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# Goblet cell appendiceal adenocarcinoma. How to deal with this rare entity. Case report & review of literature

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## ABSTRACT

Goblet Cell Adenocarcinoma (GCA) is considered a very rare entity with an incidence of 0.05 cases/100.000 per year. The aim of this report is the presentation of a case of 68-year old male who was diagnosed with GCA with a concomitant review of the recent literature. A 68 year old male presented in ED with a clinical and radiological appearance of acute appendicitis. The patient underwent a laparoscopic appendectomy. Biopsy of the specimen revealed GCA. A right hemicolectomy was performed one month later with an uneventful post-op course, followed by adjuvant chemotherapy due to one positive lymph node. A research on recent literature was performed focusing on clinical presentation, epidemiology, diagnosis, pathology, management and survival of patients with GCA. It revealed that GCA is usually first presented as acute appendicitis with the diagnosis being set only after histology report. It is not yet well established which grading system of colon cancer is more appropriate for this entity. Thus, although right hemicolectomy seems to be the treatment of choice, there are no clear guidelines about the surgical treatment of these patients. The 5 year old survival presents a great fluctuation according to tumor stage but in general it seems to be better than the one of adenocarcinoma of the colon.

**Key Words:** *Appendiceal tumours, appendicitis, goblet cell adenocarcinoma*

## INTRODUCTION

Goblet cell adenocarcinoma of the appendix (GCA) is considered a very rare entity, according to literature, found in 0.05 cases/100,000 population per year. This tumour histopathologically resembles both adenocarcinomas and carcinoids, however showing a more aggressive attitude compared to them. Because of its unexpected course, which can vary from benign and slow-growing tumour to an aggressive malignant tumour, it needs careful assessment. There is still controversy whether radical surgery (Rt. Hemicolectomy) is needed, together with adjuvant chemotherapy. This mucus-secreting tumour is usually presented with abdominal pain mimicking clinical features of acute appendicitis [1]. In this abstract, we present a case report and we review the literature about this rare malignancy.

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## CASE PRESENTATION

A 68-year-old male presented in ED, complaining of right lower quadrant abdominal pain. He also had a fever of 38.8 C, and his white blood cell count was abnormal (18.000). His clinical appearance imitated acute appendicitis. Abdominal CT scan was performed, which showed distended and inflamed appendix with possible rupture (Figure 1). During laparoscopy, the appendix was located retrocecal adherent to itself and the lateral abdominal

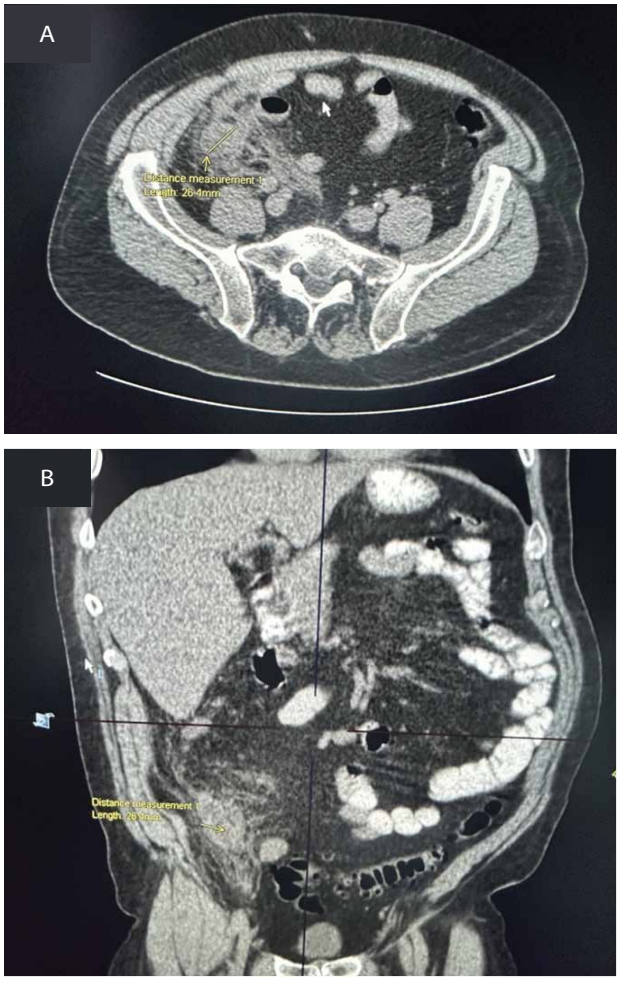


**FIGURE 1.** CT showing enlarged appendix and pericolic fat thickening.

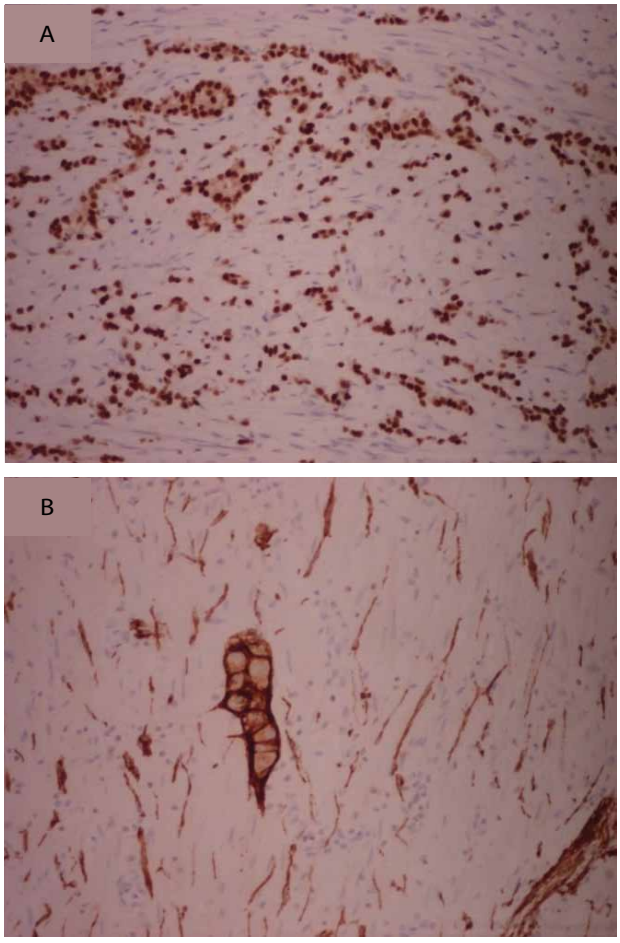


**FIGURE 2.** A: CDX-2 x 100 strain. B: CD56 X100 strain.

wall. Some purulent discharge was found around the area of inflammation. Meticulous dissection was performed and during mobilization, perforation of the apex of the appendix was found.

Laparoscopic appendectomy was performed using Harmonic endoshears (Ethicon) for the mesoappendix and 45mm GIA stapler with gold tape, stapling the base of appendix. Thorough lavage of the abdominal cavity was also performed. Patient's course following surgery was uneventful and he was discharged two days later. Biopsy of the specimen showed a 3 cm Goblet cell adenocarcinoma located mainly on the base of the appendix, extending to proximal margin of resection. Tumour was infiltrating mucosa, submucosa, muscularis propria but not the serosa. Additionally, findings of acute appendiceal inflammation with perforation at the apex were confirmed. Immunohistologic studies showed CDX2 (+), CK8-18 (+), CK7 (-), CD56 (+), Chromographin (+) and Synaptophysin (+) (Figures 2,3). Specimen was signed as GCA pT3NXR1.

A full colonoscopy was performed, in order to exclude other lesions in the rest of the bowel. After the MDT meeting, it was decided initially to proceed with right hemicolectomy. The operation was performed 30 days post appendectomy. An open limited right hemicolectomy was performed, with an uneventful post-op course. The patient was discharged seven days later. Biopsy of the specimen confirmed presence of GCA, on the appendiceal stump, extending 1.8cm in the cecum, infiltrating mucosa, submucosa, muscularis propria but not the serosa. Out of 28 lymph nodes removed, 1 was found positive (pT3N1). Patient started adjuvant chemotherapy 30 days post-op and 1 year follow-up since last operation, he is negative of tumour recurrence.

## REVIEW OF THE LITERATURE

During review of the literature for GCA cases, we found interesting data regarding its clinical presentation, epidemiology, diagnosis, therapeutic management, histopathology & genetics, grading, prognosis and survival.

**a. Clinical presentation**: In most cases GCA presents as

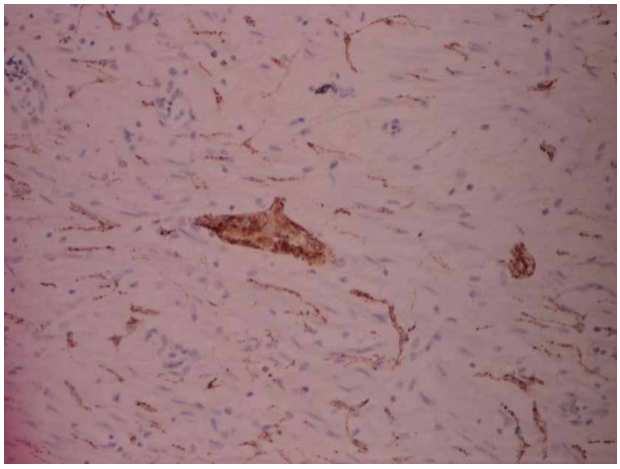

**FIGURE 3.** Synaptophysin X100 strain.

acute appendicitis. A high incidence of appendiceal perforation is reported, around 20-23% [2]. Appendicitis usually is related to low grade and localised disease. In the rest of the cases GCA could mimic non-specific abdominal pain or even abdominal mass, and in these cases most of the times we find high grade or metastatic disease. The most common sites of metastases are the liver, the small bowel and the ovaries. Regarding the location of the tumour within the appendix, no specific incidence in location (base, middle, apex) was documented in multiple studies [3-7].

b. **Epidemiology**: From literature, it is obvious that GCA is a quite uncommon entity, presenting with an incidence of 0.05-0.3 per year, per 100,000 cases. However some studies show an increased tendency of GCA recently [8]. GCA is more commonly found in Caucasian people (80-90%), with mean and median age at diagnosis reported between 50-60 years old [9].

c. **Diagnosis**: Unfortunately it is not easy to diagnose GCA, prior to histology report. CT scan is considered the main diagnostic modality, but GCA has no specific radiological features to differentiate from acute appendicitis. In some studies it is mentioned that PET (Positron Emission Tomography) scans may have better sensitivity, while in some other studies, serum carcinoembryonic antigen (CEA) [10-11] does.

d. **Pathology & Grading**: Goblet Cell Adenocarcinoma comes from pluripotent intestinal crypt base stem cells, which show combined mucinous and neuroendocrine differentiation. Focal presence of goblet shaped epithelial cells with intracytoplasmic mucin, remains the distinctive histopathologic feature of GCA. GCA stains positive on PAS (periodic acid-Schiff) staining of mucin. Grade of GCA is an independent prognostic factor, however at the moment there is a conflict between histopathologists, which grading system is more accurate regarding GCA, proposing different grading systems. There is a tendency from most studies to adopt for GCA to be classified as an adenocarcinoma, using a 4-stage grading system [12-15].

e. **Management**: There are no clear guidelines regarding appropriate management of GCA. There are some studies which imply that for a small (<1cm), low grade and apex or middle of appendix localised tumour, only appendectomy is sufficient. However, this situation is very rare, thus most of the times, if not all, additional post-appendectomy surgery is needed and more specifically right hemicolectomy [16-18]. Unfortunately, recurrence can occur, despite extensive surgery, which in some studies ranges between 16-20% and with higher possibility when positive lymph nodes are found. Use of adjuvant chemotherapy in patients undergoing right hemicolectomy, or having positive lymph nodes, or in cases of perforated appendix with appendicular abscess, seems to improve fve-year survival [19]. Metastatic disease shows an unfavorable prognosis, with five-year survival rate in Stage IV, less than 19%. In such cases palliative chemotherapy similar to colonic adenocarcinoma is used [20].

f. **Survival**: Five-year survival for GCA according to stages is estimated for ***Stage I*** 91.1%-100%, for ***Stage II*** 67%-90,5%, for ***Stage III*** 36%-57% and for **Stage IV** 4.2%-18.9%. It is evident from reviewing the literature, that GCA has worse survival than appendiceal MEN, but better than that in colonic adenocarcinoma, signet ring cell adenocarcinoma and mucinous adenocarcinoma [21-23]. Regarding independent prognostic factors, age, grade and stage, possibly have some importance, while male sex, lymph node metastases and positive surgical margins have been related to decreased survival in stage I-III [24].

## DISCUSSION

GCA is a quite rare entity, which exclusively affects the appendix. It seems that it has a more aggressive attitude than carcinoid tumours, with a shift towards colonic adenocarcinoma. It is found in 0.3-0.9 appendectomy specimens and 14-19% in primary appendiceal cancer specimens. Mean age of diagnosis is between 50-60 years old, with no predominance between males and females. Usually, it presents with signs of acute appendicitis, and in some cases it may even cause small bowel obstruction, or in disseminated disease, it may be accompanied by vague abdominal pain, which usually it may be missed by physicians. Rarely only appendectomy is adequate, being

most of the times necessary a secondary surgical procedure, right hemicolectomy with adjuvant chemotherapy in presence of positive lymph nodes. The 5-year overall survival depends on the stage of the disease, which in case of positive lymph nodes or progressed disease, is quite poor [25].

**Conflict of interest:** *The authors declare that they have no conflict of interest.*

**Consent:** *Written informed consent was obtained from the patient for the publication of this case report and accompanying images.*

**Ethical aproval:** *Ethical Approval was provided by the authors' institution.*

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