CASE REPORT

Endoscopic diagnosis of a goblet cell carcinoid tumour of the appendix

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SUMMARY

Primary malignancies of the appendix are rare. Of these, less than 5% are goblet cell carcinoid (GCC) tumours. The majority of GCC present with findings of acute appendicitis or advanced peritoneal spread. We describe a rare presentation of GCC as subtle mucosal abnormality of the appendiceal orifice seen on colonoscopy performed for iron-deficiency anaemia. Biopsies were interpreted as adenocarcinoma; however, final surgical pathology confirmed GCC of the appendix with caecal involvement. The patient recovered well from surgery, anaemia resolved and follow-up did not show metastatic disease.

BACKGROUND

Appendiceal goblet cell carcinoid (GCC), also known as mucin producing carcinoid, adenocarcinoid, intermediate type carcinoid or crypt cell carcinoma, is a rare tumour of the appendix with both neuroendocrine and intestinal-type goblet cell morphology.¹ These tumours present most commonly as acute appendicitis or widespread metastatic peritoneal disease.^{1–3} We present the case of a patient with iron-deficiency anaemia and abnormal appendiceal orifice appearance on colonoscopy that on surgical pathology was confirmed to be appendiceal GCC. This case emphasises the importance of close endoscopic examination of the appendiceal orifice and need for sampling to rule out pathology.

CASE PRESENTATION

A 69-year-old man presented with symptoms of fatigue and new-onset iron-deficiency anaemia. He denied overt gastrointestinal bleeding or other symptoms. He was otherwise healthy, on no medications. Family history was negative for colorectal malignancy.

INVESTIGATIONS

Laboratory investigations showed a haemoglobin of 103 g/L with a mean corpuscular volume (MCV) of 82 fL, ferritin of 22 µg/L, iron of 4 µmol/L and total iron binding capacity (TIBC) of 68 µmol/L. He denied overt gastrointestinal bleeding or other symptoms. Colonoscopy showed a slightly protruding appendix with subtle irregularity of the mucosa. The mucosal appearance was not typical for adenomatous tissue (figure 1A). The consistency of this area was firm when biopsies were taken. The biopsies reported

poorly differentiated adenocarcinoma positive for individual signet ring-like cells and stained positive for mucin (PAS-D and Alcian blue) but negative for neuroendocrine markers. A CT scan of the chest/abdomen/pelvis showed metastatic disease a 18 mm arterial phase enhancing lesion in segment 8 of the liver, but no evidence of metastatic disease.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for the appendiceal orifice abnormality seen on endoscopy included inverted appendix, adenomatous polyp or carcinoma arising either from the appendix or colon.

TREATMENT

The patient was referred to surgery and underwent a laparoscopic right hemicolectomy.

OUTCOME AND FOLLOW-UP

Surgical specimen pathology was consistent with GCC (pT3pN0) involving the whole appendix with focal extension to the mesoappendix and caecal base (figure 1B–D); neuroendocrine markers chromogranin A and CD 56 were positive (figure 2), perineural invasion was present and the Ki-67 mitotic index was greater than 20%. Surgical excision margins were clear with no regional lymph node metastases (0 out of 16). After pathology results showed positive neuroendocrine markers, the patient had a negative octreotide scan.

A follow-up MRI of the liver at 3 months was consistent with focal nodular hyperplasia. Abdominal CT scan at 6 months after right hemicolectomy did not show evidence of recurrence or metastases. Colonoscopy done 1 year after surgery was clear. Repeat haemoglobin was normal.

DISCUSSION

GCC is a rare tumour of the appendix, compromising less than 5% of primary appendiceal lesions.¹ This tumour has a submucosal growth pattern with invasion of the appendiceal wall characterised by goblet or signet ring cells in clusters or glands separated by smooth muscle stroma.⁴ Signet ring cells are positive for various histochemical markers including PAS, mucicarmine, pancytokeratin, CDX-2, CK20, MUC2, CEA, chromogranin and synaptophysin.⁴ While GCC is generally described to exhibit both neuroendocrine and intestinal-type morphology, up to one quarter of cases are negative for neuroendocrine markers.⁴ In the case presented above, endoscopic biopsies were

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Figure 1 (A) Endoscopic appearance of the appendiceal GCC on colonoscopy. (B) Nest of GCC tumour cells with goblet cell appearance invading the muscular wall of the appendix. (C) GCC invading into caecal mucosa. (D) GCC invading into mesoappendiceal fat. GCC, goblet cell carcinoid.

negative but final surgical specimen stained positive for neuroendocrine markers. The diagnosis of GCC requires surgical pathology as endoscopic biopsies can be mistaken for adenocarcinoma.

The majority of appendiceal GCC present as acute appendicitis; diagnosis is almost always made postoperatively on surgical pathology.³ A recent case describes GCC found within an Amyand's hernia.⁵ Other rare cases are described where GCC presented as iron-deficiency anaemia with ulcerating lesions arising from the appendiceal base.⁶ To our knowledge, this is the only case report in the literature where GCC of the appendix was discovered endoscopically as non-ulcerated lesion. Following appendectomy, prognosis is generally good in patients who present with disease limited to the appendix. Right hemicolectomy is indicated when appendectomy specimen have one or more of the following features: cellular undifferentiation, increased mitotic activity, involvement of the appendiceal base and caecal wall, positive lymph nodes, tumour measures over 2 cm.¹ In our case, biopsies from the appendiceal orifice were interpreted as adenocarcinoma with signet ring cells; as such, the patient was treated with laparoscopic right hemicolectomy. Following a diagnosis with GCC, patients should be investigated with plasma chromogranin A, 24 hours urine 5-HIAA, CT chest/abdomen/pelvis and octreotide scintigraphy.¹ Prognosis of GCC of the appendix is generally better than adenocarcinoma, but

Figure 2 (A) GCC cells staining positive on immunohistochemistry for CD56 (neuroendocrine marker). (B) GCC cells staining positive on immunohistochemistry for Chromogranin A (neuroendocrine marker). GCC, goblet cell carcinoid.

Patient's perspective

Patient consent for publication of this case report and associated images was obtained.

Learning points

- Goblet cell carcinoid (GCC) is a rare condition and typically presents as appendicitis.
- GCC can be considered as an unusual cause of iron deficiency anaemia.
- GCC has subtle endoscopic features and therefore requires careful examination of the appendix.
- Definitive diagnosis of GCC requires surgical specimen as endoscopic biopsies can be misinterpreted as mucinous adenocarcinoma.
- Right hemicolectomy for GCC is indicated if any of the following apply: cellular undifferentiation, increased mitotic activity, involvement of appendiceal base/caecal wall, positive lymph nodes, tumour size >2 cm.

worse than carcinoid. Approximately 20% of patients will have or develop metastatic disease.¹ The prognosis is worse if another carcinoma is present; associated carcinomas most commonly arise from the urinary system, prostate, ovaries, stomach and breast.¹

Appendiceal GCC is rare. Endoscopic biopsies of GCC show signet ring cells and hence the lesion is often confused with adenocarcinoma. The endoscopic appearance of the lesion can be subtle and may easily be mistaken for an inverted appendix. Final surgical specimen is diagnostic and should include stains for neuroendocrine markers. This case report highlights the importance of careful endoscopic assessment of the appendix and sampling of subtle variants from normal anatomical appearance.

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