Case Report **IJCR (2018) 3:50**

International Journal of Case Reports
(ISSN:2572-8776)

Goblet Cell Carcinoid (GCC) of the Appendix presenting as a Small Bowel Obstruction: Case Report and Literature Review

Amin Tanveer[1] MD, Shaani Sighal[2] MBBS, Asiri Arachchi[3] MBBS, Zoltan Hrabovszky[3] MBBS, FRACS, Mikhail Fisher[3] MBBS, FRACS.

Amin Tanveer: Surgical Registrar, Department of General Surgery Peninsula Health, PO BOX 52, 2 Hastings Road, Frankston, Victoria, Australia; Shaani Sighal: Surgical resident, Department of General surgery Dandenong Hospital (Monash Health), 135 David Street, Dandenong, Victoria, Australia; Asiri Arachchi: Surgical registrar, Department of General Surgery Dandenong Hospital (Monash Health), 135 David Street, Dandenong, Victoria, AustraliaZoltan Hrabovszky; General Surgeon, Department of General Surgery Dandenong Hospital (Monash Health), 135 David Street, Dandenong, Victoria, Australia; Mikhail Fisher: General Surgeon, Department of General Surgery Dandenong Hospital (Monash Health), 135 David Street, Dandenong, Victoria, Australia

ABSTRACT

Goblet Cell Carcinoid (GCC) is a rare, low grade malignancy, and GCC presenting as a small bowel obstruction (SBO) is incredibly rare.

Hereby, we presenting a 68-year-old male presented to our Emergency Department with a one-day history of right sided abdominal pain, distention and vomiting, he had no previous abdominal surgery and had no significant other medical problem. Abdominal Computed Tomography (CT) demonstrated a high grade, closed loop small bowel obstruction involving the terminal segment of the ileum, and a low-density appendiceal nodule. He had laparoscopy converted to open caecectomy, the histology, confirmed the diagnosis of Goblet Cell Carcinoid of the appendix, eventually he had right hemicolectomy, progressed well, and made a good post-operative recovery, discharged home.

As presentation of GCC of the appendix with sbo is a very rare incidence, we discussed this through a case report with its immunohistochemical, behavioral features, presentation and treatment options.

Keywords: Goblet Cell Carcinoid of appendix, small bowel obstruction, Carcinoid tumor, neuroendocrine tumor.

***Correspondence to Author:**
Amin Tanveer
Surgical registrar, Department of General Surgery, Peninsula Health PO Box 52, 2 Hastings Road, Frankston, Victoria, Australia

How to cite this article:
Amin Tanveer, Shaani Sighal, Asiri Arachchi, Zoltan Hrabovszky, Mikhail Fisher, Mikhail Fisher. Goblet Cell Carcinoid (GCC) of the Appendix presenting as a Small Bowel Obstruction: Case Report and Literature Review. International Journal of Case Reports, 2018 3:50

eSciPub LLC, Houston, TX USA.
Website: http://escipub.com/

INTRODUCTION

Goblet Cell Carcinoid (GCC) is a rare, low grade malignancy, occurring almost exclusively in the appendix. Carcinoid tumour is revealed in 1 out of every 300 appendicectomies, and off those, 6% are pure GCC [1]. Hence, pure GCC present in 0.02% of appendicectomies according to the literature.

There are no particularly discerning risk factors for GCC, until recently. A relatively new study by Jiang et al. shows a possible connection between GCC and schistosomiasis, a potential risk factor [2]. It was suggested in this study that appendiceal schistosomiasis is associated with both increased proliferation and neuroendocrine differentiation of mucosal pluripotent crypt cells, and thereby may contribute to the development of GCC.

Compared with other carcinoid tumours which are usually asymptomatic, GCC often presents with clinical symptoms; the common clinical presentations include acute appendicitis (22.5%), asymptomatic (5.4%), non-localized abdominal pain (5.15%) and the presence of an appendiceal mass (3.09%) [1]. It can also present as bowel obstruction, intussusception, gastrointestinal bleeding, and chronic intermittent lower abdominal pain [3].

It is rare for GCC to present as an infiltrative appendiceal lesion causing small bowel obstruction. In these rare settings, GCC may potentially be diagnosed on CT as the primary differential in an SBO secondary to an infiltrative appendiceal lesion.

GCCs can metastasize in 15–30% of cases, particularly in higher age groups. Spread usually occurs to the pelvic organs, abdominal cavity and associated peritoneum. Haematogenous metastasis to the liver or other distant organs is rare. The ovary is the most common site of metastasis and metastatic lesions sometimes show a histological picture of mucin-producing adenocarcinoma [4].

Even though GCC has a more aggressive phenotype than benign carcinoid tumours, the prognosis is generally good and surgery (appendicectomy VS right hemicolectomy) remains the treatment of choice.

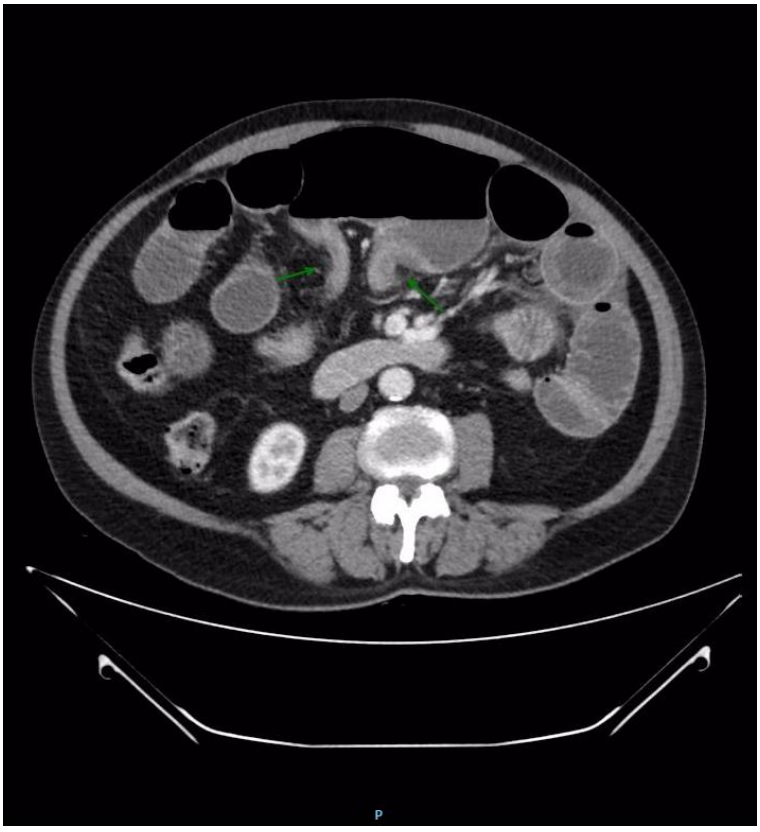

Figure 1: shows displaced caecum with appendix, 11x21 mm nodule at appendiceal tip

CASE REPORT:

A 68-year-old male presented to our Emergency Department with a one-day history of right sided abdominal pain, distention and vomiting on a background of no previous abdominal surgery. Abdominal CT demonstrated a high grade, closed loop small bowel obstruction involving the terminal segment of the ileum (Figure 1, 2), and also of significance there was a low-density appendiceal nodule (Figure 1).

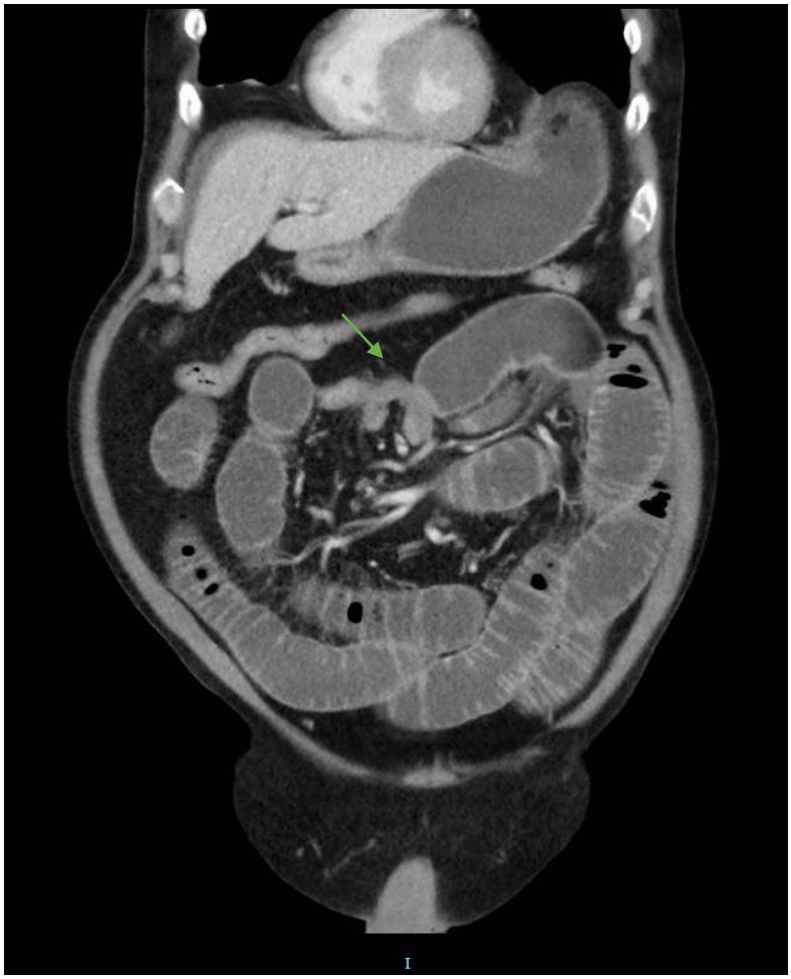

Figure 2: shows high grade small bowel obstruction with transition point

A subsequent laparoscopy revealed the tip of the appendix adherent to the meso-sigmoid colon, forming a tight band and consequent mechanical bowel obstruction. Furthermore, the meso-appendix was embedded with crystal deposits and extruding mucin. The decision was made to convert to laparotomy and perform a caecectomy.

Histology reported that the tumour cells are composed of concentric proliferation of small nests of cells with abundant intracytoplasmic mucin and eccentric, compressed hyperchromatic nuclei, resembling goblet cells/signet ring cells (figure 3). Immunohistochemistry demonstrated reactivity to synaptophysin, chromogranin A and CD56, confirming the diagnosis of Goblet Cell Carcinoid (figure 3).

A staging CT after this initial surgery revealed no metastasis. After discussion at our oncology Multi Disciplinary Meeting (MDT), the patient went on to receive a completion right hemicolectomy which revealed no further malignancy on histology. The patient progressed well, and made a good post-operative recovery, discharged home.

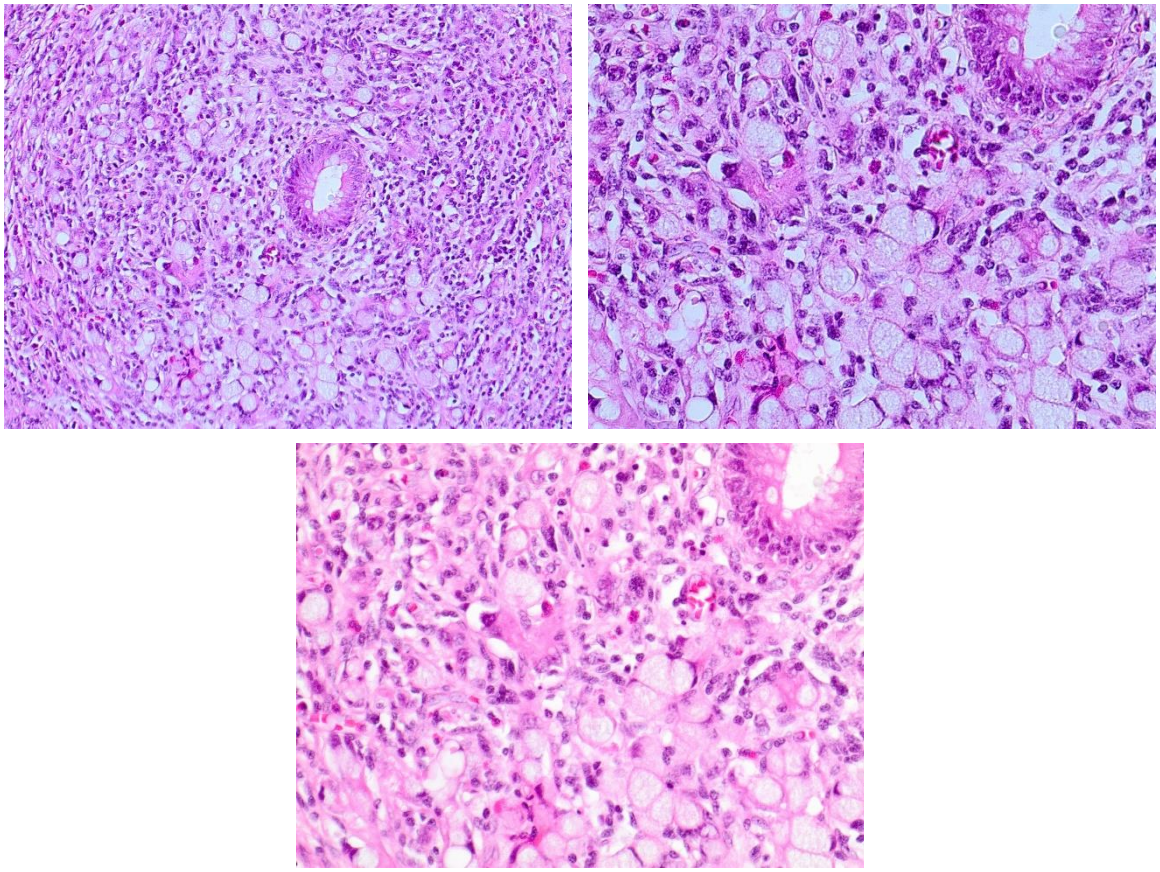

Figure 3: shows histologic picture of goblet cell/signet cell, positive for synaptophysin, chromogranin and CD56. The Ki-67 is 10%

DISCUSSION

Goblet Cell Carcinoid (GCC) is a rare, low grade malignancy, which was previously described as mucinous producing carcinoid, adeno-carcinoid, intermediate type carcinoid and crypt cell carcinoma which are largely accurate descriptions. But these alternate names, however, have been omitted from the current World Health Organization (WHO) classification [5].

Goblet cell tumours are classified as neuroendocrine tumour or carcinoma in the literatures [5]. As GCC is characteristically biphasic, derived from pluripotent intestinal stem cells that differentiate into both mucinous and neuroendocrine cells. Thus, it shares histologic features of both adenocarcinomas and carcinoid tumours respectively. The proportion of each can vary, and sub-classification along this continuum has important associations with disease progression, prognosis and treatment.

The behaviour of the tumour further complicates the tumour's classification as carcinoma versus carcinoid. Factors that demonstrate its carcinoid nature the presence of neuroendocrine cells, neurosecretory granules, organoid growth pattern, lack of atypical cytology, lack of p53 mutations, and the usual absence of a mucosal, in situ precursor lesion[1]. Features more in keeping with adenocarcinoma, or at least an entity distinct from classic carcinoid, are the presence of intracellular mucin and its characteristic trans-coelomic spread with documented cases of metastases [1].

Evaluation of the morphologic features of GCC is crucial for both clinical management and prediction of outcome. GCC immunohistochemically characterised by staining positive for synaptophysin, chromogranin A (CgA) and CD56, all markers of neuroendocrine activity. Importantly, typical appendiceal carcinoids stain homogenously for

these markers, however, GCCs tend to demonstrate a more scattered positivity. This is well in keeping with its known biphasic neuroendocrine and adenocarcinomatous nature.

This idea is complemented in a univariate analysis by Tang et al who identified an association between prognosis and the degree of positive staining [6]. Tang et al have described a sub-classification that has proved useful for predicting clinical behaviour and prognosis of GCC:

- Pure GCC (type A)
- Carcinoma ex GCC, signet ring type (type B)
- Carcinoma ex GCC, poorly differentiated type (type C)

In keeping with this classification, Tang group C specimens express the least positive neuro-endocrine activity, thus resembling poorly differentiated adenocarcinomas, and therefore associated with the least favourable prognosis.

There are other tumour markers which reflect the mucinous component of GCC. GCC shows the same CK7/CK20 immuno-expression as colorectal adenocarcinoma [7]. It is possible that the same tumour markers used to prognose colorectal adenocarcinoma can be used similarly in GCC. GCC is usually differentiated from other tumours by a raised CEA. However, in our case, the patient had a raised Ca 19-9 and a normal CEA. The raised Ca19-9 could be associated with the adenocarcinomatous component of the tumour in keeping with carcinomatous features on histopathology (Mucin pool, signet ring cells). Other documented cases of GCC with a raised Ca19-9 were in the setting of ovarian metastases.

The role of Ki-67 index in GCC, however remains controversial, its significance found to be increasingly unremarkable [8]. In one study, the Ki-67 labelling index showed no correlation to mitotic activity, angiolymphatic or Perineural invasion. Patients with Tang Group C, however, had a median Ki-67 significantly higher than patients with Tang Group A and B. Despite this, Ki-67 was concluded to have no prognostic significance for goblet cell carcinoid tumours and should not be used solely to determine treatment and surgical approach [8].

As mentioned, GCC presenting as a small bowel obstruction (SBO) is incredibly rare, and to our knowledge, only one previously reported case has been described [9]. In these rare settings, GCC may potentially be diagnosed on CT as the primary differential in an SBO secondary to an infiltrative appendiceal lesion.

The differential diagnosis for SBO with a concurrent appendiceal lesion radiologically include goblet cell carcinoid, classic carcinoid, lymphoma, and non-mucinous adenocarcinoma of the appendix [9]. This of course, is when adhesive SBO is unlikely, as with the current patient, with no previous history of abdominal surgery.

Even though GCC has a more aggressive phenotype than benign carcinoid tumours, the prognosis is generally good and surgery remains the treatment of choice. However, there is still debate about surgical management, especially whether right hemicolectomy is needed or appendectomy alone is an adequate treatment.

Byrn et al. reviewed 16 cases of gastrointestinal goblet cell carcinoid and did not support right hemicolectomy for patient with non-metastatic goblet cell carcinoid of the appendix [10]. Similarly, Varisco et al. emphasized that in patients with no concomitant caecal involvement and low-grade tumour histology; a simple appendectomy is sufficient [11]. It has been suggested that tumours confined to the appendiceal wall with a clear surgical margin and no carcinoma component can be treated by appendectomy alone.

However, right hemicolectomy is considered the standard surgical treatment of localized GCC and is recommended to take place within 3 months of the appendicectomy [12]

Indications for Right hemicolectomy include [12]:

- Tumour recognized intraoperatively
- Appendiceal margin positive
- Involvement beyond muscularis propria
- Perforation
- Presence of carcinoma component

In some patients a more radical procedure is indicated. Peritoneal carcinomatosis from GCC is as invasive as colorectal adenocarcinoma with peritoneal metastases. In such cases, complete or near-complete surgical removal, if possible, should be considered for cyto-reduction in combination with intraperitoneal chemotherapy. Some studies also suggest a prophylactic BSO in female patients, at the time of right hemi-colectomy due to the high propensity for ovarian metastases [12].

CONCLUSION

GCC presenting as a small bowel obstruction (SBO) is incredibly rare. In these rare settings, GCC may potentially be diagnosed on CT as the primary differential in an SBO secondary to an infiltrative appendiceal lesion, and surgery remains the standard treatment.

CONFLICT OF INTEREST

No conflict of interest

AUTHOR'S CONTRIBUTIONS

Amin Tanveer[1]

Group1 - Conception and design, Acquisition of data, Analysis and interpretation of data

Group 2 - Drafting the article, Critical revision of the article

Group 3 - Final approval of the version to be published

Shaani Singhal[2]

Group1 - Analysis and interpretation of data

Group 2 - Critical revision of the article

Group 3 - Final approval of the version to be published

Asiri Arachchi[3]

Group1 - Analysis and interpretation of data

Group 2 - Critical revision of the article

Group 3 - Final approval of the version to be published

Zoltan Hrabovszky[3]

Group1 - Analysis and interpretation of data

Group 2 - Critical revision of the article

Group 3 - Final approval of the version to be published

Mikhail Fisher[3]

Group1 - Analysis and interpretation of data

Group 2 - Critical revision of the article

Group 3 - Final approval of the version to be published

ACKNOWLEDGEMENTS

I acknowledge our Anatomical Pathology Department for providing the digital imaging of the histology.

REFERENCES

1. Roy P, Chetty R. Goblet cell carcinoid tumours of the appendix: an overview. World J Gastrointest Oncol. 2010; 2(6):251–8.
2. Jiang Y, Long H, Li T, Wang W, Liu H, Zhang X. Schistosomiasis may contribute to goblet cell carcinoid of the appendix. J Parasitol. 2012 Jun;98(3):565-8
3. Pham TH, Wolff B, Abraham SC, Drelichman E. Surgical and chemotherapy treatment outcomes of goblet cell carcinoid: a tertiary cancer center experience. Ann Surg Oncol. 2006; 13 (3):370–6.
4. N.H. Anderson, J.E. Somerville, C.F. Johnston, D .M. Hayes, K.D.Buchanan, J.M. Sloan Appendiceal goblet cell carcinoids: a clinico-pathological and immunohistochemical study Histopathology, 18 (1991), pp. 61-65
5. Bosman FT, Carneiro F, Hruban RH, Thiese ND (Eds). WHO Classifiication of Tumors of the Digestive System, IARC, Lyon 2010
6. Tang LH, Shia J, Soslow RA, Dhall D, Wong WD, O'Reilly E, Qin J, Paty P, Weiser MR, Guillem J, et al. Pathologic classification and clinical behaviour of the spectrum of goblet cell carcinoid tumours of the appendix. Am J Surg Pathol. 2008; 32(10):1429–43.
7. Alsaad KO, Serra S, Schmitt A, Perren A, Chetty R. Cytokeratins 7 and 20 immunoexpression profile in goblet cell and classical carcinoids of appendix. Endocr Pathol. 2007 Spring; 18(1):16-22.
8. Liu, Eric et al. The role of Ki-67 in predicting

biological behaviour of goblet cell carcinoid tumour in appendix. The American Journal of Surgery, Volume 202, Issue 4, 400-403

9. Afroz1 N, Shamim N, Sofi1 LA, Rizvi A. Incidentally discovered goblet cell carcinoid clinically presenting as acute intestinal obstruction: A case report with review of literature. Indian Journal of Pathology and Microbiology. Volume 57, Issue 1, 120-123
10. JC Byrn, JL Wang, CM Divino, *et al.*Management of goblet cell carcinoid J Surg Oncol, 94 (2006), pp. 340-396
11. Varisco B, McAlvin B, Dias J, Franga D. Adenocarcinoid of the appendix: is right hemicolectomy necessary? A meta-analysis of retrospective chart reviews. Am Surg. 2004 Jul; 70(7):593-9.
12. Plöckinger U, Couvelard A, Falconi M, Sundin A, Salazar R, Christ E, de Herder WW, Gross D, Knapp WH, Knigge UP, Kulke MH, Pape UF; Frascati Consensus Conference participants. Consensus guidelines for the management of patients with digestive neuroendocrine tumours: well-differentiated tumour/carcinoma of the appendix and goblet cell carcinoma. Neuroendocrinology. 2008; 87(1):20-30.