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Case Report

Incidental Finding of Goblet Cell Adenocarcinoma Post Appendectomy: A Rare Case Report

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Abstract

Introduction: One of the most frequent etiologies of an acute abdomen is appendicitis, which ranks as one of the primary reasons for surgical emergencies globally. Goblet cell adenocarcinoma (GCA) of the appendix, is hallmarked for displaying both endocrine and exocrine traits, presenting with symptoms similar to acute appendicitis, complicating its diagnosis before surgery.

Case Report: We present a case report of a 61-year-old male with a medical history of benign prostatic hyperplasia and depression who presented lower abdominal pain, fever, and diagnosed with acute appendicitis. A laparoscopic appendectomy was performed. Histopathology revealed GCA of the appendix with Ki-67 proliferative index of 10%. After multidisciplinary team (MDT) discussion and further evaluation, he underwent a right colectomy and hyperthermia intraperitoneal chemotherapy (HIPEC).

Conclusion: Goblet cell tumors are rare and often not readily recognized. A multi-disciplinary approach including a team of oncologists, pathologists, radiologists, and general surgeons is essential for the intricacy of diagnosis and therapy. Patients undergoing appendectomy due to appendicitis need a thorough evaluation of biopsy specimen to exclude malignancy.

Keywords: acute appendicitis, appendectomy, goblet cell adenocarcinoma, goblet cell carcinoid, hemi-colectomy

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1. Introduction

Appendicitis is one of the most common operative emergencies that necessitates an appendectomy. It is caused by fecalith obstruction, foreign bodies, gallstones, tumor of the cecum, or appendiceal tumors. Only 1% of these cases are cancer related [1]. Goblet cell adenocarcinoma (GCA) formerly known as goblet cell carcinoid is a very uncommon neoplasm. The most common location is the appendix, but it has also been documented in other locations such as the small intestine, colon, stomach, duodenum, biliary tract, and bronchus [2-4]. The typical age range of diagnosis is 52–58 years old, which is more in line with the estimated age of 60 for adenocarcinomas than the approximate age of 38 for appendiceal well-differentiated neuroendocrine tumor (NETs). Mucin-containing, goblet-like epithelial cells, which can cluster in the lamina propria of the appendix or submucosa while the mucosa itself is mostly intact, is the histologic signature of GCA [5]. With an incidence of 0.01–0.05 per 100,000 people annually, GCA is an uncommon variant of primary appendiceal adenocarcinoma, comprising 15% of all tumors arising in the appendix [6].

2. Case Report

A 60-year-old male with a medical history of long standing benign prostatic hyperplasia and depression. The patient came in with complaints of lower abdominal pain and fever. The lower abdominal pain that began suddenly the previous night, initially localized in the lower right quadrant, later spread across the entire lower abdomen. It was associated with high grade fever of 38.3°C and two episodes of loose motions. There was difficulty passing urine, flu-like symptoms, and he denied having any nausea, vomiting, and sick contacts. He had also not eaten any new foods recently.

On examination, the vital signs were as follows: blood pressure of 140/76, pulse of 110, temperature of 38.3°C, respiratory rate of 18 breaths/min, SpO2 of 99%, and BMI of 29.75 kg/m^2.

He appeared comfortable and in no distress in room temperature. In the abdominal exam, distension and tenderness were noted in the right iliac fossa (RIF) with positive rebound tenderness and suprapubic tenderness. The rest of the systemic examinations were unremarkable.

Septic markers and the rest of the biochemistry were unremarkable.

Urine analysis was pale yellow with traces of blood by strip, 5-10 RBC/HPF, occasional epithelial cells, and few mucus threads (otherwise normal). Urine culture revealed no growth.

For imaging, chest X-ray detected prominent bronchovesicular markings with peribronchial cuffing, likely indicating an inflammatory process. No obvious consolidation, pleural effusion, or pneumothorax were found. Cardiac size and configuration appeared normal.

As it is policy in Dubai Hospital to do CT scans for all patients aged >40 who present with appendicitis to rule out malignancy, a CT scan of the abdomen and pelvis with contrast was done for this patient.

The results of the CT scan (Figures **1**, **2**a, **2**b, and **2**c) demonstrated increased caliber of the appendix, measuring 8.5 mm, and mural wall enhancement and thickening with fat stranding in the surrounding tissue and minimal free fluid, pointing toward acute appendicitis. Other findings included mild fatty liver and a 4x3 cm left-sided fatty tissue inguinal herniation.

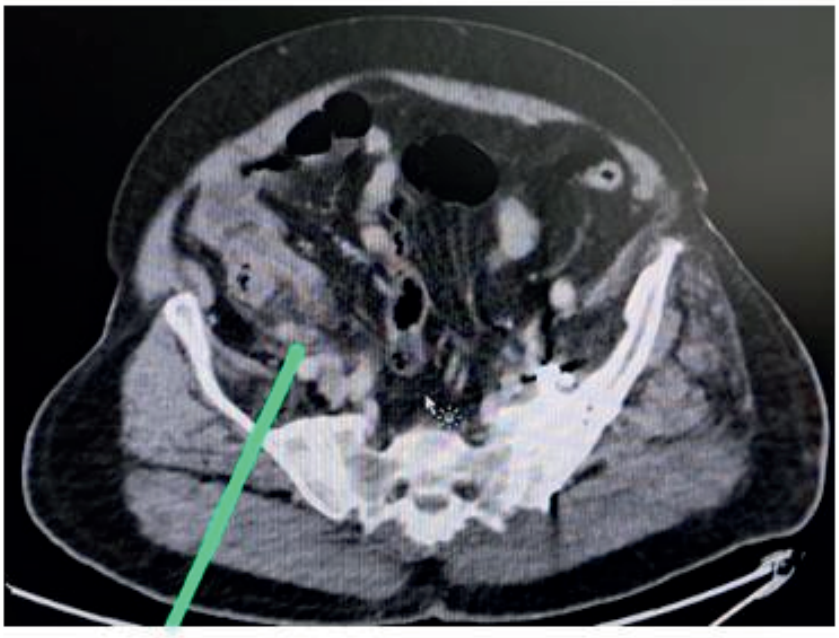

Figure 1: Pre-operative CT scan of abdomen and pelvis with contrast where the green line shows thick appendix and fat stranding.

He was diagnosed with a case of acute appendicitis with localized peritonitis based on clinical and radiological findings and was taken for a laparoscopic appendectomy.

Grossly, the appendix was an acutely inflamed retrocecal appendix with early mass formation. The body of the appendix was perforated with fecalith, and omentum wrapped around the perforation resulting in a contained perforation due to omental sealing at RIF. The base and cecum were healthy. There was free turbid fluid without any gelatinous or mucin material resembling that of infective origin in RIF and inflamed and dilated distal ileum adherent to phlegmon of the appendix was noted. There was no small bowel perforation except for congested terminal ileum and cecum near appendix phlegmon area with fibrin on serosal surface. From the diagnostic laparoscopic findings, there were no gross detection of mucin and malignancy was not suspected, so cytology was not done. The fluid was sent for analysis which showed *E. coli*, and the patient was treated with antibiotics according to the culture and sensitivity.

The final pathology report of the appendix concluded that it was a GCA of the appendix with involvement extending from the tip to the mid-portion of the appendix. The histomorphology features and immunohistochemical profile results are consistent with appendiceal goblet cell carcinoma–moderate to poorly differentiated: pT3 (Table **1**).

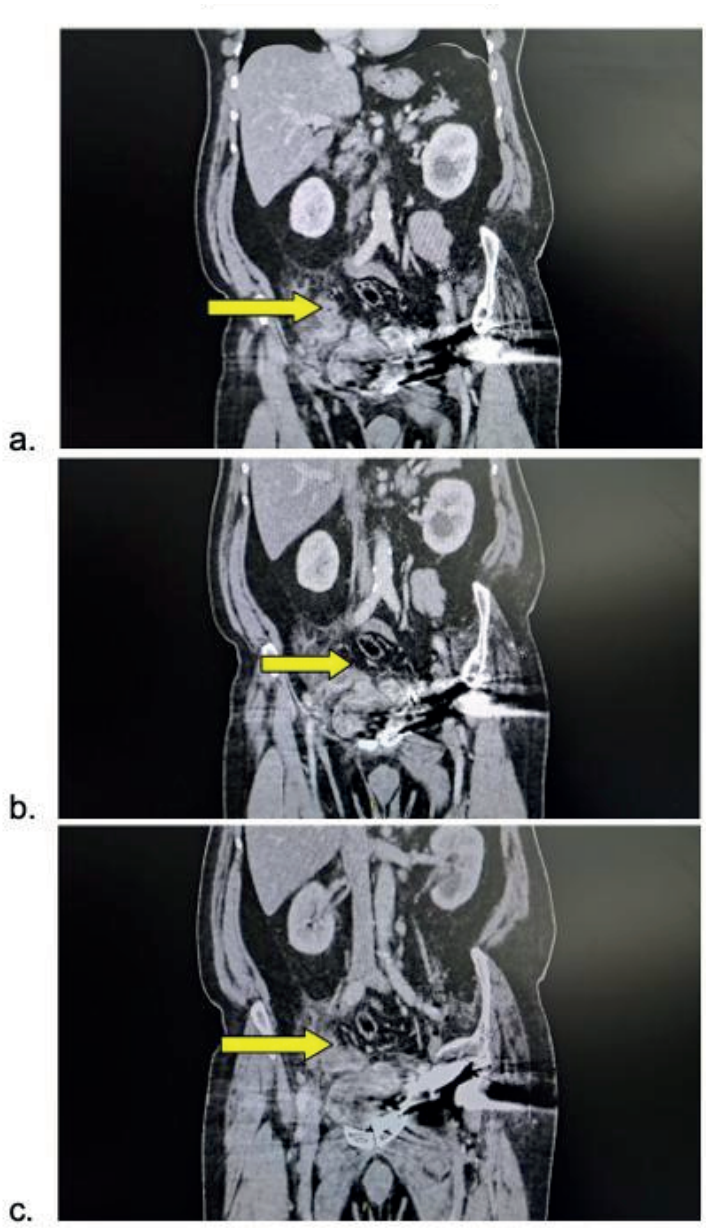

Figure 2: Pre-operative CT scans of abdomen and pelvis with contrast. Yellow arrows in all three images show thick-walled appendix with fat streaking around.

Based on the laparoscopic and histopathological findings, multidisciplinary team meeting concluded to obtain a contrast-enhanced CT scan of the chest and abdomen and to perform a colonoscopy. Because the tumor characteristics and a perforated appendix raised concern for peritoneal metastasis, they recommended proceeding with a right hemicolectomy and hyperthermic intraperitoneal chemotherapy (HIPEC) after discussing the treatment plan with the patient. The patient was brought to the clinic to discuss the findings and MDT decision. The CT scan of the abdomen, pelvis, and chest showed no suspicious findings to suggest metastatic disease. The colonoscopy revealed a small sessile polyp 6cm at the cecum, removed by cold snaring and internal piles. The mucosa of the rest of the colon

appeared normal. Histopathology of the polyp showed mild hyperplastic changes with no evidence of dysplasia or malignancy.

Table 1: Final histopathology report.

Tumor site	Half of the appendix (involving the tip and midportion)
Base of appendix involvement	Not identified
Histologic type	GCA
Tumor grade	G2-G3 (moderately to poorly differentiated)
Tumor size	1.0 cm (greatest dimension - microscopic measurement)
Tumor deposits	Not identified
Tumor extension	Invades through muscularis propria into subserosa and focally into the mesoappendix, not extending to the serosal surface
Lymph vascular invasion	Not identified
Perineural invasion	Focally present
Margin status for invasive carcinoma	All margins negative for invasive carcinoma
Immunohistochemical profile	CK7, CK20, CDX2, S100, Synaptophysin, CD56, MUC2, and MUC5AC showed diffuse positive reactions. Chromogranin was negative. Ki-67 index: 10%

The patient subsequently underwent a right hemicolectomy in addition to HIPEC and the final histopathology did not show any residual tumor.

3. Discussion

GCA was first described by Gagne et al. in 1969. GCA comprises primarily goblet cells, and Paneth and neuroendocrine cells can also be found. The cells often form tiny tubules, comparable to intestinal crypts. Tumor cells seldom exhibit cytologic atypia or mitotic figures, they include both neuroendocrine granules and mucin droplets, while also expressing epithelial and neuroendocrine markers [2]. GCA is more commonly found in the appendix, with clinical features ranging from acute appendicitis, chronic abdominal pain, to being asymptomatic [7]. These tumors have been referred to by several names, including mucinous carcinoid tumor, goblet cell carcinoid, well-differentiated adenocarcinoma, Aden carcinoid, crypt cell carcinoma, adenocarcinoma ex-goblet cell carcinoid, and mixed Aden neuroendocrine carcinoma [8]. The WHO officially classified GCA in 2019 [9].

Appendix malignancies are relatively rare, occurring in 0.5–1.4% of appendectomy patients [10]. Tumors are often discovered during a laparoscopy for a different reason or because of appendix inflammation and are seldom suspected prior to surgery [11]. In GCA, preoperative CT results vary, and no distinctive radiological characteristics are seen. This makes it difficult to diagnose until a histological evaluation. GCA is typically diagnosed incidentally based on postoperative histology. Cross-sectional imaging and postoperative staging are part of the diagnostic workup. Surveillance CT scanning is used as a follow-up to check for recurrence. To treat GCA, a right hemi-colectomy is the surgical option at

any stage of localized illness. Because women are more likely to develop gynecological metastases, a preventive bilateral salpingo-oophorectomy may also be performed. Systemic chemotherapy using a combination of 5-flurouracil (5-FU) is frequently utilized for more advanced illnesses. For patients with peritoneal spread, cytoreductive surgery combined with heated intraperitoneal chemotherapy (CRS-HIPEC) is utilized. The therapeutic efficacy of these treatment proposals is still unknown because there is limited amount of prospective data and no phase III trial evidence to back them up [12]. Indications for performing right hemicolectomy encompass lesions exceeding 2 cm, tumors situated at the base of the appendix, invasion into lymphatic channels, serosa and mesoappendix, regional lymph node metastases, mucin production (mucinous carcinoid tumors), cellular pleomorphism with a high mitotic index, and carcinoid tumor in children [13, 14].

In our case, the patient was diagnosed with GCA of the appendix based on a histopathological report post-laparoscopic appendectomy. Pre-operative CT abdomen and pelvis with contrast indicated symptoms of acute appendicitis but provided no indication of GCA, making the diagnosis practically impossible. As per the MDT approach, CT scans with contrast of the chest, abdomen, and pelvis and a colonoscopy were performed, all of which were unremarkable. Undergoing right hemicolectomy was advised. The key features in histopathology of our patient were invasion of tumor through muscularis propria into subserosa and focally into the mesoappendix with a Ki-67 proliferative index of 10% based on which he subsequently underwent right hemicolectomy in addition to HIPEC, as the appendix was perforated and there was suspicion of peritoneal spread. A Ki-67 proliferative index of 10% in GCA corresponds to a moderately proliferative tumor. The Ki-67 index is valuable for determining tumor aggressiveness, survival rates, and guiding treatment plans, as well as measuring the number of dividing cells [15, 16]. Having a high Ki-67 proliferation index indicates that the cancer is likely to grow and spread quickly. An index of Ki-67 proliferation over 30% is generally considered high. In some cancers, such as breast cancer, the Ki-67 proliferation index can help predict how well chemotherapy will work [17]. According to the WHO classification, a Ki-67 index of less than 3% signifies a low grade well-differentiated Grade 1 NET, while a Ki-67 index of 3-20% signifies an intermediate G2, and >20% signifies a high grade G3 [18]. In our case, the patient has a Ki-67 index of 10% which corresponds to G2, that is, moderately differentiated.

4. Conclusion

GCA of the appendix is usually incidentally detected on histopathological specimens of appendix taken out for acute inflammation. Ki-67 proliferation index correlates well with tumor aggressiveness and helps guide further management and prognosis. Decision for further oncological resection depends on tumor size, location, transmutation extent, and peritoneal spread. HIPEC is recommended for patients

with peritoneal spread or perforated tumors. This case emphasizes the importance of post-operative histopathology for appendectomy specimens to carefully look for any malignancy. Early detection may result in improved treatment methods and prognosis for this uncommon neoplasm.

Acknowledgments

None.

Statement of Ethics

This case report is conducted in accordance with the World Medical Association (WMA) Declaration of Helsinki.

Ethical Approval

The Institutional Review Board (IRB) at Dubai Health typically does not require formal ethical approval for case reports, as per their established guidelines and policy.

Patient Informed Consent Statement

Written informed consent was obtained from the patient to publish their case and any accompanied images.

Conflict of Interest

The authors declare that there is no conflict of interest.

Artificial Intelligence (AI) Disclosure Statement

AI-unassisted work.

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Author Contribution

Aliya Ishaq is the supervisor for the project and oversaw all stages. Shameema Alam and Fathima Hana wrote the first manuscript draft. All authors critically revised the article for important intellectual content and approved the final manuscript.

Data Sharing Statement

Data sets are included in the published article.

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