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Case Report

Gastrointestinal granular cell tumour, endometriosis and appendiceal intussusception-a unique report

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ABSTRACT

Granular cell tumours (GCT) are uncommon, typically benign growths that can appear in various parts of the body, though they most frequently manifest in the oral cavity. The overall frequency of GCT in surgical samples is under 0.05%. Between 5% and 11% of GCT cases are found within the gastrointestinal system, with the oesophagus, colon, and stomach being the most commonly affected sites. This article presents a rare case of appendiceal intussusception caused by an endometriosis nodule, which led to the discovery of a granular cell tumour in the surgical specimen.

Keywords: Granular cell tumour, Endometriosis, Appendiceal intussusception, Gynecology, General surgery, Emergency department

INTRODUCTION

Granular cell tumour (GCT) are rare, predominantly benign lesions that occur in various parts of the body, primarily in the oral cavity. The first description of GCT dates back to 1926 when Russian pathologist Abrikossoff documented 5 cases of tongue tumour. Initially it was believed that they originated from skeletal muscle, coining the term "granular cell myoblastoma." Subsequent ultrastructural and immunohistochemical studies, including the observation that these tumours are typically positive for the S-100 protein, suggest that they are of Schwann cell origin. Interestingly, a subset of GCT that do not exhibit S-100 positivity, referred to as "non-neural" GCT, has been recognized, indicating a non-neural origin for some cases. The first reported case of an S-100 negative, non-neural GCT was in 1991.[1-3] The underlying cause of GCT remains poorly understood, with limited knowledge about their genetic basis and pathophysiology. Recent advancements in whole-genome sequencing have identified recurrent mutations associated with specific syndromes, but the genetic drivers behind sporadic GCT formation are only beginning to emerge.[1-3]

Epidemiology

GCT are rare. A study conducted by Lack and colleagues at a single institution over a 32-year period reported an incidence of only 0.03% in surgical specimens.[4] These tumours can occur in individuals of all ages and genders but are most commonly seen in women in their 40s to 60s.[2,3] Two-thirds of benign GCT cases have been observed in African American patients. A more recent study involving 113 patients with malignant cutaneous GCT found that over 70% of those affected were Caucasian. In 10% to 15% of cases, especially among

African American patients, multiple GCT may develop.[3,5,6]

Presentation and location

These rare tumours most frequently arise in the skin, oral cavity, digestive tract, and subcutaneous tissue, although they can develop in other areas such as the breast, bladder, nervous system, and respiratory and genitourinary tracts.[1-3] The head and neck region are involved in 45% to 65% of cases.[3]

GCT typically present as painless, well-defined nodules smaller than 3 cm in diameter, most commonly affecting the tongue, skin, or subcutaneous tissue. Location in the gastrointestinal tract is a rare form of presentation, which accounts for only about 5% of cases, it typically presents as a well-circumscribed submucosal mass and are often discovered incidentally during endoscopic or surgical procedures.[1-3] When present in the gastrointestinal tract they are most often found in the esophagus, colon, or stomach.[6,7]

GCT of the appendix are extremely rare, with only 12 cases reported in the medical literature over the last 50 years.[2] Although GCT are usually solitary, 7% to 29% of patients may present with multiple lesions, and 30% of those involve the skin and subcutaneous tissue.[3] Approximately 1% to 2% of GCT are malignant, based on histological or clinical criteria.[7]

Prognosis

The majority of GCT are slow-growing and have a benign course. However, based on histological features or the presence of metastasis, 1% to 2% of GCT may become malignant, and in these cases, the prognosis is poor, with limited treatment options beyond surgical removal.[3]

CASE REPORT

A 39-year-old female patient presented to the emergency department with abdominal pain in the right lower quadrant. No irradiation was present and no changes in the intestinal habits were marked. Past medical history showed an iron deficiency anaemia, thyroidectomy due to goiter and infertility with 2 tries of artificial insemination. The patient was medicated with anti-depressants and thyroid hormone substitute. Abdominal evaluation revealed a painful palpation on the transition of the right iliac fossa to the hypogastric region with rebound tenderness. Blood samples showed leukopenia (2100 µl), anaemia (10.6 g/dl) and elevation on inflammatory response (C-reactive protein of 131 mg/l). A computerized tomography (CT) was performed in the same day in a private institution revealing fatty tissue densification, free liquid and localized pneumoperitoneum in an infracecal topography. Centered in these changes a tubular structure with a diameter of 15 mm was noted and the hypothesis of a complicated appendicitis was highlighted. The patient was then proposed for an exploratory laparoscopy. Intraoperatively, in the vesical-uterine pouch, serosanguineous liquid and local inflammatory process involving sigmoid colon, uterus and right fallopian tube was observed. No appendix was observed. In the confluence of the taenia coli a purple spot and local inflammation was noted. Inside of the cecum a mass was palpable. The gynecologist's opinion was sought and endometriosis was suspected, even though it did not explain the cecal mass. The surgeons opted by converting to laparotomy and an ileocecectomy with an isoperistaltic side-to-side anastomosis was performed with removal of the right Fallopian tube.

The surgical specimen and its markings are shown in Figure 1. Post-op was complicated by a superficial surgical site infection treated with antibiotics and the patient had an otherwise uneventful hospital stay and was discharge by day 12.

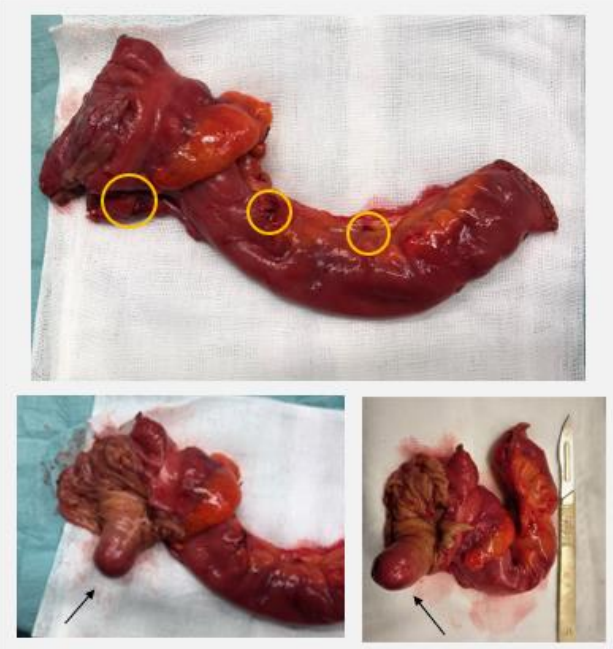

Figure 1: Top image showing the ileocectomy specimen. Notice no visualization of the appendix and yellow circles outlining purple lesions, compatible with endometriosis. Bottom images showing opened cecum with intussusception of the appendix-arrows.

DISCUSSION

As with most GCTs, colorectal GCTs are often incidentally found during colonoscopy as solitary submucosal tumors. In other cases, patients may present with hematochezia, abdominal pain, altered bowel habits, or constipation.[1] Our patient, a 39-year-old woman with no personal or family history of colorectal cancer, inflammatory bowel disease, or polyps, had never

undergone a colonoscopy prior to this diagnosis. Similar to esophageal GCTs, colorectal GCTs typically appear as small, yellow submucosal tumors. Endoscopically, they may resemble sessile or, less frequently, pedunculated polyps, with most lesions measuring less than 2 cm in diameter 1. Differential diagnoses include lipomas, adenomas, and hyperplastic polyps, which are much more common.

Following the definitive diagnosis, a thorough review of the patient's medical history was conducted to assess related symptoms. The patient reported intermittent abdominal pain without changes in bowel habits, which appeared to be more related to her underlying endometriosis than the GCT. Although iron deficiency anemia can result from chronic intestinal blood loss associated with GCT, the patient had not noticed any significant changes in her stool.

Given their small size and indolent behavior, GCTs are generally asymptomatic. However, when GCTs involve the appendix, obstruction can lead to secondary appendicitis, though intussusception of the appendix is rare regardless of etiology.[2,8] We believe that the endometriosis nodule at the base of the cecum may have contributed significantly to these findings. The diagnostic workup for colorectal GCTs typically includes colonoscopy, endoscopic ultrasound (EUS), and biopsy.

These tumors can exhibit marginal or infiltrative growth patterns, and a subset may present with reactive mucosal changes, nuclear pleomorphism, lymphoid aggregates, or focal calcifications. These pronounced surface changes can lead to misdiagnosis, particularly as tubular adenomas or adenocarcinomas on mucosal biopsy. Thus, diagnosing colorectal GCT can be challenging, even with histopathological examination.[1,8] EUS is an essential diagnostic tool, providing information on the lesion's echogenicity and depth of invasion.[8] Typical findings include a hypoechoic and homogeneous mass. However, EUS is not always reliable in distinguishing between benign and malignant lesions. While it is helpful in identifying the submucosal origin of the tumor, clinical and radiological criteria for definitive diagnosis remain limited.

Regular ultrasound is the first-line imaging modality for abdominal pain. CT scan, while not typically the first choice for imaging in the Emergency department, can be particularly useful in differentiating between potential causes of symptoms, especially in obese patients where ultrasound sensitivity may be reduced. In this case, a CT scan was performed in a private institution. There are no standard treatment guidelines for colorectal GCTs.[1,2,8] Tumors smaller than 2 cm are generally managed with endoscopic mucosal resection, which is considered safe and effective in the majority of cases, with over 70% experiencing no complications. Surgical treatment is typically reserved for cases with suspicion of malignancy, contraindications to endoscopic resection, or multiple symptomatic tumors.[1] Alternative treatment options, such as dehydrated alcohol injections, polidocanol, and YAG laser ablation, have also been proposed. Endoscopic resection remains advantageous due to the ability to obtain tissue for diagnostic purposes.

The treatment of GCT remains controversial due to its rarity. Whether these tumors should be monitored for changes in size or immediately resected is often debated.[8] If removal is necessary, endoscopic treatment is less invasive, more cost-effective, and associated with fewer complications compared to surgical resection. Nevertheless, complete excision with negative margins is the most effective treatment, achieved either endoscopically or surgically and recurrence rates are reported to be between 2% and 8%. For GCTs involving the appendix, laparoscopic appendectomy may be indicated, as these cases often present with appendicitis.

In this case, the decision to perform an ileocecectomy was based on a multidisciplinary evaluation. The presence of pneumoperitoneum on imaging raised significant concern for the potential of sepsis due to localized perforation, warranting resection. Intraoperatively, the intracecal mass was found to be of concern, with clear evidence of intussusception of the appendix and inflammatory changes. These findings were consistent with the elevated inflammatory markers observed in the patient's blood samples, further confirming the need for urgent surgical resection.

Anatomical pathology

Histology analysis revealed an intussusception of the appendix with endometriosis lesions. In the cecum, a lesion of 0.5cm was noted. The immunohistochemistry analysis revealed s100+, cd68+, ae1/ae3-, dog1- e cd117- compatible with a granular cell tumour.

CONCLUSION

Granular cell tumours are exceptionally rare, particularly when found within the gastrointestinal tract. This case highlights an unusual presentation of appendiceal intussusception caused by an endometriosis nodule, which led to the unexpected discovery of a granular cell tumour in the surgical specimen. Given the rarity of this condition, there is a limited number of articles in the literature that describe this pathology in detail.

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