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Case Report

Goblet cell adenocarcinoma of the appendix: a rolling stone for long

Renu Sharma[1]*, Pooja Chauhan[1], Amit Rattan[2]

[1]Department of Pathology, Shri Lal Bahadur Shastri Government Medical College, Mandi, Himachal Pradesh, India
[2]Department of Surgery, Shri Lal Bahadur Shastri Government Medical College, Mandi, Himachal Pradesh, India

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***Correspondence:**
Dr. Renu Sharma,
E-mail: renurattan81@gmail.com

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ABSTRACT

Appendiceal goblet cell adenocarcinoma (GCA) is a rare and aggressive epithelial neoplasm comprising goblet-like mucinous cells primarily and variable neuroendocrine cells. It is an amphicrine neoplasm with features of epithelial and neuroendocrine tumours, but behaves aggressively like an adenocarcinoma variant. GCA has undergone multiple name changes in the past; therefore, there have been inconsistencies in nomenclature, classification, reporting, and understanding of the pathology of the disease. Although it typically presents with features of acute appendicitis, it may sometimes present with subtle symptoms of gastrointestinal discomfort. In late stages, they may present with intestinal obstruction or as a metastatic ovarian mass. Diagnosis is possible only on histopathologic examination, which reveals goblet cell infiltration in sheets, singly scattered form, complex cribriform pattern, discrete clusters, and tubules. Our case report aims to increase awareness about GCA and its differential diagnosis and emphasise the need for a larger, elaborate study to bring consistency in GCA reporting. We report a rare case of metastatic high-grade appendiceal GCA in a 65-year-old female presenting with complete intestinal obstruction.

Keywords: Goblet cell adenocarcinoma, Appendiceal, Neuroendocrine neoplasm, Amphicrine neoplasm

INTRODUCTION

Appendiceal goblet cell adenocarcinoma (GCA) is a rare tumour, found in 0.3–0.9% of appendectomy specimens.[1] GCA is an amphicrine tumour composed of mucin-filled goblet-like cells bearing neuroendocrine-like features. Patient usually presents with symptoms of acute appendicitis and are detected incidentally after histopathologic examination of the appendicectomy specimen. It is diagnosed between the ages of 50 and 60 and has no sex predilection.[2]

We report a rare case of high-grade GCA in a 65-year-old adult female presenting with complete intestinal obstruction and metastatic tumour deposits.

CASE REPORT

A 65-year-old female presented to the emergency department with features of complete intestinal obstruction. After initial investigation and radiologic findings, an emergency laparotomy was done with right hemicolectomy of the intestine, which included the terminal part of the ileum, cecum, appendix, and ascending colon. Patient gave history of upset stomach, altered bowel habits, indigestion, and abdominal discomfort for the past 6 months.

Gross examination

The resected segment of intestine was 25 cm long, comprising the terminal part of the ileum, cecum, appendix, and ascending colon. On cut opening, a jumbled-up mass was seen at the ileocecal junction involving the appendix, the terminal ileum, and part of the cecum. On the cut section, grey white growth was seen to be majorly involving the appendix and extending into the adjacent ileum and cecum, completely obstructing the ileocecal junction. There was no well-defined growth; instead, there was grey white thickening of the wall of the

appendix. The growth involved serosal surfaces, and on palpation, 22 regional lymph nodes were identified, ranging in size from 0.5 to 1.5 cm in diameter, along with two tumour nodules in the mesentery.

Histopathologic examination

Showed tumour was located predominantly in the submucosa (Figure 1), concentrically involving the lumen of the appendix (tip to base). No dysplasia was seen in the overlying epithelium. The tumour was composed of diffuse sheets and singly scattered goblet cells infiltrating submucosa, muscle, and serosal layers (Figures 2 and 3). At places, moderately to severely pleomorphic cells were seen with vesicular nuclei, prominent nucleoli, and scant to moderate eosinophilic cytoplasm. In addition, goblet cells were seen in small, discrete clusters constituting a low-grade component of GCA (Figure 4). Perineural and lymphovascular invasion was seen. Mitosis was less than 2/10 high power field (hpf). The tumour involved the visceral peritoneum, part of the adjacent ileum, and cecum. Out of the total 22 regional lymph nodes resected, two showed metastatic tumour deposits, and there were two metastatic tumour nodules in the mesentery. Resected margins were free of tumour invasion. Consequently, the specimen was classified as high-grade GCA, appendix, pathologic stage pT4bN1aM1b.

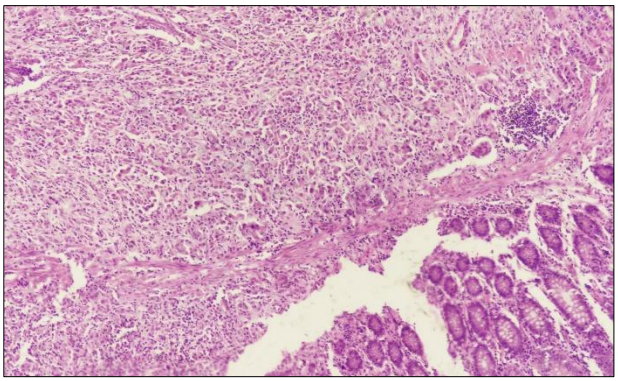

Figure 1: Predominant submucosal location of high-grade GCA (hematoxylin and eosin stain, original magnification x100).

GCA was first described in 1969 by Gagne et al as an appendiceal tumour with carcinoid and adenocarcinoma features, later termed goblet cell carcinoid (GCC) in 1974.[3,4] This tumour has undergone multiple name changes in different classifications since then. Various names given to this tumour include adenocarcinoid, mucinous carcinoid, and amphicrine carcinoma, goblet cell carcinoid, and adenocarcinoma ex goblet cell carcinoid. Then it was categorised as a subtype of mixed adeno-neuroendocrine carcinoma (MANEC) owing to its associated neuroendocrine features in the 4th edition of the WHO classification of tumours of the Digestive System published in 2010.[5] Recently, in 2019, the WHO classification of the Digestive System tumours 5th edition, it was classified as a goblet cell adenocarcinoma, highlighting its adenocarcinomatous nature.[6]

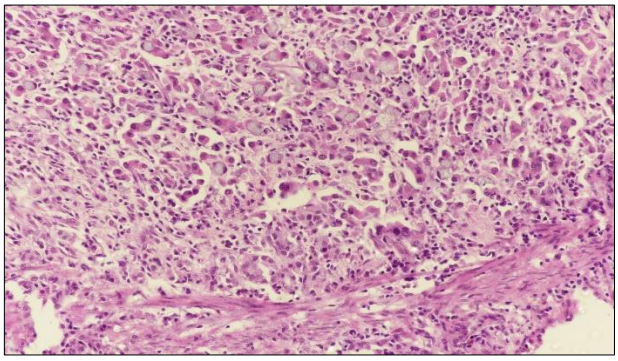

Figure 2: Mucin-filled goblet cells in sheets in high-grade GCA (hematoxylin and eosin stain, original magnification x400).

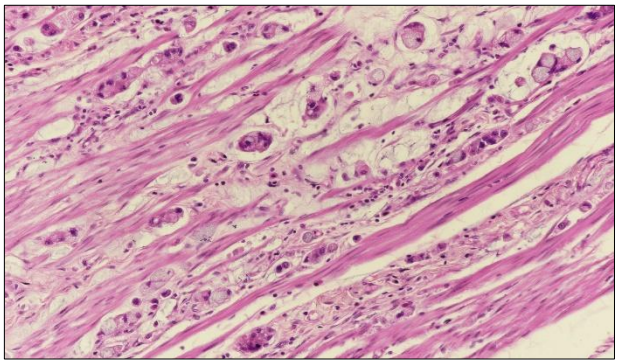

Figure 3: Mucin-filled tumour cells infiltrating into the muscle layer (hematoxylin and eosin stain, original magnification x400).

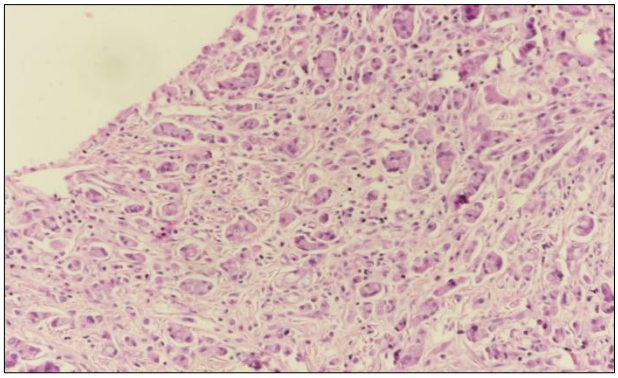

Figure 4: Low-grade component of GCA in small discrete clusters (hematoxylin and eosin stain, original magnification x400).

GCA is an amphicrine tumour composed of goblet-like mucinous cells, paneth cells, and endocrine cells. Neuroendocrine markers, chromogranin and synaptophysin, are usually expressed in mucin-containing tumour cells. But GCA is considered separate from neuroendocrine tumours because neither neuroendocrine

marker staining is consistent in this tumour nor is it associated with hypersecretory syndromes related to neuroendocrine tumours. Moreover, they behave more like typical adenocarcinoma. Therefore, usually staining with neuroendocrine markers is not required for diagnosis. However, it is important to differentiate it from neuroendocrine neoplasms (NEN), specifically from mixed neuroendocrine and non-neuroendocrine neoplasm (MiNEN) as well as conventional adenocarcinoma, and signet ring cell carcinoma, since it has a prognosis intermediate between the stage-matched tumours. While GCA has a worse survival and metastasis risk than that in appendiceal NEN, it is better than that in colonic adenocarcinoma, mucinous adenocarcinoma, and signet ring cell carcinoma.[7,8] In a study by Palmer et al, female sex, stage, and grade were associated with poor survival rate, but only the stage of the tumour was a statistically significant prognostic marker.[9] Though GCA may have a minor component of NEN, which may confuse it with MiNEN, but diagnosis of later requires each component (neuroendocrine and non-neuroendocrine) to comprise at least 30% of the lesion. Therefore, it is crucial to thoroughly examine the appendix to look not only for the presence of a neuroendocrine component but also to assess its extent.

According to the classification proposed by Yozu, GCA is graded into low-grade (tubular or clustered growth) and high-grade (loss of tubular or clustered growth).[10] High-grade tumours show single cell infiltration, complex tubular architecture, cribriform pattern, and sheets of goblet-like or signet-ring-like tumour cells. Low-grade tumours show goblet-like cells in a tubular pattern and discrete clusters with a variable number of endocrine and Paneth cells. Low-grade tumours have a favourable outcome, whereas high-grade tumours are aggressive tumours with a poorer prognosis. Sometimes differentiation of high-grade GCA from signet ring cell carcinoma becomes challenging; in these cases, focal presence of a component of low-grade GCA is essential for the diagnosis of high-grade GCA.

Generally patient presents with features of acute abdominal pain or with features of acute appendicitis. It is only after histopathologic examination that these tumours are diagnosed incidentally in early stages. They may also present as complete intestinal obstruction or in late stages as ovarian masses owing to disseminated peritoneal metastasis.[11,12] Our patient had high-grade GCA and presented with complete intestinal obstruction with peritoneal metastatic tumour deposits. However, she had symptoms of vague abdominal pain and altered bowel habits for the past six months.

CONCLUSION

Appendiceal GCA is a rare and aggressive amphicrine neoplasm. Owing to its intermediate prognosis and metastatic risk, histopathologic diagnosis requires differentiation from MiNEN, conventional adenocarcinoma, and signet ring cell carcinoma. This requires a thorough and complete examination of the appendix to look for a neuroendocrine component. Considering the rarity of GCA and the inconsistency in classification and reporting, not only is there a need for large prospective studies, but also every case of GCA should be thoroughly examined and reported.

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