

## Case Report

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# Extraappendiceal goblet cell carcinoid of the transverse colon

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## ABSTRACT

Goblet cell carcinoids (GCC) are a rare subgroup of neuroendocrine tumours which exhibit mixed endocrine and exocrine features and are almost exclusively localised to the appendix. A few cases of extraappendiceal GCC have been reported in the literature however these are exceedingly rare. They are biologically aggressive tumours that are believed to arise from pluripotent intestinal epithelial crypt base stem cells. Given their rarity, no guidelines currently exist for the management of extraappendiceal GCC, however treatment for GCC's is generally based on their tumour stage in line with staging for typical adenocarcinomas. This case gives an account of a colonic goblet cell carcinoid within the transverse colon encountered in a 66-year-old male. A literature search did not identify any previous documented cases of a GCC at this location.

**Keywords:** Goblet cell carcinoid, Goblet cell adenocarcinoma, Extraappendiceal, Mucinous carcinoid, Transverse colon

## INTRODUCTION

Goblet cell carcinoids (GCC) are rare neuroendocrine tumours first described by Gagne et al in 1969.<sup>1</sup> They are an amphicrine tumour consisting of both epithelial (adenocarcinoma) and neuroendocrine (carcinoid) components and are grouped under the category of adenocarcinoids.<sup>2</sup> They virtually solely involve the appendix with some exceptional extraappendiceal locations being reported including the stomach, duodenum, small intestine, colon and rectum.<sup>3</sup>

## CASE REPORT

A 66-year-old male was referred by his family physician for an elective colonoscopy due to a positive faecal occult blood test (FOBT). He denied abdominal pain, changes in his bowel habits or per rectal bleeding. He had no family history of gastrointestinal malignancy and had no previous colonoscopies. His past medical history consisted of hypertension, hypercholesterolaemia and a

previous non-ST-elevation myocardial infarction (NSTEMI) treated with angiography and a drug eluting stent.

His colonoscopy revealed diverticulosis of the entire colon, a 3 mm polyp in the proximal transverse colon and a 15 mm polyp in the distal transverse colon. The histopathology revealed a low grade tubular adenoma and a goblet cell carcinoid respectively. Immunohistochemically the GCC tumour cells positively reacted with neuroendocrine markers CD56 and synaptophysin and patchy chromogranin staining was seen within the infiltrative glandular structures. The Ki-67 was 30%. A computed tomography (CT) scan of the chest, abdomen and pelvis was unremarkable with no evidence of metastatic disease. A Dotate PET (positron emission tomography) scan identified no dotatate-avid disease. Carcinoembryonic antigen (CEA) and chromogranin A (CgA) levels were within normal limits.

A repeat colonoscopy was performed for inspection and tattooing of the polypectomy site. The patient was discussed at the colorectal multidisciplinary team (MDT) meeting and a decision was made to proceed with a laparoscopic left hemicolectomy. Histopathological analysis of the surgical specimen revealed sections of colon showing an area of submucosal fibrosis believed to represent the polypectomy site. Tattoo pigment was identified adjacent to this area. No residual goblet cell carcinoid or dysplasia was identified. There were six unremarkable lymph nodes within the specimen (0/6).

## DISCUSSION

Goblet cell carcinoids, also known as goblet cell adenocarcinoma, mucinous carcinoid or mixed crypt cell carcinoma, are biphasic neoplasms comprised of both neuroendocrine and epithelial cells which are believed to arise from multipotential stem cells within the crypts of intestinal mucosa.<sup>2,4</sup>

GCCs are very rare neoplasms with an approximate incidence of 0.01 to 0.05 per 100,000 per year and account for less than 15% of all malignant tumours of the appendix.<sup>5</sup> Evidence has not revealed a variation in incidence between gender however an ethnic preference for Caucasians is described.<sup>4,6,7</sup> The average age at presentation is between 52 to 58 years which is closer to the average age of patients presenting with adenocarcinomas than of appendiceal neuroendocrine tumours (NET).<sup>4,6-8</sup> To date the only possible risk factor which has been described is schistosomiasis.<sup>6</sup> Only a few cases of extraappendiceal GCC have been reported in locations including the stomach, ampulla of Vater, jejunum, ileum, caecum, ascending colon and rectum.<sup>4,7</sup>

Histologically, the hallmark of GCCs is the presence of mucin-containing goblet-shaped epithelial cells, which may cluster in the lamina propria or submucosa.<sup>7,9</sup> On immunohistochemical staining, there is scattered expression of the neuroendocrine markers chromogranin A and synaptophysin, with the expression of CEA and CK20 differentiating them from appendiceal neuroendocrine neoplasms.<sup>4,8,9</sup> Ki-67 immunostaining increases with decreasing differentiation however it has not been found to have a prognostic significance, as a correlation between Ki-67 levels and clinical outcomes has not been definitely shown.<sup>4</sup>

Their biological behaviour and prognosis is intermediate between carcinoid tumours and adenocarcinomas.<sup>5</sup> GCCs have shown an increased risk for local lymph node metastases and have the potential to spread intraperitoneally even in the absence of any nodal metastases.<sup>4</sup> In the case of disseminated disease, the peritoneum (as carcinomatosis) and ovaries are frequently involved whereas metastasis to the lungs are rare, in contrast to adenocarcinomas and classic intestinal carcinoid tumours.<sup>6</sup>

Treatment recommendations for GCCs are similar to that for colonic adenocarcinomas.<sup>4</sup> At a minimum these tumours are treated with surgical resection based on their location.<sup>4</sup> Given the vast majority of GCCs have primary origin from the appendix, localised stage I tumours are usually treated with either appendectomy alone or a right hemicolectomy.<sup>2,4,6</sup> There has been some debate as to whether simple appendectomy is sufficient to secure radicality, however generally in higher stages (T3 or T4) a right hemicolectomy is recommended for nodal sampling.<sup>4,6</sup> Some authors also recommend removal of the ovaries in post-menopausal women given the high affinity these tumours have for metastasis to this site.<sup>2</sup> If residual disease remains in the colectomy specimen or metastasis to lymph nodes is present, adjuvant FOLFOX, like in colorectal cancer is recommended.<sup>2,5</sup> Peritoneal carcinomatosis is treated in a similar manner to epithelial tumours of the colon and ovary with cytoreductive surgery (CRS) followed by hyperthermic intraperitoneal chemotherapy (HIPEC), as this appears to provide the best long term survival.<sup>2,5,8</sup> In patients with systemic disease or unresectable peritoneal disease, 5-fluorouracil (5-FU) based chemotherapeutic regimens offer progression-free survival of up to 12 months.<sup>5</sup>

Post-treatment surveillance is recommended using a comparable regimen to colorectal cancer, usually over a five year period, however the optimal duration of follow-up has not been established.<sup>6</sup> This includes surveillance with blood tests and imaging modalities such as CT or magnetic resonance imaging (MRI).<sup>6</sup> In contrast to classical neuroendocrine tumours, chromogranin A serum levels are normal and of no value for detection or monitoring of GCC.<sup>4,6,9</sup> Instead it is suggested to use CEA, CA-19-9 and CA-125 as tumour markers at presentation and during surveillance as these epithelial cell markers have been shown to be elevated in GCC in up to 80% of patients.<sup>4,5,6,8</sup> FDG-PET scans are of limited value as only high grade GCC tumours appear to be FDG-PET avid.<sup>5</sup>

As a general rule, prognosis of GCC is worse than with malignant NETs but better than with appendiceal adenocarcinoma.<sup>6</sup> For appendiceal GCCs, the TNM staging is a significant prognosticator, with 5-year overall survivals in stage I, II, III and IV being 100%, 76%, 22% and 14% respectively, as reported in a retrospective series of 57 patients with GCC.<sup>8</sup> Given the rarity of extraappendiceal GCCs with only a few reported cases in literature, there is little available data on prognosis or recommended treatment protocols.

## CONCLUSION

GCC are rare tumours which are comprised of both neuroendocrine and glandular components.<sup>2</sup> Extraappendiceal locations for GCC such as the transverse colon are extremely rare with only a few reported cases in the literature.<sup>4,7</sup> Management of extraappendiceal GCC's is challenging due to both a

limited understanding of the neoplasms molecular biological characteristics and their rarity, which precludes the formulation of evidence-based therapeutic algorithms for optimal treatment and surveillance guidelines.<sup>4,8</sup>

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