Appendiceal Goblet Cell Carcinoid: An Unexpected Histology Following Simple Appendicectomy

Apendiks Goblet Hücreli Karsinoid: Basit Apendektomi Sonrası Beklenmedik Bir Histoloji

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ABSTRACT

Goblet cell carcinoid (GCC) is an enigmatic and rare tumour involving the appendix almost exclusively. It is a rare, aggressive subtype of appendiceal tumours with neuroendocrine features, and controversy exists with regards to therapeutic strategy. We herein highlight a 56-year-old lady with GCC whom she presented initially with a typical presentation of acute appendicitis. The histologic hallmark of this entity is the presence of clusters of goblet cells in the lamina propria or submucosa stain for various neuroendocrine markers, though the intensity is often patchy. GCC of the appendix is rare and challenging. In advanced form, it can present with carcinoid symptoms but occasionally mimics classical presentations of acute appendicitis. A tumour measuring less than 1 cm and located at the tip of the appendix is sufficient for a simple appendicectomy which warrants a promising prognosis.

Keywords: Appendectomy; appendicitis; goblet cell carcinoid

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ÖZET

Goblet hücreli karsinoid (GCC), neredeyse sadece apendiksi tutan esrarengiz ve nadir bir tümördür. Nöroendokrin özelliklere sahip, nadir, agresif bir apendiks tümör alt tipidir ve terapötik strateji ile ilgili tartışmalar mevcuttur. Burada, başlangıçta tipik bir akut apandisit sunumu ile sunduğu GCC'li 56 yaşındaki bir kadını sunuyoruz. Bu antitenin histolojik özelliği, yoğunluk genellikle düzensiz olmasına rağmen, çeşitli nöroendokrin belirteçler için lamina propria veya submukoza boyasında goblet hücre kümelerinin varlığıdır. Ekin GCC'si nadirdir ve zordur. İleri formda, karsinoid semptomlarla ortaya çıkabilir, ancak bazen akut apandisitin klasik sunumlarını taklit eder. Apendiksin ucunda yer alan ve 1 cm'den küçük bir tümör, umut verici bir prognozu garanti eden basit bir apendektomi için yeterlidir.

Anahtar Sözcükler: Apendektomi; apandisit; goblet hücreli karsinoid

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INTRODUCTION

Well-differentiated neuroendocrine tumours (NETs) of the appendix, formerly known as carcinoids, are rare incidents usually detected incidentally following appendicectomies (1,2). Embryologically, they are derived from the subepithelial endocrine cell population which is different from other NETs (3). Gastrointestinal (GI) NETs are traditionally classified based on the embryonic origin of the alimentary tract, whereby those originating from the mid-gut are notorious for secreting vasoactive agents such as serotonin into the systemic circulation, whereby giving carcinoid syndrome – an after-effect from a high level of vaso-active agents within the circulation (1,2).

Anatomically, appendicular NETs are commonly found at the tip of the appendix (2-4). A tumour measuring less than 1 cm and its location at the tip of the appendix are sufficient for curative intention by simple appendicectomy (3,5). Tumours of larger size and tumour location at the base of the appendix will require formal oncological right hemicolectomy due to its significant risk of metastasis (2). Nonetheless, treatment for lesions measuring 1-2 cm is controversial (2,6,7). Other factors and considerations from tumour classification, invasion into surrounding structures, and careful patient risk evaluation need to be assessed (2,7). We report a 56-year-old lady, diagnosed with appendiceal GCC and the subsequent therapeutic pathway utilized in treating such conditions.

CASE REPORT

A 56-year-old lady came to the emergency department with a typical presentation of acute appendicitis, which she described as having a sudden onset of fever, right iliac fossa pain 1-day duration, pricking in nature with a pain score of 5-7, and anorexia since the symptoms started. Otherwise, no other associated GI symptoms. This was her first-ever presentation as such with no prior similar pain experienced before. Clinically, she appeared alert and comfortable with no stigmata of chronic illness. Vital signs were within the normal range. Respiratory and cardiovascular system assessments were unremarkable. Abdominal examination revealed tenderness over the right iliac fossa, typical of acute appendicitis.

Biochemical parameters showed leucocytosis with a reading of 18 $\times 10^9$/L (normal value: 4-11 $\times 10^9$/L); otherwise, all other blood and urine investigations including C-reactive protein, urea, electrolytes and glucose values within the normal range. Plain abdominal radiography was unremarkable. She subsequently had an emergency laparoscopic appendicectomy whereby the appendix appeared classical to inflamed appendicitis. No other alarming features such as lymphadenopathy or mucin materials were noted intraoperatively. The appendicectomy was created using a usual manner. A formal histopathological examination report, however, revealed a GCC (grade 2) indicated at the tip of the appendix; no tumour beyond the appendiceal wall (Figure 1A, 1B). Immunohistochemistry showed chromogranin A (Figure 2A) and synaptophysin positivity (Figure 2B). Her post-operative recovery was uneventful.

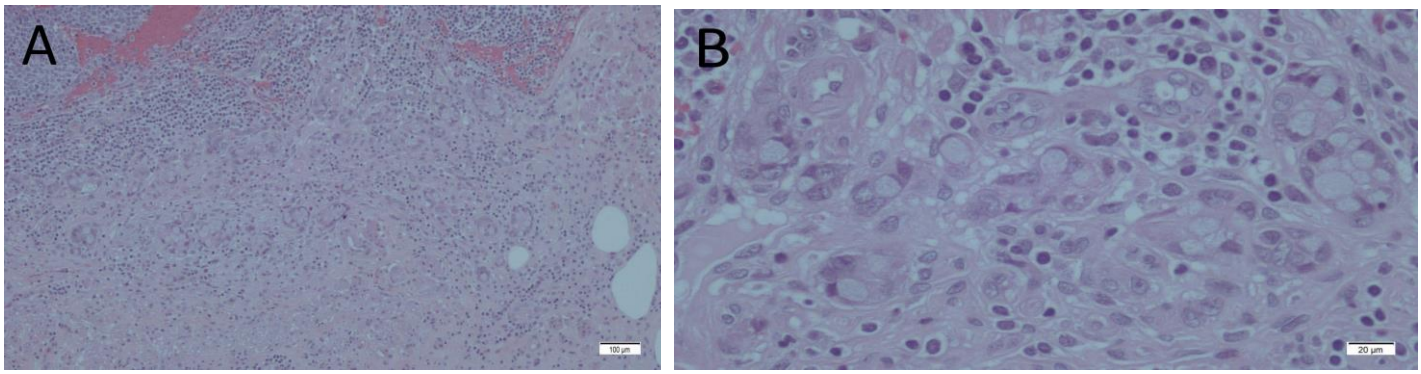

Figure 1: (A) The tumour is composed of goblet cells (haematoxylin and eosin (H&E), x10). (B) The goblet cell has eosinophilic and vacuolated cytoplasm (H&E, x40).

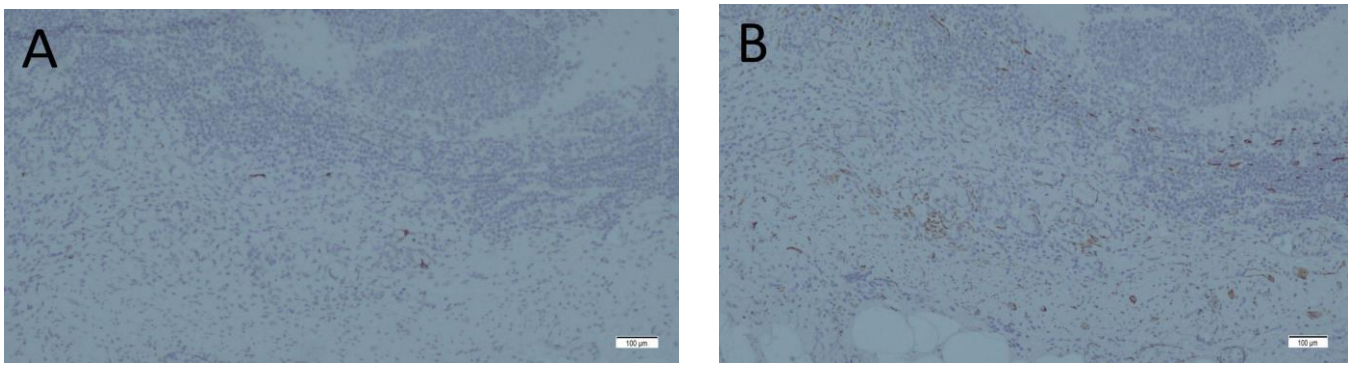

Figure 2: The tumour shows chromogranin (A) and synaptophysin (B) positivity

DISCUSSION

Acute appendicitis is the commonest aetiology of acute abdominal pain. However, acute right iliac fossa pain is not always ended with a pathological diagnosis of simple acute appendicitis (8-10). This includes GCC. The term GCC was first introduced in 1974 for the appendix tumours exhibiting histological features that differ from both ordinary carcinoid and adenocarcinoma (2). It accounts for less than 14% of all appendiceal tumours (5). Overall, the prognosis of small appendiceal NET as a whole is excellent in all ages (3). The median age at diagnosis of 58.9 years with no significant gender disparity has been reported in a systematic review of 600 patients (2).

GCC displays a degree of neuroendocrine differentiation with an expression of chromogranin A and B, synaptophysin, and allelic loss of chromosomes 11q, 16q, and 18q which have been observed to possess similarities to other neuroendocrine neoplasms, jejunum/ileum NEN (2,3).

The proliferation index as measured by Ki-67 is often much higher than in intestinal NEN (8). Both ANEN and GCC are generally diagnosed post appendectomy incidentally, however, patients with GCC may present symptomatic and at advanced tumour stages in 10–63% of cases (2).

Surgical resection is the primary mode of treatment for GCC (2,3,5). The natural history of this disease is intermediate in aggressiveness in comparison to classical adenocarcinomas and carcinoids; overall survival sits in between (2,3).

Due to its rarity, there is a lack of evidence and high-level consensus with regards to the optimal extent of resection of different stages of this disease. Treatment recommendations, in general, are similar to adenocarcinomas. Stage I GCC may be treated with appendectomy alone (2,3). In more advanced stages, right hemicolectomy is still the most commonly performed surgical option, despite various controversies; stop at appendicectomy alone versus oncological resection as per colonic adenocarcinomas (3).

The peritoneum is the commonest site of metastasis, assumed to be via the trans-coelomic spread, and is also the most common site of disease relapse (3). The precise roles and benefits of chemotherapy in GCC have not been extensively tested under prospective trials (3). GCC may be treated with regimens extrapolated from those utilised in colorectal adenocarcinomas, which include regimes such as FOLFOX (5-fluorouracil and oxaliplatin) and CAPOX (capecitabine and oxaliplatin) (11). However, small series of studies have failed to identify a significant difference in survival between patients undergoing adjuvant chemotherapy, and those who did not (2). The advocated plan of management recommended for patients with tumours that involve the adjacent caecum or with high-grade tumours requires completion of right hemicolectomy due to the high possibility of local recurrence with a 20% risk of metastatic behaviour (3). In female patients with GCC of the appendix regardless of age, bilateral salphingo-oophorectomy is advocated (2,3). In cases with an obvious spread of the disease, chemotherapy, mostly with 5-FU and leucovorin is advised. Cytoreductive surgery with adjuvant intraperitoneal chemotherapy can offer improved survival in cases with advanced peritoneal dissemination (3).

The prognosis of GCC is good overall. According to the SEER data compiled between 1973 and 2001, the 5-year overall survival for GCC was 76% (3,11). The stage is the most important prognostic factor. Literature reported 5-year disease-specific survival of 100%, 76%, 22%, and 14% for stage I to IV respectively according to the AJCC stage groups (3). The reported 5-year survival rates have ranged between 58% and 83% (3).

Since this is merely a case report, further descriptive researches need to be conducted in the future to obtain significant outcomes on the management of GCC.

CONCLUSION

GCC of the appendix is rare and challenging. In advanced form, it can present with carcinoid symptoms but occasionally mimics classical presentations of acute appendicitis. A tumour measuring less than 1 cm and located at the tip of the appendix is sufficient for a simple appendicectomy which warrants a promising prognosis.

Conflict of interest
No conflict of interest was declared by the authors.

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