Original Article

Does it matter if it is appendix mucocele instead of appendicitis? Case series and brief review of literature

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ABSTRACT

Aims: Appendiceal mucocele (AM) is a rare pathology, and its reported incidence is 0.3% in all appendectomy specimens. Here, we report a case series of AM and make a brief review of literature.

Subjects and Methods: We conducted a retrospective review of a prospectively collected data of patients who diagnosed as AM by histopathological evaluation between January 2009 and June 2015 were demographic data including age and gender, intraoperative findings, and histopathological reports were recorded. All cases were followed-up by routine examination and telephone interview.

Statistical Analysis Used: Definitive statistical methods (mean, standard deviation, median, frequency, and percentage) were used to evaluate the study data.

Results: Twelve patients were examined in the study with diagnose of AM. The mean age was 51.8 ± 18.6 years (26–83). Female-to-male ratio was 1.4 (7/5). Indications for surgery were acute abdomen in 8 (72.7%) patients with presumptive diagnosis of acute appendicitis and were AM in four patients diagnosed by imaging. Histopathological evaluation revealed mucinous cystadenoma in eight patients, simple retention cysts in three, and borderline mucinous tumor (pseudomyxoma peritonei) in one. The neuroendocrine tumor was obtained on the remaining portion of the appendix in one of the simple retention cysts patients. None of the patients died because of the AM with an average follow-up of 43 months (range: 7–74).

Conclusions: Surgical resection is the first choice therapy for AM. Precise treatment modality can remain unclear in some patients because of insufficient preoperative diagnosis. It is nonmalign AM mostly however having mucocele matters because of the significant association with synchronous tumors.

KEY WORDS: Appendicitis, mucocele, neoplasms, synchronous

INTRODUCTION

Appendiceal mucocele (AM) is rare in clinical practice and it is characterized by a distended, mucus- filled appendix. AM is classified into the following histologic subtypes: Mucosal hyperplasia which has comparative histology such as a hyperplastic colon polyp, simple or retention cyst which is described by degenerative epithelial changes due to obstruction (e.g., fecalith) and distention; mucinous cystadenoma which is morphologically reminding adenomatous colon polyp or villous adenoma; mucinous cystadenocarcinoma which shows glandular invasion into the stroma.[1]

AMs are uncommon and are found in approximately 0.3% of appendectomy specimens.[2] Among AMs, the nonneoplastic mucoceles (mucosal hyperplasia and simple retention cysts) have a higher occurrence as compared with neoplastic mucoceles (mucinous cystadenomas and cystadenocarcinomas).[1-3]

AMs are usually presented as acute appendicitis and are detected as an incidental finding during operation and pathological evaluation of appendix or imaging techniques such as radiologic or endoscopic evaluation of unrelated complaints.[2-4] Specific imaging findings taken from computed tomography (CT) or ultrasound helps physicians to diagnose this condition.

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Patients are frequently asymptomatic or have nonspecific symptoms. The most frequent symptom is acute or chronic right lower quadrant abdominal pain. An abdominal mass is occasionally palpable. Less frequently, patients can present with intermittent colicky pain and gastrointestinal bleeding associated with intussusception of the mucocele, intestinal obstruction from mass effect, genitourinary symptoms due to obstruction of the right ureter or bladder, acute abdomen from mucocele rupture, or sepsis.[5,6]

In this report, we aimed to present case series of AM and discuss the presentation, treatment strategy, and outcome of the disease under the review of literature.

SUBJECTS AND METHODS

This study was a retrospective review of prospectively collected database. The local internal review board approved the study protocol. The patients who diagnosed as AM by histopathological evaluation between January 2009 and June 2015 were reviewed retrospectively, in this observational study.

Preoperative presumptive diagnoses were evaluated. Patients with definitive preoperative diagnose of malignancy confirmed by histopathology were excluded from the study. Demographic data including age and gender as well as operation notes regarding suspicious intraoperative findings and pathology results were recorded. Additional interventions after pathological examination and during follow-up were noted. All cases were followed-up by routine examination and telephone interview.

Normally-distributed continuous variables were expressed as mean ± standard deviation. Categorical variables were expressed as frequencies and percentages.

RESULTS

After exclusion of four patients with colonic cancer, a total of 12 patients with the diagnosis of AM were studied. The mean age was 51.8 ± 18.6 years (26–83). Female-to-male ratio was 1.4 (7/5). Indications for surgery were acute abdomen in eight (66.7%) patients with presumptive diagnose of acute appendicitis and were AM in four (33.3%) patients diagnosed by CT. During the study, 2533 patients operated for acute abdomen with the presumptive diagnosis of acute appendicitis. Eight (0.3%) of them were diagnosed as AM after histopathological evaluation. Detailed information about cases is summarized in Table 1.

All patients had a complaint of abdominal pain, two had nausea and vomiting. Eight patients had acute abdomen during admission and operated emergently. Remaining four patients had complaints of pain intermittently, and physical examinations were nonspecific for acute condition. In these patients, diagnoses were revealed by imaging techniques (ultrasound and CT), and patients were prepared for elective surgery. Ten patients had directed to the ultrasound examination before operation, and four of them were directly taken to the operation without further imaging modalities such as CT because of highly possible acute appendicitis suspicion of ultrasound [Table 1]. CT was preferred in the remaining two patients, showing cystic formation at appendiceal area. Ultrasound reported suspicion of acute appendicitis in six patients, tubular formation in two, and normal findings in one. CT scans were taken from seven patients, and with the help of multiplanar reconstruction, tubular formation was detected in seven patients, suggesting the diagnosis of AM [Figures 1-4].

Preoperative laboratory evaluation revealed leukocytosis in seven patients (13.072 ± 5.219, range: 7.200–26.500/μL) and anemia in four (hematocrit: 36.6 ± 8.2%, hemoglobin 12.1 ± 2.8 g). Three of anemia patients required a blood transfusion. Tumor markers, for example, carcinoembryonic antigen and CA 19-9 were available and normal in three patients.

Only appendectomy performed in nine cases. Perforated appendicular mass with the involvement of cecum and mucinous dissemination was seen in one of the cases, and the operation of choice was right hemicolectomy. Another right hemicolectomy was performed in one of the cases with the nonperforated huge appendicular mass. Ileocecal excision was performed in one of AM cases.

Histopathological evaluation revealed mucinous cystadenoma in nine patients, simple retention cysts in two, and borderline mucinous tumor (pseudomyxoma peritonei) in one. The average size of lesions was 3.6 cm ranging from 0.5 to 12 cm. The neuroendocrine tumor was obtained on the remaining portion of the appendix in one of the simple retention cysts patients. High-grade dysplasia was detected in one of the cystadenoma patients, and acute phlegmonous appendicitis was detected in another cystadenoma patient.

The mean length of stay was 4.8 ± 1.3 days with a range of 1–27 days. Surgical site infection developed in three patients (7%). Two of them were treated by conservative therapy. Fournier's gangrene developed in the remaining patient, and the patient was treated with repeated surgical debridement successfully.

At follow-up, the patient with pseudomyxoma peritonei was operated with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy at 31 months after the first operation with a CA 19-9 level >1200 U/mL, and magnetic resonance imaging findings of 8 cm × 14 cm mass invading the right iliopsoas muscle [Figure 5]. Four months later, the patient was reoperated with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy due to recurrence in iliopsoas area with magnetic resonance imaging finding of 5 cm mass located posterior to iliopsoas muscle. One of the patients deceased

Table 1: Demographic, histopathological findings of appendiceal mucocele cases

Sex	Age	Size (cm)	Preoperative diagnose	US findings	CT findings	Operative findings/operation	Pathology
Male	26	0.5	AA	AA		Normal/open appendectomy	Mucinous cystadenoma
Female	31	4	AA	AA		Normal/open appendectomy	Neuroendocrine tumor and retention cyst
Male	32	3	AM	6 cm tubular formation	3 cm mucocele	Normal/laparoscopic appendectomy	Mucinous cystadenoma
Female	39	0.5	AA		2 cm cystic formation	Normal/open appendectomy	Retention cyst
Male	42	12	AA	AA		Perforated mucoid mass/right hemicolectomy	Mucinous cystadenoma, Pseudomyxoma peritonei
Female	49	0.5	AA		4 cm cystic formation	Normal/open appendectomy	Mucinous cystadenoma
Female	52	1	AM	AA, 3 cm fluid collection	1 cm tubular formation	Mucocele/ileocecal excision	Mucinous cystadenoma
Female	61	4	AA	4 cm tubular formation	4 cm tubular formation	Normal/open appendectomy	Mucinous cystadenoma
Male	62	5	AA	AA	2 cm cystic formation	Mucocele/open appendectomy	Mucinous cystadenoma
Female	69	1	AM	Normal	1 cm tubular formation	Mucocele/open appendectomy	Mucinous cystadenoma
Male	76	2.5	AA	AA, 3 cm fluid collection		Normal/open appendectomy	Mucinous cystadenoma
Female	83	9	AM	AM	10 cm appendicular mass	Appendiceal mass/right hemicolectomy	Mucinous cystadenoma

US=Ultrasound, CT=Computed tomography, AA=Acute appendicitis, AM=Appendiceal mucocele

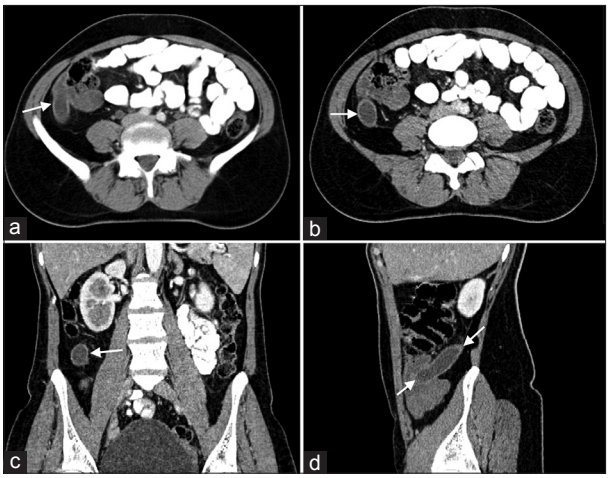

Figure 1: (a) Contrast enhanced computed tomography axial view showing the lesion entering cecum (white arrow), (b) axial view showing the lesion as cystic mass with the size of 19 mm × 25 mm, (c) coronal view demonstrating the cystic mass (white arrow), (d) sagittal view showing extension of the lesion (29 mm × 84 mm between two arrows)

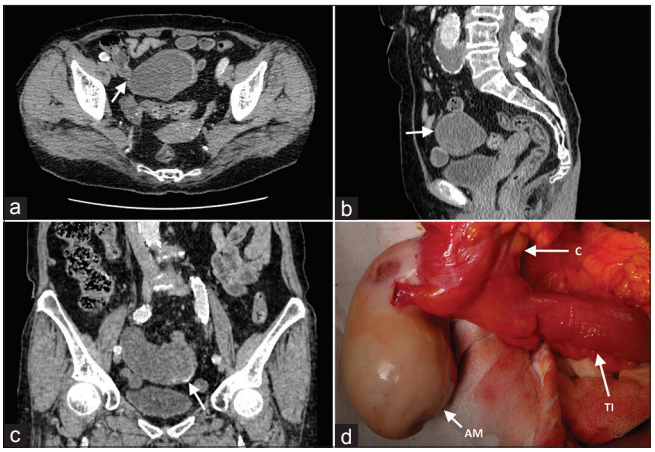

Figure 2: (a) Contrast enhanced computed tomography axial view showing the lesion entering cecum (white arrow) with the size of 72 mm × 51 mm, (b) coronal view showing the lesion as cystic mass, (c) sagittal multiplanar reconstructed image demonstrating the cystic mass with mural calcifications (white arrow), (d) operative view of appendicular mass (arrow with appendiceal mucocele tag), terminal ileum (arrow with TI tag), and cecum (arrow with C tag)

41 months after the operation due to exacerbation of chronic respiratory disease. No other death or morbidity occurred with an average follow-up of 43 months (range: 7–74 months).

DISCUSSION

AM is a rare disease of the appendix vermiformis which is detected in 0.3% of all appendectomies. In literature, AM is misdiagnosed as acute appendicitis, adnexal, or pelvic mass in almost half of the cases.[4,5,7] In our series, eight (73%) AM cases were misdiagnosed as acute appendicitis and it constituted 0.3% of patients with presumptive diagnosis of acute appendicitis. Surgeons suspected the pathology during operation in most of the cases; however, definitive diagnoses were achieved by histopathological evaluation.

There are various results about gender and age distribution of AMs. Some of reports have showed female or male predominance; others have showed similar incidences in men and women.[2,4,8] In our study, there was a slight female predominance. Fifth and sixth decades of life have been reported as the most common age group.[2,4] In our study, mean age was 51.8 and range was variable from 26 to 83 years. Although this study presented low volume of AM cases, this study showed that AM can be diagnosed at any age, and it should be considered in the differential diagnosis of acute abdominal pain in any age.

AM is generally evaluated in four different histological groups as simple mucocele or retention cysts, mucosal hyperplasia,

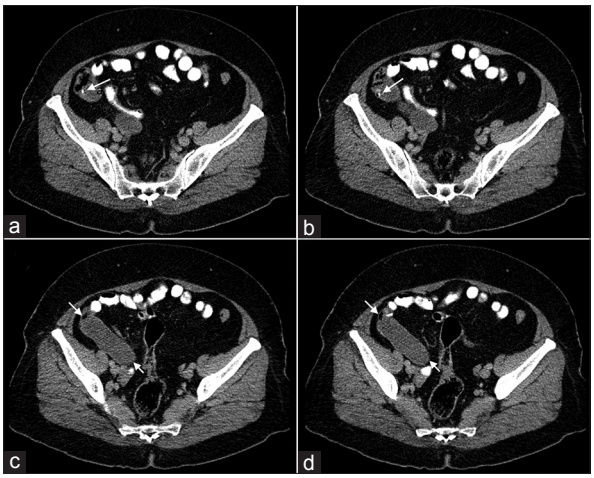

Figure 3: (a and b) Contrast enhanced computed tomography axial view showing mural calcifications (arrow) and cystic mass, (c and d) axial view shows tubular mass with the size of 26 mm × 86 mm (between two arrows)

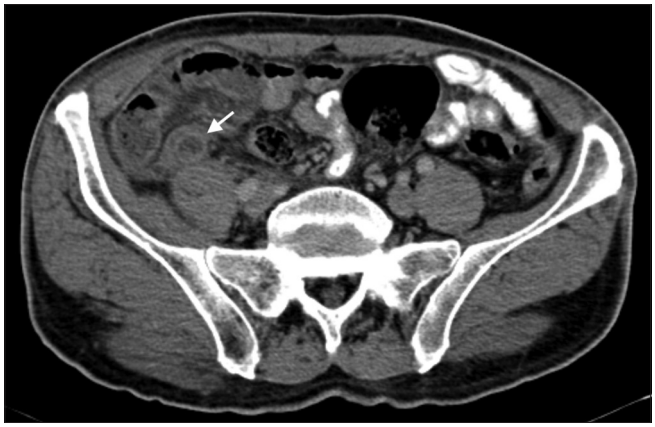

Figure 4: Contrast enhanced computed tomography axial view showing tubular mass in appendiceal area

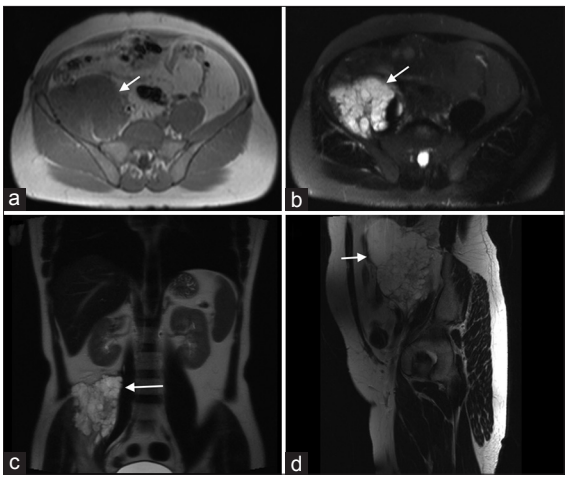

Figure 5: Multi-planar magnetic resonance imaging of patient with psuedomixoma peritonei, scan was performed during follow-up at 31st month after first operation of appendiceal mucocele, (a) axial T1-weight image shows 8 cm mass (arrow) in the right lower quadrant, (b) axial T2-weighted scan show multiple cystic lesions (arrow), (c) coronal section shows mass (arrow), (d) sagittal section shows mass (arrow)

mucinous cystadenoma and mucinous cystadenocarcinoma with prevalence rates of 52%, 20%, 18%, and 10%, respectively.[1-3,9] Prognosis differs according to subtypes, and they need different survey and treatment modalities. Therefore, its preoperative diagnosis is an important issue for differential diagnosis of several acute and elective abdominal conditions.[2,5] In our study, retention cyst and mucinous cystadenoma were detected in 16.7% and 75% of cases, respectively. There was no mucosal hyperplasia and cystadenocarcinoma. However, the borderline mucinous tumor was detected in one (8.3%) of the patients.

Laboratory findings are nonspecific include anemia. Elevated tumor markers (e.g., carcinoembryonic antigen, CA 19-9) have been reported in neoplastic AM cases.[5,10] In our study, anemia detected in four of eleven patients, and three of them required blood transfusion before the operation. Although only two patients were tested for a tumor marker, no elevated levels were detected preoperatively in our patients. At follow-up of the patient with borderline mucinous tumor, CA 19-9 level was elevated over 1200.

Radiologic studies, specifically CT and ultrasound, can prompt a possible determination of an AM. On the other hand, their discoveries are nonspecific. On abdominal ultrasound, an AM resembles an ovoid cystic mass with or without mural calcification. Ultrasound may show variable inner echogenicity relying on the consistency of the mucocele.[11,12] In our series, all patients were admitted with abdominal pain and it has been preferred to use ultrasound examination in nine (81.8%) of 11 patients as a first-line imaging technique. Only two (22%) of ultrasound examination was suspected AM with a cystic mass like tubular formation located in the right iliac fossa, seven of nine ultrasound was negative for AM diagnose.

The average CT finding in a patient with an AM is a low weakening, well-encapsulated round, or tubular cystic mass in the right lower quadrant neighboring the cecum, and the most part of which can be retrocecal. The vicinity of curvilinear or punctate line calcification at the site of the appendix can be informative to supplement an AM; however; it is seen in <50% of cases.[11,12] Cystic dilatation of the appendix, mural calcification of the wall, and luminal diameter >15 mm are important imaging findings for AM diagnosis.[13] In our study, seven (63.6%) patients received CT, and CT revealed pathology as cystic (in three) and tubular (in three) formation with a possible diagnose of AM in all of them. Mural calcification detected in one of the patients.

CT has the advantage of clearly showing the anatomic relationship of the cystic mass and the cecum over ultrasound or barium enema. Imaging findings cannot differentiate the histologic subtypes of AM; however, certain characteristics of malignancies may be helpful. Neoplastic AM (cystadenomas and cystadenocarcinomas) are generally larger than nonneoplastic AM (mucosal hyperplasia and retention cyst). Soft tissue thickening and wall irregularity without an increase in wall thickness are suggestive of malignancy.[9,14,15]

Benign AMs, hyperplasia, and retention cysts are not associated with recurrence once they rupture. In contrast, AMs that develop from true neoplasms (cystadenomas or cystadenocarcinomas) secrete mucin. Rupture can lead to the intraperitoneal spread of neoplastic cells resulting in mucinous ascites, with adhesions and intestinal obstruction. Pseudomyxoma peritonei can be developed after the rupture of these lesions.[16] In our study, one of the patients had spontaneously perforated AM and consequently pseudomyxoma peritonei during operation, and histopathology revealed borderline mucinous tumor.

The differential diagnosis of an AM includes acute appendicitis and other appendiceal neoplasms (e.g., leiomyoma, fibroma, carcinoid, lipoma, and adenocarcinoma of the appendix).[17] These conditions can be differentiated by the help of imaging techniques such as abdominal CT scan. The presence of periappendiceal inflammation or abscess suggests an acute appendicitis.[12] In our study, CT helped to differentiate pathology as AM in seven cases. In remaining patients, only ultrasound was performed and failed to diagnose AM in all four patients.

The presence of AM and other tumors involving the gastrointestinal tract, ovary, endometrium, breast, and kidney has been reported.[18-20] A concurrent colorectal adenocarcinoma has been reported in approximately 20% of patients with AM. Examination of the colon, rectum, and ovaries are suggested at the time of surgery to reveal an incidental tumor.[1,5] The relation of these concurrent pathologies is not clear in literature because most of the studies are case reports or case series.[18-21] In our study, after pathological evaluation of appendix, the neuroendocrine tumor was detected at remaining part appendix in one of the patients. However, we did not detect concurrent tumor at other organs during operation. Operations were performed by open surgery technique with McBurney incision in eight patients, mid-line incision in two patients, and laparoscopic surgery in one patient. It can be assumed that definitive exploration with Mc-Burney incision may be insufficient. Nevertheless, no other additional incision was performed for any of patients. We scheduled routine examinations for example, colonoscopy, breast, and gynecologic examination, for all AM cases. No other pathology was detected.

AM can be detected in the operation of other abdominal pathology. Farah-Klibi *et al*.[22] reported a case of primary cystadenocarcinoma of the appendix that detected at the operation of mucinous adenocarcinoma of the colon. In our clinic, we detected four AM; all were cystadenoma, in the operation of colon cancer at the period of study. Three of them were adenocarcinoma, and one of them was neuroendocrine carcinoma. These cases were not presented in our series because the presence of other malignancy can change the efficacy of the imaging techniques and also these situations not changed the patients' survey. However, surgeons have to be aware of the risk of concurrent malignant conditions, and should plan a follow-up program for patients with AM, even in benign AM cases. New studies are needed to explain the relation of concurrent pathologies for example, neuroendocrine carcinoma and AM.

Surgical resection should be offered to all AM cases. Although CT is appropriate to detect AM, benign appearing AM may harbor a cystadenocarcinoma which could not be differentiated in imaging studies.[5,15,18,23] Standard simple appendectomy, open or laparoscopic, has been suggested for retention cysts, mucosal hyperplasia, or cystadenomas.[5] In patients with a complicated mucocele with the involvement of adjacent organ, the right hemicolectomy is suggested. Rupture of a neoplastic mucocele may result in peritoneal dissemination, careful surgical methods for handling, and resection of the lesion is imperative to avoid this complication.[16,24] In our study, we performed appendectomy for nine cases. We detected a perforated mucoid mass in one the patients, the operation of choice was right hemicolectomy. Pathology of patients revealed borderline mucinous tumor, pseudomyxoma peritonei. At follow-up, the malignancy recurred.

The prognosis of AM is related with their histologic subtypes. Survival is excellent (91–100%) after standard appendectomy of retention cysts, mucosal hyperplasia, or cystadenoma. However, patients with appendiceal cystadenocarcinomas have 5-year survival rate of 6–100% based on stage.[4,25] In our study, the survival rate was 100% with an average follow-up of 43 months.

In this study, some limitations are available including its retrospective design, lack of advanced imaging technique like CT in some of the patients. However, after this study, we implemented a diagnostic algorithm to increase the awareness of this pathology for cases of suspected acute appendicitis and a follow-up protocol for AM cases. New clinical studies with larger series are needed to develop follow-up protocol for this pathology.

CONCLUSIONS

Despite the use of advanced imaging studies, definitive diagnosis of AM could not be achieved in some cases. Simple appendectomy can be curative in most the patients. Detailed operative examination and systematic screening after operation may be overlooked; however, it matters because of the significant association with synchronous tumors.

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Conflicts of interest
There are no conflicts of interest.

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