A Giant Low-Grade Appendiceal Mucinous Neoplasm in a Middle-Aged Female: A Case Report and Review of Literature

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Abstract
Appendiceal mucoceles represent abnormal accumulation of mucin in the appendix. They are rare and can be due to neoplastic and nonneoplastic causes, the most common cause being low-grade appendiceal mucinous neoplasm (LAMN), also known as mucinous cystadenoma of the appendix. We present the case of a 48-year-old woman who had complaints of abdominal pain for 2 months. Imaging showed mucocele of the appendix. She was taken for open appendectomy which revealed a huge (16.5 × 7 × 6 cm) mucocele, and histology proved it to be a LAMN with negative margins.

Introduction
Appendiceal mucoceles occur due to abnormal mucin accumulation, resulting in abnormal distension of the vermiform appendix due to different neoplastic and nonneoplastic causes, histologically categorized into mucus retention cysts due to obstruction (most commonly due to an appendicolith), mucosal hyperplasia, mucinous cystadenoma of the appendix (most common), and mucinous adenocarcinoma of the appendix. Appendiceal mucoceles have a prevalence of 0.2–0.3% at appendectomy, are seen most commonly in middle-aged individuals, particularly women, and are the most common appendiceal tumors detected on imaging [1].

Low-grade appendiceal mucinous neoplasms (LAMN), previously known as appendiceal mucinous cystadenomas, are rare mucinous tumors of the appendix, showing low-grade cytological atypia. Patients are asymptomatic in around 25% of cases, others presenting with right iliac fossa (RIF) pain similar to acute appendicitis [2]. Perforation of the tumor can lead to pseudomyxoma peritonei (mucinous intraperitoneal ascites) [3]. Mucinous cystadenocarcinoma, a well-differentiated, slowly progressive tumor, represents the second most common etiology of appendiceal mucoceles [4], the treatment of which is right hemicolectomy, plus debulking if associated with pseudomyxoma peritonei [5].

Here, we present a case of a 48-year-old woman who came with complaints of lower abdominal pain and was found to have a giant LAMN (16.5 × 7 × 6 cm), treated by open appendectomy. We follow our case presentation by a review of the relevant literature.
Case Report

A 48-year-old woman, with no past medical or surgical history presented to our surgical department after having been investigated for complaints of lower abdominal pain for 2 months, with imaging results suspicious of appendiceal mucocele. Initial ultrasonography of the abdomen (done a month earlier to presentation), shown in Figure 1a, b, reported the right ovary harboring a large cyst with internal echoes that have a reticular or fishnet pattern, measuring approximately 11.1 × 6.8 × 5.7 cm. Doppler scan showed no vascularity within the cyst.

Repeat pelvic ultrasonography, shown in Figure 2a, b, showed a large abdominal-pelvic cystic mass lesion, measuring approximately 14 × 5.7 cm, tubular in shape with internal echoes that have a reticular or fishnet pattern at the right hypochondrial region, reaching the uterine fundus. This lesion was thus unrelated to the ovaries or uterus.

Computed tomography (CT) of the chest, abdomen, and pelvis with intravenous, oral, and rectal contrasts was done and reported a large distended fluid-filled thin-walled tubular mass lesion contiguous with the base of the cecum and running horizontally superior to the uterine fundus, measuring around 6.2 × 15.5 × 7.6 cm, shown in Figure 3a–c. Multiple prominent ileocolic lymph nodes with minimal adjacent fat stranding were noted. No obvious internal vascularity could be appreciated. The ovaries were spared with preserved fat planes. Complementary transabdominal ultrasound focused on the right iliac region showed a cystic mass lesion with characteristic multilayered onion skin appearance shown in Figure 4a–c.
Therefore, this characteristic ultrasonographic multilayered onion skin appearance of the large RIF tubular cystic lesion, which seemed contiguous with the base of the cecum, was thought to most likely represent a large uncomplicated appendiceal mucocoele (appendiceal mucinous cystadenoma). Other differentials were appendiceal mucinous cystadenocarcinoma or a peritoneal inclusion cyst. Colonoscopy was done prior to admission and showed inflamed appendiceal orifice with no prominent submucosal lesion, but there was evidence of segmental inflamed mucosa which was circumferential with superficial erosion and exudate with loss of underlying vascular pattern in the sigmoid and descending colon and cecum.

Biopsy was taken which reported moderate chronic active colitis with surface erosion and no evidence of granulomas or infectious agents. This suggested the possibility of Crohn’s disease or indeterminate colitis or treated ulcerative colitis with focal patchy chronicity and activity. However, our patient was not previously diagnosed with inflammatory bowel disease and denied having diarrhea or weight loss.

On presentation, the patient was vitally stable. Hemoglobin was 103.0 g/L, white blood cell count was $9.3 \times 10^9$/L, and beta human chorionic gonadotropin was negative (<5 IU/L). Creatinine was 44.21 μmol/L, alkaline phosphatase was 103 U/L, alanine aminotransferase was 17 U/L, and total bilirubin was 1.71 μmol/L. C-reactive protein was 66.7 nmol/L. Tumor markers including cancer antigen (CA) 125, CA 19-9, and carcinoembryonic antigen were negative. CA 125 was 10.6 U/mL, carcinoembryonic antigen was 8.4 ng/mL, CA 19-9 was 8.2 U/mL.

The patient was consented and planned for elective laparoscopic/open appendectomy with possible right hemicolectomy. Surgical resection of the lesion without biopsy or preoperative drainage was done to prevent pseudomyxoma peritonei.
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Lower midline laparotomy was carried out electively. The findings included a 16.5 × 7 × 6 cm appendix, shown in Figure 5, filled with likely mucinous material and mass at the tip. One enlarged lymph node was seen at the base of the appendix. The cecum was not involved. Dissection was done at the white line of todt’s lateral to the cecum to allow delivery of the appendix. Using blunt and sharp dissection, the enlarged appendix was freed from peritoneal attachments, and a window was created at the base of appendiceal mesentery. A 60-mm purple stapler was applied at the base of the appendix. Mesoappendix was divided, and hemostasis was secured using 0 vicryl ties. The appendix was delivered, hemostasis checked, patency of ileocecal junction confirmed, and fascia was closed using 0 loop PDS. Skin was closed using stapler.

The patient underwent an uneventful recovery. Histopathology confirmed the diagnosis of LAMN, with extension of the mucinous material into the submucosa. It was focally confined within muscle layers. The serosal fibrocollagenous tissue was uninvolved by the lesion. The base of the appendix was uninvolved by the lesion (with a distance of 0.5 cm from the lesion to the resected margin).

There was evidence of early acute appendicitis. The appendiceal serosa and periappendiceal adipose tissues showed areas of vascular congestion and foci of hemorrhage. One mesenteric lymph node was identified which proved to be reactive (nonneoplastic). The mesoappendix was unaffected.

On 1-month follow-up, the patient is doing well with no active complaints. Since the diagnosis proved to be a LAMN with negative margins, no further treatment was needed.

Discussion

On the literature review, we found most of the cases describing appendiceal mucocoele to have occurred in elderly females and most were treated with open appendectomy. A case described an open surgery performed on a 64-year-old female for an appendiceal mucocele with retrocecal location. Frozen section confirmed clear resection lines, and hence, an open appendectomy was done [6].

An 80-year-old woman was described to have an appendiceal mucocele, initially misdiagnosed as an ovarian cyst, with the final diagnosis only being made intraoperatively during exploratory laparotomy, where a routine appendectomy was then carried out. The authors highlighted the dilemma faced by surgeons in such cases and the need to keep appendiceal mucocele among the differential diagnoses of women presenting with a RIF pain and mass and features not indicative of gynecological pathology [7].

Similarly, in our case, the initial abdominal ultrasound was suspicious for an ovarian pathology. However, repeat ultrasound confirmed the mass to be unrelated to the ovaries and uterus. This stresses on the need to repeat ultrasound or perform other modalities of imaging such as CT scan when diagnosis is in doubt, to allow surgeons to arrive to a better conclusion about the most likely underlying pathology and avoid complete dependency on intraoperative findings.

Moreover, arriving at a diagnosis preoperatively is preferable to prevent the devastating outcome of spillage of malignant cells into the abdominal cavity in case it was a malignant cystadenocarcinoma. However, CT diagnosis of malignant cystadenocarcinoma can be quite challenging, and the final diagnosis is reached upon histopathological examination [8].

Another case is of a 38-year-old male who presented with recurrent attacks of RIF pain and was subsequently taken for emergent surgery with the suspicion of chronic appendicitis. The diagnosis of appendiceal mucocele was confirmed by histology postoperatively [9].

One more case described a 47-year-old female who had ultrasonographic features of cholelithiasis as well as an incidental cystic tubular swelling in the right lower abdomen, reported as a right adnexal cyst. She was taken for open surgery with the findings of gallstones, as well as a 13.0 × 3.5 cm cystic mass of the appendix, with thinned walls without perforation. Due to suspicion of appendiceal mucocele, appendectomy was performed along with the cholecystectomy, and histopathology confirmed the diagnosis to be a simple retention cyst [10].

With regards to patients who had undergone right hemicolectomy, a case described a 70-year-old female with appendiceal mucocele who had undergone open extended right hemicolectomy with ileotransverse anastomosis, due to suspicion of carcinoma and unavailability of a frozen section. Later on, histopathology proved it to be mucinous cystadenoma with mucocele, and she had an uneventful postoperative recovery [11].

Additionally, a 43-year-old female with dull aching pelvic pain for 2 years was taken for laparotomy which showed a giant intact cystic distended appendix with involved base, displacing the cecum cranially. Right hemi-

Fig. 5. Intraoperative finding of appendiceal mucocele measuring 16.5 × 7 × 6 cm.
colectomy was performed, and histology revealed a low-grade appendicular mucinous neoplasm with free surgical margins and no lymph node involvement [12].

A comparison of three different presentations of patients with appendiceal mucoceles was made by Cestino et al. [13]; The first case was of a 48-year-old male who was taken for laparoscopic appendectomy, electively following CT scan diagnosis of appendiceal mucocele and had an uneventful recovery. Histopathology reported mucinous hyperplasia with appendicular mucocele, with disease-free resection margin.

The second was of an elderly female admitted with hip fracture for which she underwent surgery and developed pneumonia with abdominal pain postoperatively. CT showed a RIF lesion mimicking intestinal intussusception. Ileocecal resection with lateral ileocolic anastomosis was performed as the dilated appendix had a large base, implanted on a dilated cecum, and its body was strictly adherent to the posterior wall of the pelvis. The pathology reported appendicular mucocele due to mucinous papillary cystadenoma with epithelial high-grade dysplasia and 13 pericolic nodes negative for neoplastic cells. The patient was kept on radiological follow-up.

The third case was of a 53-year-old male with clinical features of acute appendicitis and raised inflammatory markers who had undergone laparoscopic appendectomy, and the pathology reported mucinous cystadenoma of the appendix with low-grade dysplasia. This proves the varying presentations of patients with appendiceal mucoceles and further highlights the necessity to perform appropriate imaging prior to operation, keeping in mind that intraoperative findings may still prove different to preoperative provisional diagnoses.

Of the reported cases, we found our patient to have the biggest reported appendiceal cystadenoma to date, with a size of 16.5 × 7 × 6 cm. Due to the imaging finding of the huge appendiceal mucocele and to avoid spillage of contents and possible dissemination of malignancy should this prove to be a carcinoma, the decision was made to proceed with open surgery.

Some may argue that the choice of operation is dependent on the size of the mucocele, with right hemicolectomy being the more favorable option for bigger mucoceles. However, to avoid unnecessary morbidity to our patient, we decided to proceed with appendectomy and follow up the histopathology to decide if there is a need to proceed with right hemicolectomy in case of malignancy.

Since our patient proved to have a LAMN with negative margins, and the base was not involved, an appendectomy was in fact the operation of choice. Our patient is currently doing well with scheduled follow-ups and yearly colonoscopy surveillance.

Conclusion

In conclusion, appendiceal mucoceles are a rare entity, which can be neoplastic (benign or malignant) or non-neoplastic. Our patient presented with a giant (16.5 × 7 × 6 cm) appendiceal mucocele which was removed by open appendectomy and later proved to be a LAMN. This should alert physicians and surgeons to the possibility of this diagnosis especially in a middle-aged female presenting with chronic abdominal pain and hence warrant radiological diagnosis, in order to assess the extent of tumor progression and to decide on the proper surgical management, with referral to oncological services for further treatment should the lesion prove to be malignant.

Statement of Ethics

This case report study complies with the guidelines for human studies and was done ethically in accordance with the World Medical Association Declaration of Helsinki. Ethical approval is not required in accordance with the Dubai Health Authority Ethics Committee policies. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

The authors did not receive any funding.

Author Contributions

Y.H.A. and A.H.S. contributed to writing and data collection. L.S.A.-O. contributed to study design and review.

Data Availability Statement

All data generated during this case report study are included in this article. Further inquiries can be directed to the corresponding author.
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