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Case Report

Combined appendiceal goblet cell adenocarcinoma and low grade mucinous neoplasm: a case report with unusual presentation

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ABSTRACT

Appendiceal tumours are uncommon. They mostly present with abdominal pain due to appendicitis or as an incidental finding in an appendicectomy specimen. After neuroendocrine tumours (NETs), mucinous neoplasms are the most common appendiceal tumours. Goblet cell adenocarcinoma (GCA) is rare and exclusive in appendix. This is a distinctive subset of amphicrine tumour composed of both goblet and endocrine cells. They are more aggressive as compared to the conventional appendiceal tumours. Presence of both the tumours in the same patient is a rare instance. These synchronous tumours pose challenges for diagnosis as well as management. Here, we present a case of an 80 years old female with combined GCA and low grade appendiceal mucinous neoplasm.

Keywords: Appendix, Mucinous neoplasm, Carcinoma of the appendix, GCA, Appendectomy, Right hemicolectomy, NETs

INTRODUCTION

Primary appendiceal neoplasms are rare, however, their incidence has increased over the years.[1,2] These are usually detected incidentally in less than 1% of the appendicectomy specimens.[1] They are categorized into epithelial and non-epithelial tumours.[2] Rare cases have been reported with synchronous GCA and mucinous neoplasms in the same appendix.[3]

GCA are unique tumours with a debated histogenesis and variable biological behaviour which may range from indolent to aggressive, based on the tumour grade and stage.[4] They are graded into low, intermediate and high-grade tumours depending upon the percentage of tubular or clustered/ confluent pattern and single cell infiltration. As these tumours are mainly composed of mucin secreting goblet cells, these are considered as type of adenocarcinoma.[4,5] These tumours show immunostaining for neuroendocrine markers. However, in comparison to conventional colonic adenocarcinomas and neuroendocrine neoplasm, GCA have better survival rate.[6]

Only a few cases of GCA have been reported in combination with other appendiceal neoplasms. These are known as collision tumours. However, their relationship and pathogenesis are not ascertained. This is suggested to arise from independent progenitor cells and are caused by alterations in WNT signalling.[7,8] In this case report, we present a case of combined appendiceal GCA and low-grade mucinous neoplasm.

CASE REPORT

An 81-year-old female presented with change in her bowel habits. She was known for having active haemorrhoids and bleeding per rectum associated with abdominal bloating and flatulence. Past medical history included total thyroidectomy, emergency caesarean section, essential hypertension, total mastectomy for fibro-myxoid sarcoma, cardiac disease (left ventricular

hypertrophy, non-ST segment elevation myocardial infarction, triple vessel disease, second non-ST segment elevation myocardial infarction, coronary angioplasty) and pre diabetes. There was no history of bowel cancer in family. Investigations revealed ferritin of 26, HB of 144, MCV 86.2 and her FIT was positive at 325.9.

Computed tomography (CT) of the abdomen and pelvis identified an annular T3N0M0 caecal tumour obstructing the appendix. There was a mucocele at the tip of the appendix (Figure 1). There was a 6mm polyp in the caecum and 9 mm polyp in ascending colon. There were some more polyps which were not of significant size on both the sides of the colon. The patient underwent laparoscopic right hemicolectomy.

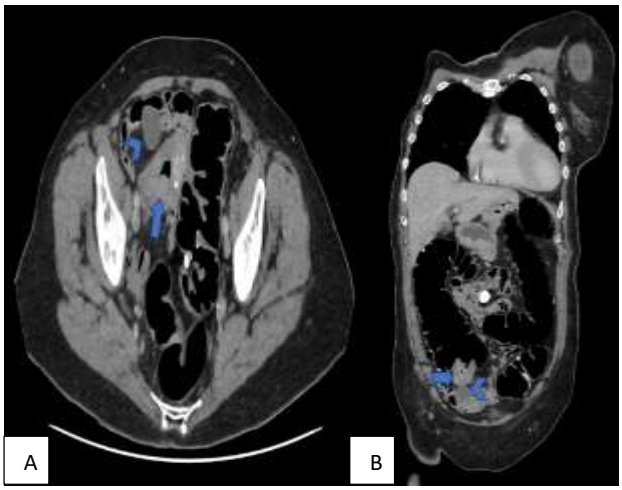

Figure 1 (A and B): Abdominal CT revealed a caecal tumour (arrow) and cystic mass in the appendix (arrowhead), indicating coexistence of GCA involving caecum and LAMN of appendix.

Right hemicolectomy specimen was received in our department. Appendix measured 60 mm long and was kinked in an 'L' shape. Distal 30 mm segment of appendix was distended to a diameter of 25 mm and contained thick luminal mucin. The proximal 30 mm of appendix appeared to be adherent to both terminal ileum and to some extent to the caecum. There was a 35 mm circumferential tumour in the caecum. A 10 mm segment of terminal ileum also appeared indurated.

Histopathology confirmed low grade mucinous neoplasm (LAMN) at the tip of the appendix (Figure 2 A) and GCA (Figure 2 A-C) immediately adjacent to this cystic lesion. Goblet cell adenocarcinoma comprised of small tubules and clusters of goblet-like mucinous cells. Bulk of the tumour was composed of single scattered mucinous and signet ring-like cells (Figure 2 A-C). The tumour cells extended beyond the subserosal fat into the serosa (pT4) and also reached the mesoappendiceal margin. The tumour involved both the mucosal and serosal aspect of the terminal ileum. There was extensive lymphatic, venous and perineural invasion. Eleven out of sixteen (11/16) lymph nodes, including the apical node, showed metastatic carcinoma (Figure 2 D).

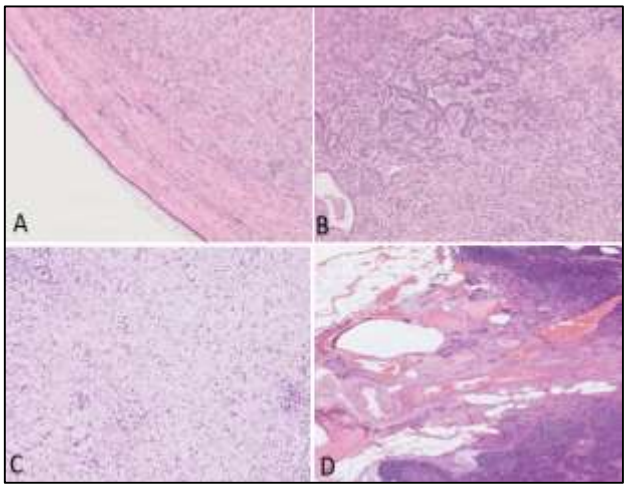

Figure 2 (A-D): Histopathological features of LAMN and GCA in appendix (H and E). It was consistent with LAMN and GCA. The tumor cells of LAMN and GCA were adjacent. Low grade GCA consisted of tubules and clusters of goblet-like mucinous cells. High grade GCA consisted of signet ring lie cells. Lymph node involvement by GCA.

Immunohistochemically, tumour cells of GCA were positive for synaptophysin (Figure 3 A), chromogranin (Figure 3 B) and CD56 (Figure 3 D), which are neuroendocrine markers. Patchy staining for CK7 (Figure 3 C) and CDX2 was also present. Ki-67 index was 10-20% in GCA. Tumours cells of LAMN were highlighted with CK20 and showed no immunostaining with neuroendovcrine markers.

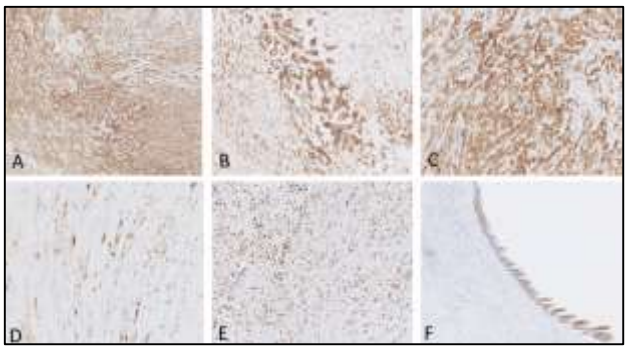

Figure 3 (A-F): Immunohistochemical staining revealed immune-expression for-synaptophysin, chromogranin, CK7, CD56, Ki-67 in GCA tumor cells, while LAMN tumor cells showed staining for CK20.

The case was reviewed at the colorectal multidisciplinary team meeting with a recommendation for chemotherapy. As the patient was not fit for debulking surgery, so she was not referred to Basingstoke. On follow up, the patient presented with ascites with presence of pools of mucin and mucinous tumour cells after a year.

DISCUSSION

Appendiceal tumours are rare. Mucinous neoplasms are detected in only 0.4-1% of all the gastrointestinal tumours. These are found in 0.2-0.3% of the total appendectomy specimens, however, these are considered to be the most common appendiceal tumours.[9]

GCA is rare appendiceal tumour with both mucinous and neuroendocrine differentiation.[6] The tumour cells rise from the pluripotent stem cells present at the base of the crypt.[10] They represent a variant of adenocarcinoma with features similar to NETs i.e. immunostaining with synaptophysin, chromogranin and CD56.[11]

NETs of appendix are staged by size with key role of mitotic activity and Ki67. In contrast, GCA follows identical UICC TNM 8 staging system as for appendiceal adenocarcinoma, due to their more aggressive nature than NETs. Hence, pathological T stage is based on depth of invasion rather than size of tumour, as is case with colorectal adenocarcinoma.[12] Unlike neuroendocrine tumours, Ki-67 and mitotic count are not required for grading GCA.[11]

The coexistence of mucinous neoplasm and GCA is a rare occurrence. The appendiceal collision tumours are incidentally detected as they cause non-specific symptoms. These tumours present most often with abdominal pain as acute appendicitis, as an incidental finding or rarely with metastasis.[6] The synchronicity of these tumours is established by pathological examination.

CONCLUSION

The collision tumours of appendix are extremely rare. They are incidental and cause diagnostic challenges. These are diagnosed on histopathological examination, which is further confirmed by immunohistochemical staining. The management is potentially challenging and depends upon grade, stage and biological behaviour of the tumour. This report discusses a rare case who presented as a caecal tumour, however, on pathological examination, two synchronous appendiceal tumours, LAMN (Tis) and GCA (T4) with GCA infiltrating into the caecum and terminal ileum, were identified. However, further investigation is required to support their association as their occurrence has been described to arise from two distinct cellular lineages.

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