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# Unusual case of intraluminal cecal recurrence of a low grade appendiceal mucinous neoplasm (LAMN)—Case report and brief literature review

Nick Givalos<sup>a,\*</sup>, Georgios Manolidis<sup>a</sup>, Nikolaos Kochylas<sup>a</sup>, Vasiliki Vrachni<sup>a</sup>, Sofia Tsakona<sup>a</sup>, Christos Eftychiadis<sup>b</sup>, Panos Vrachnos<sup>a</sup>

<sup>a</sup> 2nd Department of General Surgery, General Hospital of Attica “KAT”, Nikis 2, PC14561, Kifissia, Athens, Greece

<sup>b</sup> Pathology Department, General Hospital of Attica “KAT”, Nikis 2, PC14561, Kifissia, Athens, Greece

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## ABSTRACT

**INTRODUCTION:** Appendiceal mucinous neoplasms exhibit a wide spectrum of clinical behavior, ranging from neoplasms which are relatively slow-growing but with considerable risk for recurrence and eventual death and those neoplasms that are highly aggressive with increased likelihood of early death. Clinical behavior depend mainly on mucinous neoplasms grading and staging.

**PRESENTATION OF CASE:** We present the incidental finding of a mucinous appendiceal neoplasm in a 52 years old woman during her follow up for an operated breast carcinoma. The patient underwent appendectomy and a low grade appendiceal mucinous neoplasm (LAMN) confined into the appendiceal wall was diagnosed. Resection margin showed fibrous replacement of the appendiceal wall and some acellular intraluminal mucin. Three months later the tumor recurred inside the cecal lumen and a right hemicolectomy was performed showing again a LAMN confined into the bowel wall.

**DISCUSSION:** According to the latest AJCC eighth edition patients with pTis LAMN, as in our case, (LAMN confined to the muscularis propria after histologic examination of the entire appendix) have essentially no risk of recurrence. Moreover, some authors suggest follow up for LAMN confined into the appendix even with a positive surgical margin.

**CONCLUSION:** Rarely, LAMN may recur in the form of a polypoid protrusion into the cecal lumen and this recurrence may originate from the buried stump of the appendix, especially when the surgical margin is positive.

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## 1. Introduction

Mucinous neoplasms of the appendix consist a complex, diverse group of epithelial neoplasms often causing cystic dilation of the appendix due to accumulation of gelatinous material, morphologically referred to as mucocoeles [1]. First described by Rokitansky in 1842 [2], mucocoeles are often incidentally detected radiologically in asymptomatic patients and often raise various therapeutic dilemmas. In the present study, we report the incidental discovery of a low grade appendiceal mucinous neoplasm (LAMN) which

recurred inside the cecal lumen, three months after appendectomy. The work has been reported in line with the SCARE criteria [3].

## 2. Presentation of case

A 52 year old woman was diagnosed in 2014 with an invasive breast carcinoma of no special type (NST) in her left breast, for which she underwent a lumpectomy with lymph node dissection followed by chemotherapy, radiation therapy and administration of aromatase inhibitors. Three years later, in 2017, during her routine follow up, an abdominal CT demonstrated a cystic lesion in the right iliac fossa, with some mural calcifications, measuring 4.3 × 4.5 × 7.7 cm (Fig. 1). The patient underwent a laparoscopic investigation in another surgical department, during which the cystic lesion was found located in the appendix, with features reminiscent of a mucocoele. The operation was converted to open and a typical appendectomy was performed. No extra-appendiceal mucin was found after meticulous investigation.

\* Corresponding author at: 2nd Department of General Surgery, General Hospital of Attica “KAT”, Iras 5 Str., Palaio Psychiko, PC15452, Athens, Greece.

E-mail addresses: [nickgival@hotmail.com](mailto:nickgival@hotmail.com)

(N. Givalos), [georgemanol@yahoo.com](mailto:georgemanol@yahoo.com)

(G. Manolidis), [nickkohilas1979@hotmail.com](mailto:nickkohilas1979@hotmail.com) (N. Kochylas), [v-aly-v@hotmail.com](mailto:v-aly-v@hotmail.com)

(V. Vrachni), [sofia.e.tsakona@gmail.com](mailto:sofia.e.tsakona@gmail.com) (S. Tsakona), [ceftychiadis@yahoo.gr](mailto:ceftychiadis@yahoo.gr)

(C. Eftychiadis), [pvrachnos@yahoo.gr](mailto:pvrachnos@yahoo.gr) (P. Vrachnos).

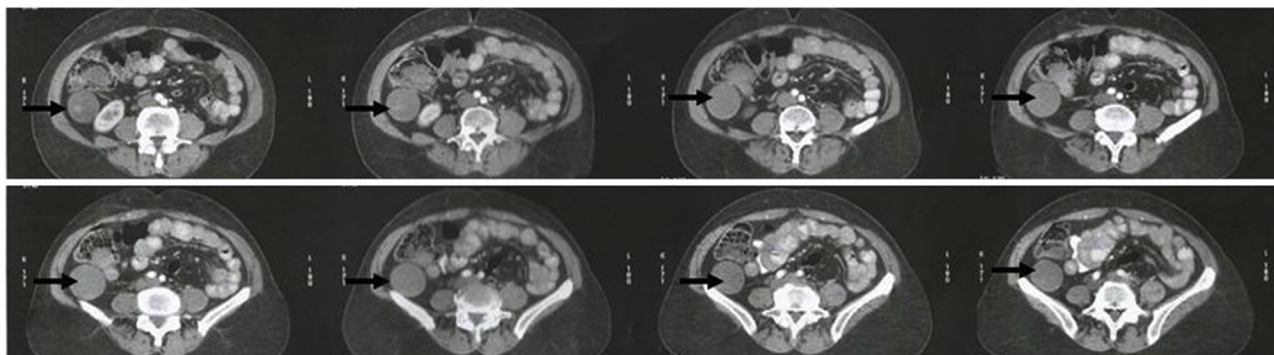


Fig. 1. Abdomen CT showing a cystic lesion with some mural calcifications in the right iliac fossa (arrows).

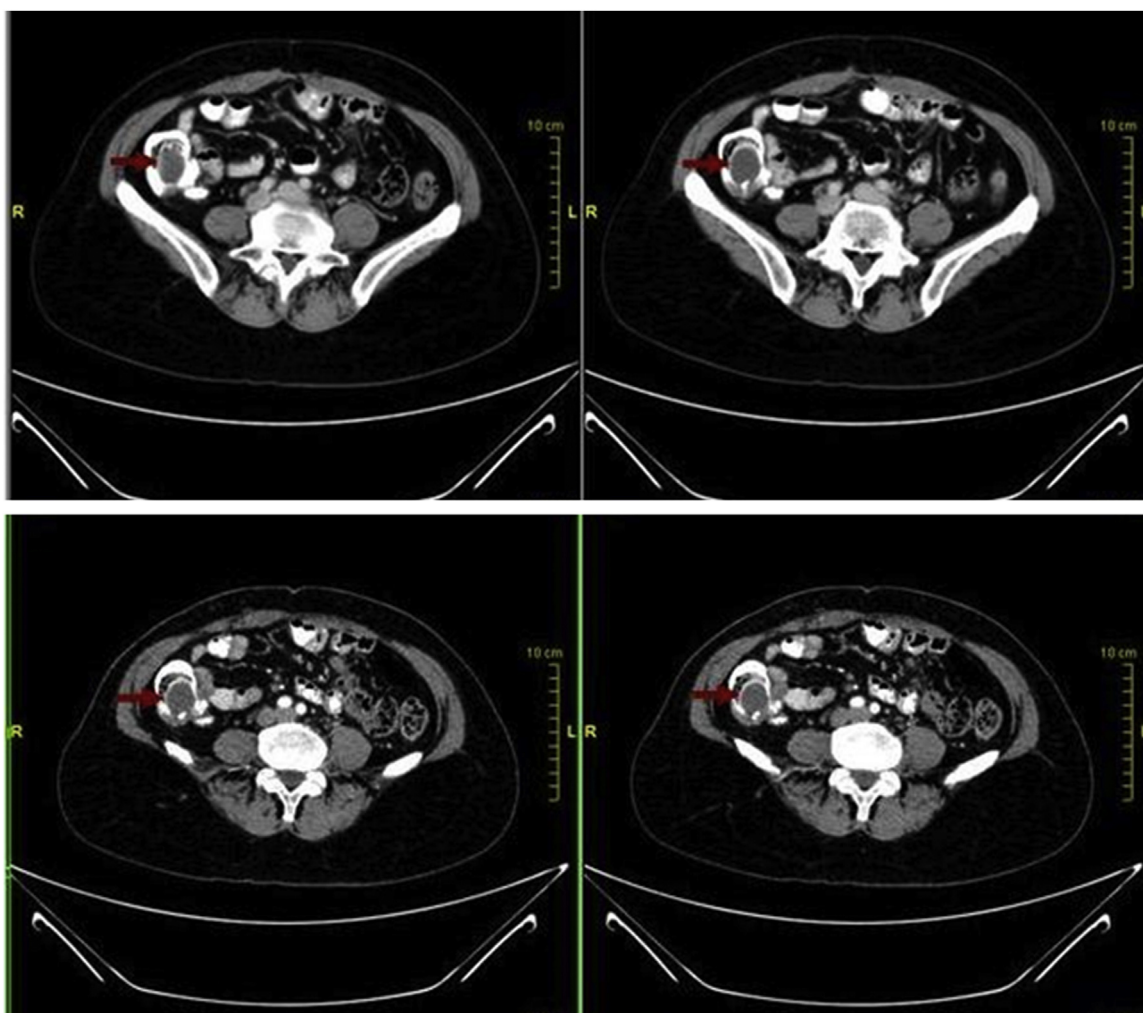


Fig. 2. CT of the abdomen after the appendectomy showing a low density cystic lesion with mural calcification, protruding into the cecal lumen (arrows).

### 2.1. Histological examination of the appendectomy specimen

Grossly, the appendix showed cystic dilatation through its whole 7.5 cm length with a maximum diameter of 4 cm. The lumen was filled with mucin. Microscopically, and after examination of the entire appendix included in 27 paraffin blocks, in all sections, replacement of the lamina propria, muscularis mucosa and submucosa by fibrous tissue was seen. Muscularis propria showed various

thinning. In sections from the base, some mucin producing columnar epithelium with low grade dysplasia was detected. In the apex area an acellular pool of mucin was observed inside the wall. Serosa and subserosa were free of changes. In the section from the surgical margin the epithelium was not preserved but some acellular intraluminal mucin was seen as well as fibrosis of the lamina propria and the muscularis propria.





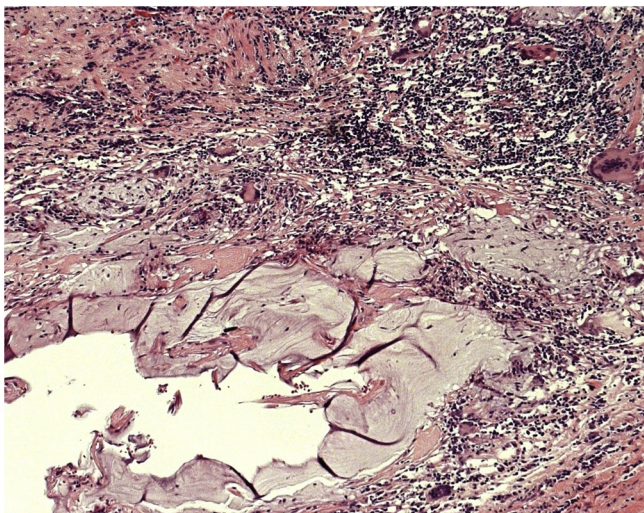
**Fig. 3.** Gross examination of the colectomy specimen showing a cystic lesion filled with mucin, protruding into the cecal lumen.

Three months later a follow up with US and a second CT were performed in our department. According to the US examination, a cystic lesion with peripheral calcifications, measuring 2 cm in its greatest diameter, was found in the right iliac fossa and in the anatomical position of the appendix. There were no signs of rupture neither free intraperitoneal fluid.

According to the CT, a cystic lesion  $2.5 \times 2 \times 2.6$  cm seemed to protrude inside the cecal lumen (Fig. 2). A right hemicolectomy was decided.

### 2.2. Histological examination of the colectomy specimen

Grossly, a cystic lesion  $2.5 \times 2 \times 2$  cm, filled with mucin, protruding into the cecal lumen and extending near the ileocecal valve was observed (Fig. 3). The origin of the lesion seemed to be the buried stump of the appendix. Histological diagnosis was again that of a LAMN confined within the bowel wall without extension to subserosa, with free margins and free lymph nodes (Fig. 4).



**Fig. 4.** Pools of acellular mucin occupying the lamina propria. Some multinucleated giant cells in the underlying stroma probably as a result of the previous appendectomy.

### 3. Discussion

In the present study we report on a rare case of a recurrent appendiceal LAMN which occurred in a 52 years old woman. Appendiceal mucinous neoplasms exhibit a wide spectrum of clinical behavior, ranging from neoplasms which are relatively slow-growing but with considerable risk for recurrence and eventual death and those neoplasms that are highly aggressive with increased likelihood of early death [1,2,4–9].

On the basis of the imaging findings and after a laparoscopic investigation suggesting a mucocele, our patient underwent an open appendectomy and the diagnosis was that of a LAMN confined into the appendiceal wall. The 2010 WHO classification recognizes 3 main categories of mucinous neoplasms: mucinous adenoma, LAMN and HAMN [10]. The presence of any mucin outside the appendix excludes the diagnosis of an adenoma while morphologic characteristics are used to distinguish low-grade from high-grade tumors [10]. The current eighth edition of the American Joint Committee on Cancer (AJCC) Staging Manual now uses a 3-tiered approach (low-grade tumors are classified as grade G1 or well differentiated, but high-grade tumors are classified as grade G2 or moderately differentiated and grade G3 or poorly differentiated based on the absence or presence of signet ring cells respectively) [11].

Moreover, the latest AJCC eighth edition initiated significant changes to the staging of appendiceal mucinous neoplasia, particularly for low-grade tumors, pointing out that their prognosis depends on their staging [11]. Patients with pTis LAMN (LAMN confined to the muscularis propria after histologic examination of the entire appendix) have essentially no risk of recurrence [11]. Patients with LAMN pT3 (LAMN with acellular mucin or neoplastic mucinous epithelium extending into the subserosa or mesoappendix but without involvement of the visceral peritoneal surface after histologic examination of the entire appendix) have an unknown risk of developing peritoneal recurrence [11]. Longterm clinical follow-up for ~10 years is suggested until additional data on recurrence risk becomes available. Patients with LAMN pT4a due to acellular mucinous deposits (LAMN with acellular mucinous deposits on the visceral peritoneal surface after histologic examination of the entire appendix) show an ~3% risk of developing peritoneal recurrence [11]. Long-term clinical follow-up for ~10 y with periodic abdominal and pelvic imaging is recommended [11]. Finally, patients with LAMN pT4a due to cellular mucinous deposits (LAMN with mucinous deposits on the visceral peritoneal surface containing low-grade neoplastic mucinous epithelium) show a ~36% risk of developing peritoneal recurrence [11]. Longterm clinical follow-up for ~10 y with periodic abdominal and pelvic imaging is recommended [10]. The role for additional surgery or intraoperative hyperthermic intraperitoneal chemotherapy (HIPEC) is uncertain but is used in some reference centers [11].

So, penetration of the visceral peritoneum by a mucinous neoplasm consists the cardinal point in the management and prognosis as it is associated with risk of peritoneal dissemination. Ronnet et al classified mucinous appendiceal neoplasms on the basis of prognosis as: disseminated peritoneal adenomucinosis (least aggressive) and peritoneal mucinous adenocarcinoma (most aggressive) [8]. According to Sugarbaker, patients with a less aggressive disease treated by cytoreductive surgery plus perioperative intraperitoneal chemotherapy and achieving a complete cytoreduction, have a 70% survival rate at 20 years [12].

In our case, no evidence of extrappendiceal mucin was found during the appendectomy while according to the histological report, we had to deal with a low grade mucinous neoplasm confined into the appendiceal wall. In the study of Misdraji et al., all 27 patients with tumors confined to the appendix and adequate

follow-up were disease free at a median of 6 years (range 0.2–20 years) [4].

A major concern in our case was the interpretation of the surgical margin of the appendectomy specimen. According to the histological report, the clearness of the margin was not clear-cut since the epithelium was not preserved but some acellular intraluminal mucin was seen as well as fibrosis of the lamina propria and the muscularis propria. Even if the observed intraluminal mucin could be interpreted as drifted from somewhere else from the appendiceal lumen or as a result of surgical or pathological manipulations, the described fibrosis of the appendiceal wall consists part of the LAMN histology and so the most prudent interpretation was that of a positive resection margin.

There are no clear guidelines regarding appropriate management of patients with appendiceal LAMNs who have positive surgical margins on their appendectomy specimens, particularly when the tumors are confined within the serosa [13]. Some experts suggest a simple cecectomy in the case of a mucinous neoplasm with positive margins of resection and negative appendiceal lymph nodes [14]. On the other hand, in the series reported by Arnason et al, 16 patients (14 female, 2 male) with LAMN (15 patients) or adenoma (1 patient) and an involved proximal resection margin were identified, including 9 with neoplastic epithelium within the lumen and 7 with acellular mucin in the appendiceal wall at the margin. Six patients underwent cecal resection and the others were non-surgically followed [13]. No cecal resection had residual neoplasia. No patient developed recurrence or pseudomyxoma peritonei in a mean follow-up of 4.7 years [13]. A conservative approach to managing these patients was suggested [13].

In our case, the patient was followed but in the CT performed three months later, a mass was observed at the base of the cecum and inside its lumen, with a partially calcified wall. Our hypothesis was that we had a tumor recurrence due to a positive appendectomy resection margin. No evidence of extra-appendiceal disease was demonstrated on imaging studies and this was confirmed during the right hemicolectomy subsequently performed. According to the histological report a neoplasm with the same characteristics as the previous one was seen inside the bowel wall.

According to Arnason et al., a possible explanation for the observed in their study absence of residual tumor in the cecum of patients re-operated because of a positive appendiceal margin, is that many appendectomies have a stapled resection margin, and the tissue designated as the margin is in fact not the true surgical margin [13]. It seems logical that in our case both the “designated as the margin” and the “true margin” as well, had residual tumor. Moreover, in most of the previous studies describing a positive resection margin, the pattern of margin involvement was mainly in the form of neoplastic epithelium or dissecting acellular mucin [9,13]. In our patient, the pattern of margin involvement was mainly in the form of fibrotic lamina propria and muscularis propria, raising the possibility that this pattern of margin involvement might show a higher association to a subsequent presence of residual tumor in the cecum.

#### 4. Conclusion

Our case shows that despite favorable prognosticators (low grade histology and tumor confined into the appendiceal wall/pTis) a mucinous appendiceal tumor may rarely recur inside the cecum and this recurrence seem to be attributable to a positive resection margin.

#### Conflicts of interest

None.

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None.

#### Ethical approval

Ethical approval has been exempted by our Institute.

#### Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

#### Author contributions

Nick Givalos: Conception and design of the study, interpretation of data and writing the article.

Georgios Manolidis: acquisition of data.

Nikolaos Kochylas: interpretation of data.

Vasiliki Vrachni: acquisition of data, literature review.

Sofia Tsakona: acquisition of data.

Christos Eftychiadis: interpretation of histologic findings.

Panos Vrachnos: Surgeon, performed the operation and approved the paper.

#### Registration of research studies

N/A.

#### Guarantor

Nick Givalos.

#### Provenance and peer review

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