important since GCTs have a propensity for local recurrence if incompletely excised, which could have been easily missed. Even though GCTs with atypical features have low rates of recurrence and metastasis, they require close and careful attention in the absence of specific management guidelines due to potential aggressive behavior.

Keywords: Granular cell tumor, atypical features, colonoscopy

Introduction

Granular cell tumors (GCTs) are rare soft tissue tumors with neuroectodermal differentiation and Schwannian derivation. They typically present as small, nodular, non-ulcerative, and solitary growths with minimal symptoms [1]. Imaging narrows the differential diagnosis, while a careful microscopic examination is needed to confirm the diagnosis because some non-neural tumors show similar granular accumulations in the cytoplasm [2]. Alterations in V-ATPase accessory genes are seen in more than 70% of GCTs and are considered pathognomonic [3]. GCTs exhibit a female predominance, peak incidence in the fifth to sixth decades, and are overrepresented in black versus white populations [4]. Most GCTs occur in the head and neck region [4]. Fewer (5-11%) lesions are in the gastrointestinal tract, where the esophagus is the preferred site [5]. The incidence of GCTs in the colon may be increasing due to screening, either performed during a routine medical examination or when indicated for other symptoms [6].

Of the approximately 150 cases of colonic GCTs [7], only a few are with tumors with malignant histopathologic features or malignant behavior [8].

Our case describes a right-sided colonic GCT in a 65-year-old woman with a history of colorectal concerns and multiple comorbidities. The primary aim was to emphasize aspects of our patient's GCT, including its borderline histopathologic features of malignancy. The tumor arose in the submucosa and extended into the pericolic adipose tissue, where it showed its predominant growth, mimicking a lymph node metastasis. These findings are pertinent because GCTs are generally benign and reside superficially in the submucosa or mucosa. Regional and distant metastasis is rare. Our secondary aim was to highlight our case as the first on a colonic GCT co-occurring with an ileal

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neuroendocrine tumor. Improvements to management require continued effort to describe these tumors' idiosyncrasies.

Case report

A 65-year-old woman with a history of diverticulosis, diabetes, smoking, and a family history of colorectal and renal cancers underwent a recommended colonoscopy for a 10-month history of intermittent pain in the right lower quadrant and cramps in the lower pelvis.

The colonoscopy identified a 5 mm mass that was consistent with a well-differentiated neuroendocrine tumor (NET) grade 1 in her terminal ileum. The margin was positive for the tumor. A partial laparoscopic ileocolectomy was performed. After tumor resection, a round mass measuring 1.8 × 12.5 cm was identified in the adjacent mesentery with 68 Ga-DOTATATE PET/CT. No areas of focally increased radiotracer uptake were seen in the terminal ileum.

On gross examination, the mucosa was unremarkable. However, a 3 mm focus of subserosal fibrosis and a 2.3 × 2.1 × 1.9 cm subserosal white-tan solid mass at the ileal-colonic junction were identified. The 2.3 cm mass was located 4.5 cm from the ileal resection margin, 9.4 cm from the colonic resection margin, 3.2 cm from the radial margin, and no serosal puckering was identified.

Microscopic examination demonstrated two distinct tumors. The first tumor was identified in the ileal submucosa and was consistent with a residual NET measuring 3.5 mm in the greatest dimension. Two mitoses per 2 mm^2 were identified. Immunohistochemical stains showed that the tumor cells were positive for synaptophysin and chromogranin. Ki-67 showed a low proliferative index (<3%). The resection margins were negative for tumor. No lymphovascular or perineural invasion or serosal involvement was identified. One of 19 lymph nodes was positive for metastatic NET.

The second tumor consisted of a 2.3 cm well-circumscribed mass composed of eosinophilic cells with polygonal shape, abundant granular cytoplasm, and small round-to-ovoid nuclei. The tumor arose in the submucosa but was predominantly located in the pericolonic tissue at the ileocecal junction (**Figure 1A**). Most of the tumor showed well-circumscription (mimicking a lymph node metastasis of the NET). However, it spread in an ill-defined manner into the adjacent adipose (**Figure 1B-D**) and abutted but did not invade the serosa or the lymph node hilum (**Figure 1E**). Focal atypia was identified. Focal nuclear enlargement with and without prominent nucleoli (**Figure 1F-J**) and tumor spindling (**Figure 1K-M**) were identified. However, no mitoses, pleomorphism, or necrosis was seen. The cytoplasmic granules were Periodic acid Schiff-positive and diastase-resistant (**Figure 1N**). The tumor cells were strongly and diffusely positive for CD68, S100, SOX10 (**Figure 1O-Q**) and inhibin. The Ki-67 proliferative index was <2% (**Figure 1R**). The morphology and immunoprofile supported the diagnosis of a GCT with focal atypical features. The resection margins were negative for tumor, and no lymph node metastasis was identified in 19 lymph nodes submitted for microscopic examination.

The clinical team did not recommend additional treatment. However, the patient has been scheduled for further follow-up.

Discussion

GCTs were first described in the tongue by Abrikosoff in 1926. Since then, GCTs have been reported in various anatomic locations, but colonic GCTs remain rare. The ascending colon, followed by the cecum, are the most common sites. Most colonic GCTs are detected incidentally on endoscopy, where they appear as submucosal masses that are yellow-white, sessile, small (<20 mm), and round masses covered by normal mucosa. Endoscopic ultrasound is also helpful for detecting the depth of tumor invasion to facilitate assessment. Still, endoscopic methods and macroscopic examination can confuse colonic GCTs for similarly sized, shaped mimics. Histopathology remains the gold standard for definite diagnosis [9].

The histopathologic features of colonic GCTs have been extensively described and aligned with those seen in our patient. Most colonic GCTs are <2 cm, well-separated from the muscularis propria, and tend to follow a benign course [10]. GCTs with non-benign histology may behave malignantly. In 1973, Fanburg-Smith determined six histologic features predictive of malignant behavior: 1) presence of necrosis, 2) spindling, 3) vesicular nuclei with

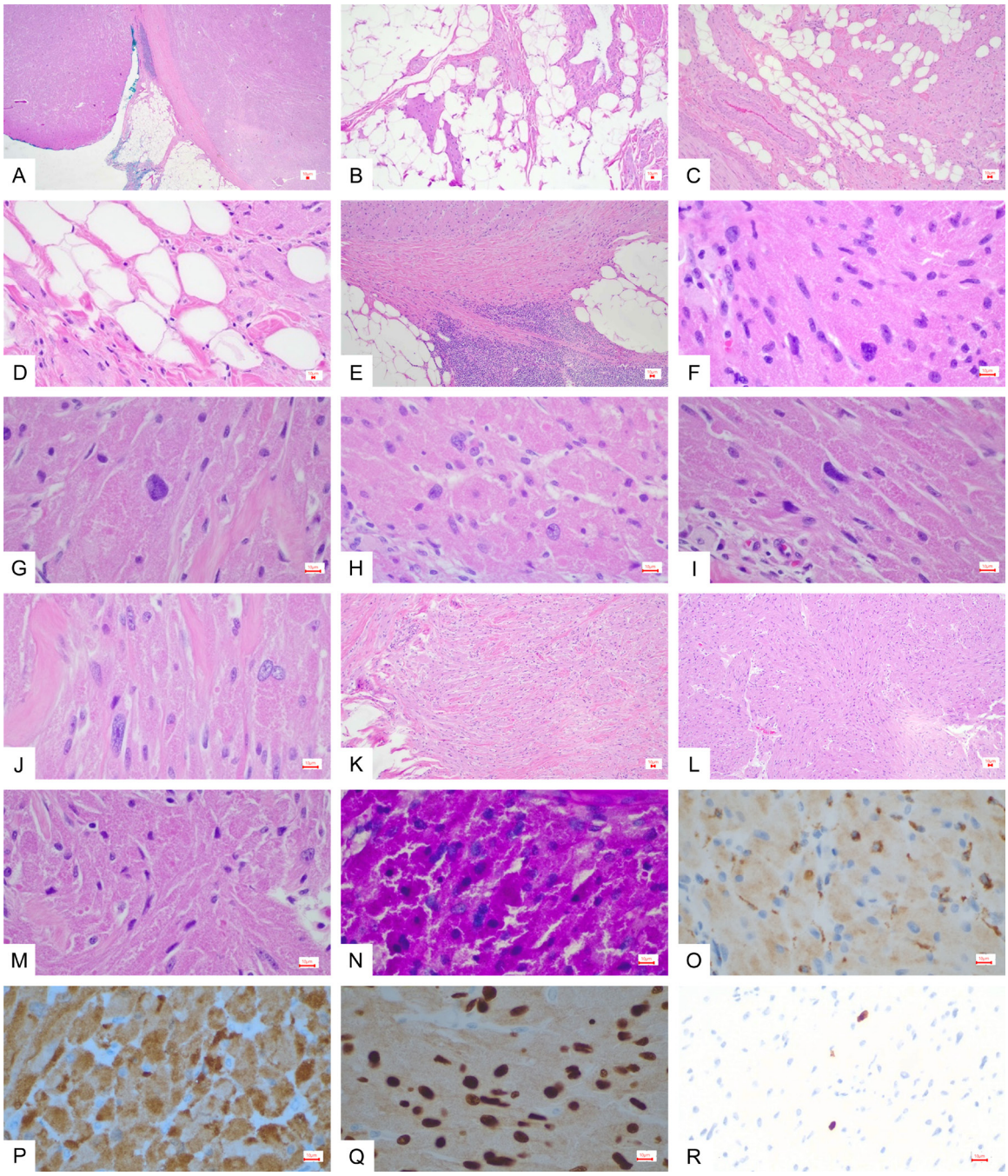

Figure 1. A. Granular cell tumor identified in the pericolonic tissue abutting the serosa (H&E, 2×). B-D. Representative images of the tumor showing wide infiltration into the pericolonic tissue (H&E, 4×, 10×, and 40×, respectively). E. Tumor abutted but did not invade the lymph node hilum (H&E, 10×). F-J. High magnification of the tumor displays foci of nuclear enlargement with hyperchromatic nuclei. J. Focal vesicular nuclei and prominent nucleoli are well-visualized (H&E, 60×). K-M. Foci of tumor spindling (H&E, 10×, 10×, and 60×, respectively). N. Cytoplasmic granules of tumor cells were diastase-resistant (Periodic acid Schiff stain, 60×). O-Q. Tumor cells were positive for CD68, S-100, and SOX10 (Immunohistochemistry stains, 60×, respectively). R. The tumor had a low proliferative index <2% (Immunohistochemical stain, 60×).

prominent nucleoli, 4) mitotic activity (at ×400 magnification >2 mitoses/10 high power field), 5) high nuclear to cytoplasmic ratio, and 6) pleomorphism. GCTs with three or more are considered malignant, and those with 1 or 2 are atypical [11].

Epidemiological factors (older patient age), tumor features (atypia, larger tumor size), and clinical behavior (local recurrence, metastasis) have been identified as independent risk factors of poor survival in GCT patients [11]. Malignancy can be proven only by clinical findings, especially metastasis; therefore, clinical suspicion and not histologic malignancy have guided tumor management [12]. However, metastasis of atypical tumors is rare, and local recurrence rates are akin to those seen in incompletely excised benign tumors [13]. Most colonic GCTs reported in the literature are histologically benign [9]. To date, there are 2 case reports of colonic GCTs - sigmoid colon and ileocecal valve - with atypical histology. Lymph node and vessel invasion and rapid tumor growth were appreciated for the sigmoid colon GCT at 1-year follow-up [12]. It is unclear whether aggressive behavior was reported for a GCT on the ileocecal valve [6]. In our patient, focal atypia was identified without concomitant lymph node metastasis.

Our case mimicked lymph node metastasis due to its roundness on imaging and detection in the pericolonic adipose tissue. GCTs may have infiltrative growth patterns, but invasion of surrounding tissues has not been shown to confer unfavorable outcomes in benign tumors [13]. Infiltration has not been reported in histologically atypical GCTs before now.

Best management practices for GCTs in the gastrointestinal region with suspicion of malignancy are lacking because only 1-2% of GCTs are malignant. Most authors are in favor of endoscopic resection, and a strict 1-year follow-up has been encouraged due to local recurrence rates of malignant tumors. Others advocate for conservative management following biopsy to prevent complications from endoscopic resection [6]. In our case, the tumor showed focal atypical features and infiltration of the fat without lymph node metastasis, which could have been missed with biopsy. Lymph node metastasis could have also been missed without careful examination and sampling of the regional lymph nodes. As information on colonic GCTs grows, efforts to record and monitor tumor invasion into pericolic fat should, too. Local infiltrative behavior could be an adverse prognostic factor for local recurrence and malignant potential in atypical GCTs.

Few reports of synchronous gastrointestinal neoplasms have been documented [14]. GCTs, in general, have been associated with carcinomas [15]. To our knowledge, this is the first reported case of an ileal NET and colorectal GCT collision tumor, widening the spectrum of associations for these pathologies.

In summary, GCTs with atypical or borderline malignant features complicate the management of an already understudied, rare tumor. Further understanding of GCTs' histology and behavior, especially atypical GCTs, is warranted.

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Disclosure of conflict of interest

None.

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References

[1] Rehan S, Paracha H, Masood R and Wang R. Granular cell tumor of the abdominal wall, a case report and review of literature. AME Case Rep 2021; 5: 28.

[2] Aggarwal A, Joshi S and Bhullar JS. Affinity of colonic granular cell tumor within the right colon: case report and review of literature. Open Access Surgery 2023; 16: 115-119.

[3] Torrado C, Camaño M, Hindi N, Ortega J, Sevillano AR, Civantos G, Moura DS, Dimino A and Martín-Broto J. Antiangiogenics in malignant granular cell tumors: review of the literature. Cancers (Basel) 2023; 15: 5187.

[4] Saleh M, Sarahneh HA, Hroub SI, Diab LK, Elatawneh TM, Wredat SB and Abubaker AN. A rare case of malignant granular cell tumor of the cheek in a 16-year-old child: a case report. Ann Med Surg (Lond) 2023; 85: 4581-4585.

[5] Dias E, Santos-Antunes J, Santos AL, Coelho R, Melo D and Macedo G. Colonic granular cell tumor identified in an adenomatous polyp. Gastroenterol Hepatol 2022; 45 Suppl 1: 41-42.

[6] Gapp J, Gross J, Chintalacheruvu L and Reddymasu S. Coexisting granular cell tumor and tubular adenoma of the ileocecal valve. Case Rep Gastroenterol 2018; 12: 7-12.
[7] Dhruv S, Atodaria KP, Gurala D, El Imad T and Abergel J. Granular cell tumor of the ascending colon. Case Rep Gastroenterol 2023; 17: 104-108.
[8] Cha JM, Lee JI, Joo KR, Choe JW, Jung SW, Shin HP and Lim SJ. Granular cell tumor of the descending colon treated by endoscopic mucosal resection: a case report and review of the literature. J Korean Med Sci 2009; 24: 337-341.
[9] Chen Y, Chen Y, Chen X, Chen L and Liang W. Colonic granular cell tumor: report of 11 cases and management with review of the literature. Oncol Lett 2018; 16: 1419-1424.
[10] Ramai D, Lai J, Changela K and Anand S. Colonic granular cell tumor: an endoscopic and histopathologic review with case illustration. Cureus 2018; 10: e2015.
[11] Fanburg-Smith JC, Meis-Kindblom JM, Fante R and Kindblom LG. Malignant granular cell tumor of soft tissue: diagnostic criteria and clinicopathologic correlation. Am J Surg Pathol 1998; 22: 779-794.
[12] Choi SM, Hong SG, Kang SM, Chae BG, Kim SJ, Park PK and Park HS. A case of malignant granular cell tumor in the sigmoid colon. Clin Endosc 2014; 47: 197-200.
[13] Machado I, Cruz J, Lavernia J and Llombart-Bosch A. Solitary, multiple, benign, atypical, or malignant: the "Granular Cell Tumor" puzzle. Virchows Arch 2016; 468: 527-538.
[14] Alshammari T, Alshammari S, Hakami R, Alali M, Aljohani T, Zayed MA and Bin Traiki T. Two histologically different primary malignancies: synchronous obstructive descending colon adenocarcinoma and appendicular carcinoid tumor. Am J Case Rep 2020; 21: e921810.
[15] Said-al-Naief N, Brandwein M, Lawson W, Gordon R and Lumerman H. Synchronous lingual granular cell tumor and squamous carcinoma. A case report and review of the literature. Arch Otolaryngol Head Neck Surg 1997; 123: 543-547.