MUCOCELE OF THE APPENDIX: THROUGH 8 CASES AT MILITARY HOSPITAL 175

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ABSTRACT

Appendiceal Mucocele (AM) is a very rare disease, believed to be more common in middle-aged women, and includes both non-neoplastic and neoplastic lesions. If not diagnosed and treated early, it can lead to mucin leakage, spilling into the peritoneal cavity, resulting in severe consequences, particularly the complication of pseudomyxoma peritonei (PMP), which has a very poor prognosis. Although it is not difficult to preoperatively diagnose AM using imaging diagnostic tools such as computed tomography and ultrasound, but screening and early detection of appendiceal mucocele still face many difficulties because the clinical symptoms of AM are quite faint.

Accurate and thorough surgical resection is the main treatment method, and the subsequent histopathological analysis forms the basis for the next treatment steps. We report 8 cases of AM diagnosed and treated at the Abdominal Surgery Department of Military Hospital 175 with positive treatment outcomes.

**Keywords: Appendiceal Mucocele, appendiceal cyst.*

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1. Introduction

The term Appendiceal Mucocele (AM), nowadays often referred to as appendiceal mucinous lesions, describes a cystic lesion with the accumulation of mucin in the appendix. This is a rare disease and is found in 0.2–0.7% of appendectomy specimens, predominantly occurring in females and individuals over 50 years of age (1, 2).AM can be caused by either benign or malignant processes, with the most common symptom being pain in the right iliac fossa, resembling the clinical picture of acute or chronic appendicitis, and sometimes presenting without symptoms. In severe cases, the disease can spread to the peritoneal cavity in the form of semi-solid adhesive mucin, with a very poor prognosis (1).

According to the Peritoneal Surface Oncology Group International (PSOGI), classification in 2012, AM is divided into two main types: The first type of non-cancerous (non-neoplastic) appendiceal mucosal lesions, including simple mucocele and retention cysts without proliferation, and mucosal neoplasia. The second type includes neoplastic lesions such as serrated polyps, appendiceal mucinous cancer: Low-grade appendiceal mucinous neoplasm (LAMN), High-grade appendiceal mucinous neoplasm (HAMN), and Mucinous adenocarcinoma (MACA) (3).

In 2019, the World Health Organization (WHO) removed non-neoplastic lesions from the AM classification. PSOGI proposed a new classification, which was accepted by WHO in 2020, according to which AM includes only: appendiceal serrated polyps, LAMN, HAMN, and MACA (with or without signet ring cells) (2, 4).

Preoperative diagnosis of AM is not difficult and can be easily detected using common imaging diagnostic tools such as ultrasound and CT scan, but early screening and detection remain very difficult (1, 2). The best treatment is accurate radical surgery to prevent mucin from spreading in the peritoneum (5, 6).

In this study, we report the characteristics, classification, and treatment outcomes of patients with AM received at our facility from 2021 to 2023.

2. Clinical Cases

Over the three years from 2021 to 2023, we performed an appendectomy on 2508 patients and recorded 8 patients diagnosed with AM, accounting for a rate of 0.32%, with an average age of 63.4±12.1 (49–83) years; male/female ratio: 1/1; underlying diseases: 62.5%; history of abdominal surgery: one patient. Among the patients, 7/8 patients, exhibited right iliac fossa pain: four patients (50%) presented with acute pain; three patients (37.5%) presented with chronic pain, and one patient (12.5%) was asymptomatic,

incidentally discovered while being treated for another disease. All patients had no clear signs of infection, white blood cells increased slightly in 3/8 cases (37.5%), while the percentage of neutrophils (N%) was within the normal range for all cases. Ultrasound diagnosed AM in 4/8 patients (50%), while CT scan detected AM in 100% of the patients.

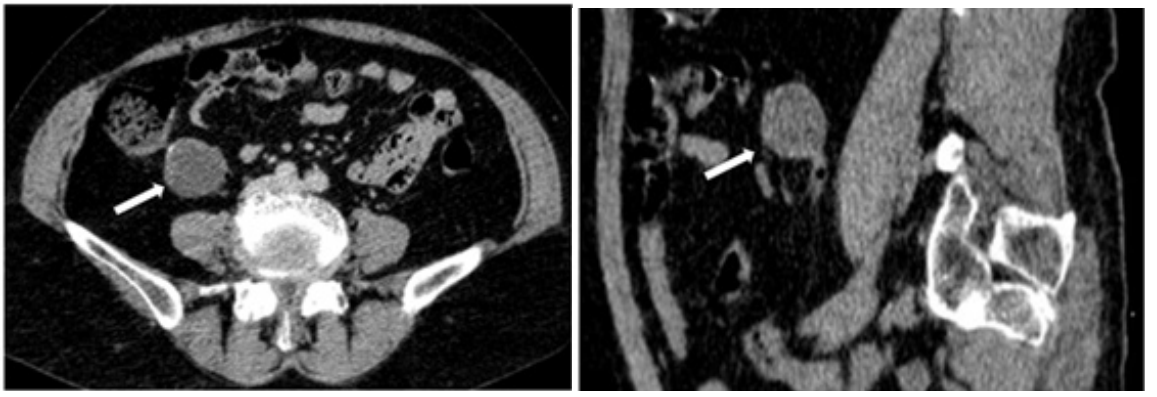

Figure 2.1. Mucocele at the tip of the appendix on CT scan with contrast agent

The lesions of the appendix on the CT scan showed abnormal swellings of the appendix, which could be localized at the tip, body, or entire appendix, with the fluid in the swelling usually having high density (Figure 2.1). Six/eight patients had lesions confined to the appendix, while two patients had accompanying abdominal fluid suspected to be due to tumor rupture. Colonoscopy detected a suspected tumor at the base of the appendix in only one out of eight patients (12.5%), indicated by a mass pushing into the cecum. All eight patients were indicated for surgery, with seven cases undergoing laparoscopic surgery and one case converting from laparoscopy to open surgery. The average surgery duration was 90.6 ± 47.7 (45–180) minutes. Injury during surgery: appendix in normal position in 6/8 cases (75%) and a retrocecal appendix in 2/8 cases (25%). The tumor location was at the tip, body, and base of the appendix in 37.5%, 37.5%, and 25% of cases, respectively, the largest diameter of the tumor ranged from 16 to 80 mm. There were two cases where the tumor progressed to cause pseudomyxoma peritonei (PMP) (Figure 2.2).

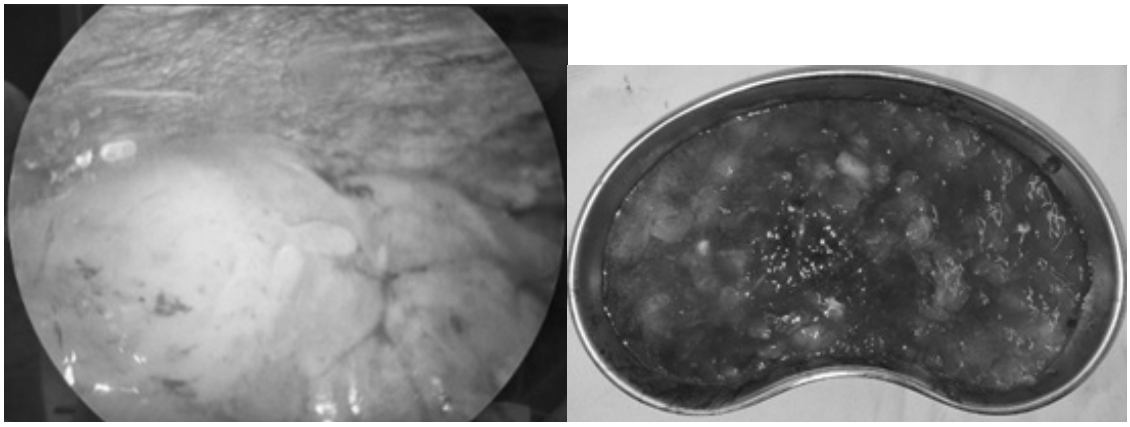

Figure 2.2. Images of mucinous appendiceal tumor progression leading to pseudomyxoma peritonei (PMP) observed through abdominal endoscopy and fluid extraction.

Treatment of the lesions: All tumors were excised according to the principle of at least 1 cm margin from the tumor, depending on the actual extent of the lesion during surgery to determine the extent of resection, without performing frozen section biopsy.

Specifically, we performed: simple appendectomy, appendectomy with cecumectomy, appendectomy with ileocecal resection, right hemicolectomy, appendectomy with mucin extraction, tumor biopsy with mucin extraction, with proportions of 37.5%, 12.5%, 12.5%, 12.5%, 12.5%, and 12.5%, respectively; there were no intraoperative complications (0%).

All appendectomy cases included ligation of the base and clamping of the appendix on the resection margin using Hemolock to prevent mucin dissemination (Figure 2.3). One case of AM-causing PMP complication underwent conversion to open surgery for maximum mucin extraction and thorough abdominal lavage (Figure 2.2). Postoperative specimens were examined for tumor histopathology and sectioned areas.

Postoperative outcomes included an average flatus time of 2 (1–3) days, a postoperative hospital stay of 5.4±3.2 (2–11) days, and one postoperative complication (12.5%) of surgical site infection, there were no perioperative deaths.

Histopathological results of the eight appendectomy specimens showed: 2 simple mucoceles (25%), 2 serrated polyps (25%), 2 LAMN (25%), and 2 MACA (one poorly differentiated, one moderately differentiated) (25%); all seven cases with tumor excision had negative margins.

Postoperative treatment: two cases of MACA were treated with chemotherapy alone (fluoropyrimidine and oxaliplatin),

while the remaining cases were placed under regular surveillance. Long-term follow-up results at the time of evaluation, ranging from 1 to 33 months, showed 100% overall survival, with one case of MACA undergoing tumor resection and mucin extraction, successfully restoring mucin production after 3 weeks, and six non-MACA cases showed no recurrence at the original site or elsewhere.

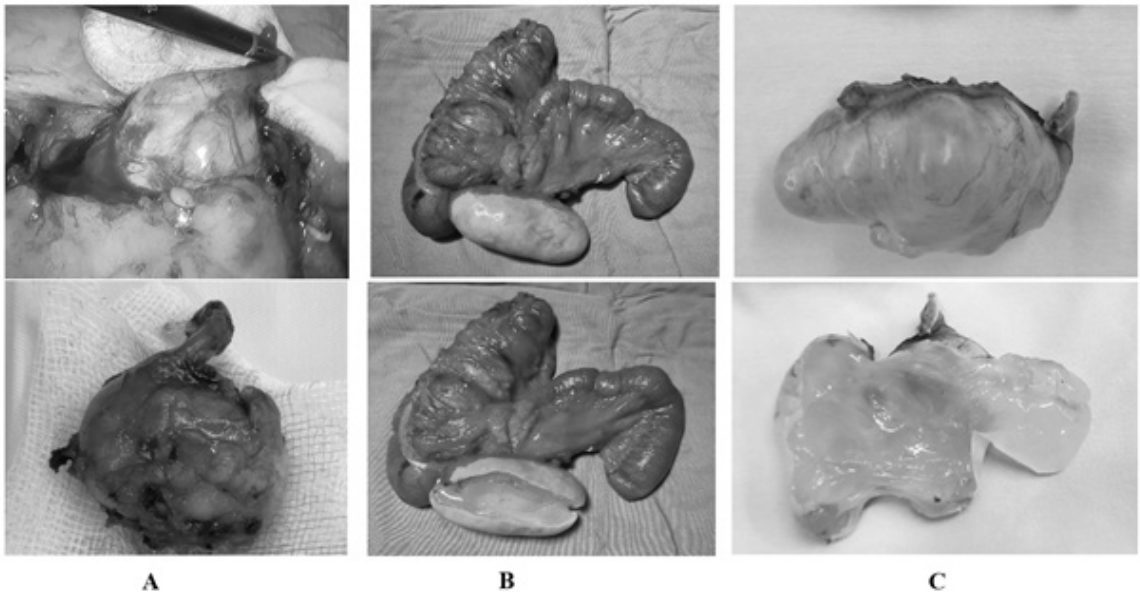

Figure 2.3. Reversal of appendiceal mucocele excision (A), examination of the

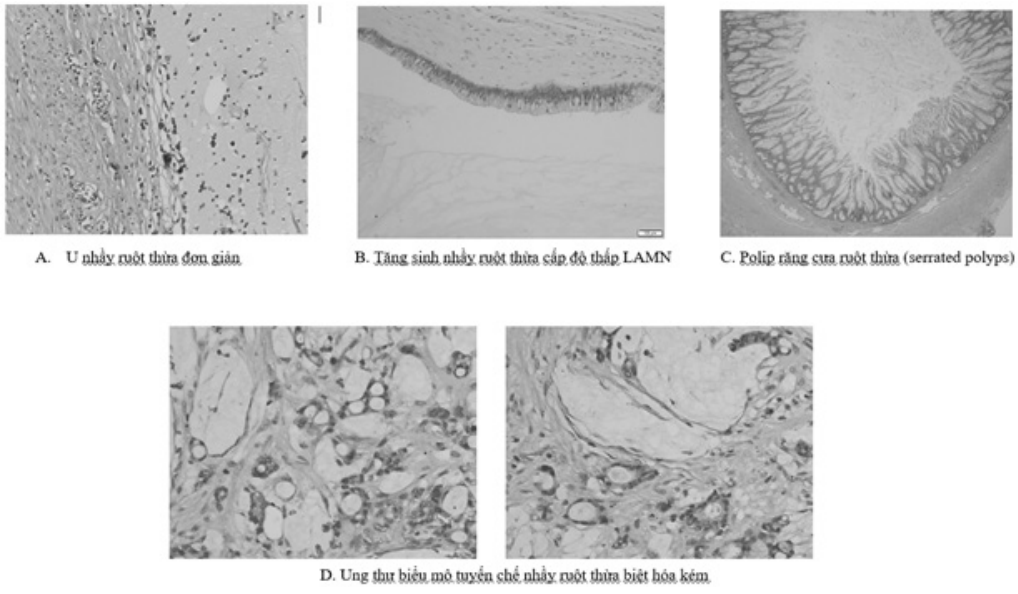

Figure 2.4. Histopathological images after surgery

A. Simple appendiceal mucocele; B. LAMN; C. Serrated appendiceal polyp; D. Poorly differentiated mucinous adenocarcinoma of the appendix.

3. Discussion

Appendiceal Mucocele (AM) was first described in 1842 by Rokitansky, and since then, this term has become a general concept encompassing various mucinous lesions of the appendix mucosa (3). The term mucocele refers to the dilation forming a cyst of the appendix with mucin accumulation, which can result from obstruction or mucin-secreting tumors.

AM is reported as a rare disease, with an incidence of 0.2% to 1.4% of appendectomy cases, more common in the age group of 50 to 60, with a female predominance (2, 5). In our study, this incidence was 0.32%, with a mean age of 63.4 years, evenly balanced between males and females.

According to PSOGI (2012), AM is divided into two main groups: non-neoplastic lesions (mucocele) and neoplastic lesions (serrated polyps, adenomatous polyps, LAMN, HAMN, and MACA) (3).

For non-neoplastic lesions such as simple mucoceles, simple retention cysts, inflammatory mucinous cells, or obstructed mucoceles, did not belong to the group of neoplastic lesions, so they were not included in the 2019 WHO gastrointestinal tumor classification. Therefore, subsequent classifications by PSOGI (2020) no longer refer to the non-neoplastic lesion group of the appendix but only classify neoplastic lesions: LAMN, HAMN, MACA, and serrated polyps as appendiceal mucinous lesions (4).

All these lesions can potentially lead to PMP, the accumulation of mucin in the peritoneal cavity due to rupture of appendiceal mucinous neoplasms (2, 3). Thus, with this classification in our study, only 6/8 cases were classified as AM, while the remaining 2 cases were simple appendiceal mucoceles. According to this classification, in our study, the 6 cases of AM still had a mean age of 63 years, belonging to the high-risk AM group, and the male-to-female ratio remained 1:1, despite the change in classification, indicating no significant gender differences.

In our study, 7/8 patients (87.5%) presented with symptoms of right lower quadrant pain, with clinical manifestations resembling acute appendicitis in 50% of cases, chronic pain in 37.5% of cases, and 12.5% asymptomatic. Although patients had pain symptoms, infection-related tests were inconclusive, with increased white blood cell counts showing no significance. This clinical characteristic was similar to some previous studies (4).

Despite performing ultrasound and colonoscopy in all 8 cases, the detection rates were 50% for ultrasound and 12.5% for colonoscopy, whereas CT imaging detected lesions in 100% of cases. Several other studies have also concluded similarly regarding the value of CT (1, 6). Some

studies have indicated localized or total aneurysm lesions, with a size increase >15 mm suggesting AM with a sensitivity of 83% and specificity of 92% (1, 2).

This imaging characteristic could be clearly observed on CT. In our study, the smallest tumor size recorded was 16 mm, and it was likely that AM smaller than 15 mm often did not cause symptoms, or smaller AM was often misdiagnosed as simple appendicitis. Furthermore, if AM imaging was accompanied by increased high-density fluid in the peritoneal cavity, then AM progressing to rupture causing PMP should be considered. Since AM was typically diagnosed after 50 years of age, CT scanning was recommended for patients over this age with signs of right lower quadrant abdominal pain.

In our study, all patients were scheduled for laparoscopic exploratory surgery and lesion management, with successful outcomes in 7/8 cases and one case requiring conversion to open surgery. Surgical treatment was not only aimed at resolving localized lesions but even when progressing to PMP, taking specimens was still of great significance in treatment. The surgical principle for localized AM was the complete removal of the tumor with negative margins and the prevention of mucin dissemination within the tumor (5).

Therefore, to ensure the principle of negative margins, the tumor should be excised with a margin of at least 1 cm, and efforts should be made to avoid tumor rupture. Hence, we applied clamping at both ends of the resection margin before excision and retrieved the tumor using a specimen bag.

In this study, we refrained from performing frozen section biopsy due to difficulties associated with specimen transfer; therefore, we opted for wide resection. We performed simple appendectomy in 3/8 cases with tumors located distally from the base, appendectomy with cecum resection in one case, appendectomy with ileocecal resection in one case, and right hemicolectomy in one case for tumors involving the body or base of the appendix and/or suspected invasion into the cecum wall.

In two cases with tumors causing PMP: we performed biopsy specimen retrieval in one case, and in the other case, we attempted appendix tumor resection and thorough mucin removal; however, mucin restoration occurred after only three weeks. Thus, for AM progressing to PMP, surgical excision or mucin extraction should not be performed; rather, biopsy should be prioritized for histological diagnosis. Treatment for PMP will vary depending on subsequent histopathological results.

According to Carr, N. J. (2020), for cases of AM progressing to PMP, the lymph nodes were generally unaffected

(4). Therefore, according to the author, for intact mucinous tumors, extensive colon and mesentery resection was unnecessary; it suffices to excise the tumor with a wide margin to ensure negative resection margins was enough., and right hemicolectomy was only recommended when there was a risk of cecal serosal injury due to surgical manipulation or tumor protrusion towards the cecal serosa (4).

For benign mucinous lesions, or localized AM with confirmed negative margins, postoperative drug therapy was usually unnecessary, and patients should be reassessed periodically according to guidelines, with a low risk of recurrence (2, 7). For AM progressing to PMP, according to the latest recommendations from PSOGI, hyperthermic intraperitoneal chemotherapy (HIPEC) with oxaliplatin instead of mitomycin C (5). The ideal protocol involves a combination of fluoropyrimidine and alkylating agents such as oxaliplatin. Adjuvant chemotherapy should be considered for patients with high-grade PMP or Signet ring cell PMP who have undergone complete or near-complete tumor cell reduction (R0-1) and HIPEC (5). Additionally, cytoreductive surgery (peritoneal stripping) was also used to treat PMP, with overall survival rates at 5 and 10 years for patients undergoing cytoreductive surgery and HIPEC due to disease dissemination being 77% and 66%, respectively (5, 7). Incomplete cytoreduction was significantly associated with lower survival rates compared to complete cytoreduction (7). In our study, two cases of AM progressing to PMP were only treated with chemotherapy alone, a combination of fluoropyrimidine and oxaliplatin; we were not treated with HIPEC or cytoreductive surgery due to our inability to perform these techniques.

Results of Long-term follow-up after surgery at the time of evaluation, ranging from 1 to 33 months, showed 100% overall survival. The case of AM progressing to PMP underwent tumor resection and mucin extraction, successfully restoring mucin production after three weeks. Six cases of benign AM showed no recurrence at the original site or elsewhere. Two cases of PMP, assessed at 17 and 20 months respectively showed abdominal cavity mucinous filling but no mortality.

4. Conclusion

Appendiceal mucoid tumors were rare diseases with nonspecific clinical symptoms and sometimes no symptoms. An abdominal CT scan was a valuable diagnostic tool for AM. Radical tumor resection was the main treatment method in the localized stage with positive treatment results.

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