

A general overview of mucocele of appendix

Mahendra Pratap Singh

Consultant Surgeon, Private Clinic, Katara, Bhopal, Madhya Pradesh, India

ABSTRACT

Mucocele of the appendix is a very rare disease entity that often discovered incidentally during surgery. It can result from both non-neoplastic and neoplastic lesions and histopathological examination is needed for confirmation. Failure to make an early preoperative diagnosis may result in its rupture and spillage of mucin contents into the peritoneal cavity leading to a disastrous complication of pseudomyxoma peritonei (PMP) that has a very bad prognosis. A clear pathological terminology and management strategies of appendiceal mucocele (AM) is lacking. This literature review aims to derive detailed information related to clinical significance of AM to avoid complication of PMP and plan appropriately during surgery according to the current evidence. The relevant articles from scientific databases such as Medline, PubMed, Google Scholar were searched and extracted using the keywords “mucocele appendix” “cystadenoma”. Data based on epidemiology, clinical manifestations, complications, pathology, diagnostic work up and management were analyzed and summarized. A meticulous surgical excision is the mainstay of treatment and open surgical approach is still preferred over laparoscopy. Preoperative diagnosis of AM is very imperative as it may harbour neoplasm and can be made utilising the imaging tools like computed tomography and ultrasonography. Primary care physicians can have a crucial role in making early detection and timely referral for appropriate management in order to avoid complications. After appendectomy, 5-year survival rate for the simple AM is 91%-100% but it reduces to 25% for the malignant AM.

Keywords: Appendiceal mucocele, cystadenoma, pseudomyxoma peritonei, rupture

Introduction

Appendectomy is a common surgical procedure done globally, every year, to manage common clinical pathology of the appendix. An appendiceal lesion termed mucocele of the appendix is very rarely encountered in 0.2 - 0.7 % of dissected specimen of the appendix.^[1] Mucocele of the appendix is a descriptive, morphological term given to an obstructive, distended appearance of the appendix due to intraluminal accumulation of mucous substance irrespective of the pathology that could be both non-neoplastic and neoplastic. Appendiceal mucocele (AM) was described first in 1842 by Rokitsky and later in 1976 defined by Feren.^[1] Some authors have favoured

for more specific term based on pathology discarding the “mucocele” as nonspecific, however, surgeons and radiologists are still preferring it.^[2] AM is commonly seen after the age of 50 years, with slight female preponderance. Clinical presentation is delayed, atypical, often with a vague lower abdomen pain or palpable lump mimicking appendicitis or tubo-ovarian mass in the female. Preoperative diagnosis is difficult even with the use of abdominal sonography or computed tomography. A meticulous surgical resection avoiding spillage of the contents is the mainstay of treatment. Histopathological examination of the dissected specimen is needed for a definitive diagnosis. Delayed diagnosis or missed diagnosis can result in spontaneous rupture of the appendix, or spillage of the mucinous contents into the peritoneal cavity during surgery resulting in a disastrous complication of PMP which has a very bad prognosis.^[3]

Owing to its rarity, a clear pathological terminology and management strategy of AM is lacking. In this literature review, the articles from scientific databases such as Medline,

Address for correspondence: Dr. Mahendra Pratap Singh,
CS-23, Sector-5, Global Park City
Katara Hills, Bhopal, Madhya Pradesh - 462043, India.
E-mail: drmpsingh2012@gmail.com

Received: 28-07-2020

Revised: 29-09-2020

Accepted: 28-10-2020

Published: 31-12-2020

Access this article online

Quick Response Code:



Website:
www.jfmpc.com

DOI:
10.4103/jfmpc.jfmpc_1547_20

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Singh MP. A general overview of mucocele of appendix. *J Family Med Prim Care* 2020;9:5867-71.

PubMed, Google Scholar were searched and extracted using the keywords “mucocele appendix” “cystadenoma”. Data based on epidemiology, clinical manifestations, complications, pathology, diagnostic work up and management were analysed and summarised in order to understand the clinical significance of mucocele of the appendix and to manage it appropriately.

Discussion

AM is commonly seen after the age of 50 years, with slight female preponderance. The majority of AM are detected incidentally during surgery, during imaging or colonoscopic work up of unrelated conditions or at the time of pathological examination of dissected specimen of appendix.^[3] The risk of occult mucocele is more in individual with features of acute appendicitis rather than in general population.^[4-6]

The patients with AM are largely asymptomatic or may present with vague nonspecific manifestations. Chronic or acute right Lower quadrant pain is more common presentation and a vague mass may be palpable, therefore, lesion is often mistaken for appendicitis.^[7] In female, AM may often mimic adenexal pathology with a palpable pelvic mass and poses a challenge to diagnose preoperatively during imaging work up or even at the time of surgery.^[8-10]

Nausea, vomiting, changes in bowel habits, gastrointestinal bleeding, genito-urinary symptoms can be the initial presentation. AM may also results in intussusception and bowel obstruction.^[7,11]

Owing to its rarity and atypical clinical feature, AM is very difficult to diagnose correctly resulting in misdiagnosis or delayed diagnosis. This increases the possibility of spontaneous rupture or delayed or inappropriate treatment. Mucin cells spillage into the peritoneal cavity resulting in PMP which has very poor prognosis if not treated properly.^[3,12] Therefore, an awareness and in-depth knowledge of the entity is imperative to make an early diagnosis. Here comes the role of primary care physician, seeing patients of such age group, at local level, making a differential of mucocele of the appendix by utilising basic clinical acumen with detail history taking and imaging study with ultrasonography, counselling, referral to appropriate centre and adding in early detection and subsequent follow-up care.

AM needs to be differentiated from bowel pathologies like appendicitis, intestinal obstruction, inflammatory bowel disease, diverticulitis, mesenteric ischemia and inguinal hernia. Urolithiasis, pyelonephritis, cystitis, and benign prostatic hypertrophy also need to be excluded. In female, tubo-ovarian mass, rupture ovarian cyst, pelvic inflammatory disease, uterine fibroid and adenomyosis need to be excluded.^[3]

The appendiceal epithelium contains mucin producing goblet cells more than colon. Based on the nature of the lining epithelium, AM has been classified into four subgroups. These are simple, hyperplastic, cystadenoma and mucinous cystadenocarcinoma.

This classification however, failed to provide a realistic perspective of lesions. To resolve this confusion, a consensus classification was developed by the Peritoneal Surface Oncology Group International (PSOGI) in 2012.^[13,14] This has two categories of appendiceal mucinous lesions

1. Non-neoplastic: Simple mucocele, retention cysts, inflammatory or obstructive mucocele comes under this category. They have degenerated epithelium without any evidence of mucosal hyperplasia or neoplasia.

2. Neoplastic: (a) Serrated polyp with or without dysplasia (b) Mucinous neoplasms are dysplastic mucinous tumours with epithelium showing pushing front going outward into muscularis mucosa, confined by muscularis propria. They are non-infiltrating and lack desmoplastic reaction. These lesions are further divided into low-grade appendiceal mucinous neoplasms (LAMNs) and high-grade mucinous neoplasms (HAMNs) depending on the cytological grades. World Health Organisation (WHO) classified most of the noninvasive lesion as LAMNs.^[15,16] (c) Mucinous adenocarcinoma demonstrates frank infiltrations and desmoplastic stromal reactions, high-grade cellular atypia and extracellular mucin in more than 50% of lesion. The extracellular matrix in these lesions is proteoglycon-rich, with abundant fibroblasts, myofibroblasts. Depending upon cellular differentiations, these are further classified. The presence of signet ring cells is a feature of poor differentiation. Adenocarcinoma can be non-mucinous as well.^[15,16]

Appendiceal neoplasms may rupture and mucin spill into peritoneal cavity. The term pseudomyxoma peritonei (PMP) is used to describe a diffuse spread that includes abundant mucin production, rather than mucin deposits near the appendix. It is considered as a malignant condition and its prognosis is determined by the level of cellularity within the mucin.^[15,16]

Imaging studies with plain abdominal radiographs showing soft tissue mass with a curvilinear or punctuate calcifications in right lower quadrant or poor filling of contrast in the appendix on barium enema study are usually non-specific. Computed tomography (CT) scan and ultrasonography (USG) can suggest AM with acceptable level of certainty of neoplasm but to confirm the lesion as neoplastic or non-neoplastic, the histopathological examination is a must. Certain characteristics like diameter larger than 1.5 cm, “onion skin” appearance, nodular enhancing of wall on USG are suggestive of AM.^[17] CT scan is considered the most accurate imaging tool with accuracy rate of 89.7%.^[18] The presence of larger lesion, soft tissue thickening, wall irregularity, egg cell calcifications with normal wall thickness on CT are suggestive of neoplastic nature of lesion.^[19] The presence of peri-appendiceal inflammation or abscess is suggestive of appendicitis and is not usually found in appendiceal mucinous lesions.^[20] The presence of ascitis, lesion on liver surface may suggest intraperitoneal spread of neoplastic lesion rather than peritoneal mucine alone although MRI is superior in predicting peritoneal lesions. Positron emission tomography (PET) study

is not indicated as it may result in high false-negative rate due to the mucin content of the lesion.^[21,22]

When an appendiceal mucocele is demonstrated on imaging study, a colonoscopy can be indicated to further examine other appendiceal lesions, colonic lesions and also to ascertain if caecum is also involved indicating local invasion from an adenocarcinoma. In approximately 13%-42% of patients with appendiceal neoplasm, a synchronous colonic lesion is present. On colonoscopy, appendiceal mucinous lesion is seen as shiny, rounded mass protruding from appendiceal orifice, moving in and out with respiration producing a “volcano sign”. Exudates may be seen coming out through the orifice. Probing with the biopsy forceps may reveal consistency as firm or soft, with central smooth indentation called “cushin sign”. Mucosal biopsy is not diagnostic as the overlying mucosa is normal and the lesion is submucosal. Once the diagnosis of mucocele is suspected, needle biopsy should never be attempted.^[23-27]

An endoscopic ultrasound (EUS) can detect the cystic nature of AM. It is also helpful in excluding other submucosal lesions like lipomas, neuroendocrine tumors, lymphangiomas and stromal invasion of mucinous adenocarcinoma.^[27] For patients with an incidentally detected appendiceal mucinous lesion on colonoscopy even without EUS, a CT of the abdomen needs to be done for further confirmation of the diagnosis and to exclude other lesions like coexisting ovarian mucinous tumor which is seen in approximately 27% of cases. Despite the extensive imaging investigation, the correct diagnosis of AM may remain elusive. The reported incidence of preoperative diagnosis for chronic setting is 15%-29% and in acute setting is even less (7.5%). AM has potential for malignant transformation and co-existence with other malignancy. The selection of appropriate operative procedures and to avoid complication of rapture during surgery and resultant PMP necessitate correct preoperative diagnosis. Misdiagnosis may delay surgical intervention and may lead to spontaneous rapture.^[28]

As there is no reliable criteria to exclude malignant lesions on imaging studies, histopathological examination of the appendiceal specimen after surgery is required to make a definitive diagnosis.^[3]

Tumor markers like carcinoembryonic antigen, CA 19-9 and CA-125 are nonspecific but need to be measured after diagnosis of AM and routinely repeated to monitor disease progression as available evidence suggest that their elevated level correlates with the advance stage of tumor in the majority of patients.^[29-32]

Early surgical resection is recommended for all AM to exclude mucinous neoplasm and to prevent spontaneous rapture in the future.^[33] Careful intraoperative handling is paramount for the intact appendix and to prevent iatrogenic rapture. There is no consensus exist regarding the optimum surgical procedure.^[34] Standard appendectomy is the initial procedure. The extent of surgery depends on several factors and should be guided by pathological diagnosis. Tumor size, location, mucin content,

caecal and ileum involvement, lymph nodes involvement, margins status and the final pathology report need to be considered.^[3] Additionally, co-existing ovarian or colonic tumor should also be considered in decision making and exploration of the abdomen should be done.^[35,36]

As obstructive lesion is frequently palpated near the base of the appendix, to ensure complete resection, a cuff of the caecum is included in specimen without encroaching on ileocaecal valve. If base of appendix is involved and clear margin cannot be achieved by stapling, a partial caecectomy, ileocectomy, or right colectomy can be performed following the oncological principles with high ligation of ileocolic pedicle at its origin. This is usually determined intraoperatively.^[36]

There is continuous debate on the suitability of open surgery over the laparoscopic approach. The chances of rapture is found to be less in open approach due to more careful and meticulous handling keep it intact. Tumor palpation and choosing optimum resection is possible during surgery. Moreover, if detected during a diagnostic laparoscopy, conversion to open can be considered. However, the laparoscopic approach is increasingly being done by surgeons having expertise in nuances of careful atraumatic handling and adhering to the safety rules in order to avoid inadvertent rapture. After resection the specimen need to be placed in an impermeable retrieval bag for safe and careful extraction. More research efforts are needed to prove its safety and efficacy.^[37,38]

If lesion has ruptured and rapture is walled off, a right hemicolectomy may be performed followed by thorough peritoneal wash. Findings of peritoneal cavity spillage should be documented and patient should be transferred to specialised center for further management according to final pathology report. PMP is noninvasive and it responds well with cytoreductive surgery and heated intraperitoneal chemotherapy (HIPEC).^[39] With multidisciplinary approach in specialised centers 5-year survival rate is around 50%-96% in the selected case. However, modality is still not standardized and follow up strategy is not clear. For non-neoplastic mucinous lesion, no further treatment is needed after appendectomy even it get ruptured.^[40,41] Prognosis is dependent on histology and presence and extent of peritoneal spread and invasion which determine the recurrence. After appendectomy 5-years survival rate for the simple AM is 91-100% but it reduces to 25% for the malignant AM.

Conclusion

AM is a rare morphological entity of immense clinical significance that may harbour mucinous neoplasm and so it continues to intrigue the surgeon, radiologist and pathologist alike. AM is commonly seen after fifth decade and clinical presentations are atypical. Preoperative diagnosis is difficult and delayed even with imaging studies but is very important in order to avoid rapture and resultant complications of PMP. A definitive diagnosis is made at pathological examination. Recent classification based

on pathology has largely succeeded in clearing dilemma as far as management is a concern. Meticulous surgery is the mainstay of treatment and open surgery is the preferred approach however laparoscopic method is increasingly being used recently. More research effort is needed toward the management of PMP. Awareness is needed and primary care physician can help to make early differential and appropriate referral.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Idris LO, Olafe OO, Adejumbi OM, Kolawole AO, Jimoh AK. Giant mucocele of the appendix in pregnancy: A case report and review of literature. *Int J Surg Case Rep* 2015;9:95-7.
2. Misdraji J. Mucinous epithelial neoplasm of the appendix and pseudomyxoma peritonei. *Mod Pathol* 2015;28:67-79.
3. Morano WF, Gleeson EM, Sullivan SH, Padmanaban V, Mapow BL, Shewokis PA, *et al.* Clinicopathological features and management of appendiceal mucocele: A systematic review. *Am Surg* 2018;84:273-81.
4. Choudry HA, Pai RK. Management of mucinous appendiceal tumors. *Ann Surg Oncol* 2018;25:2135-44.
5. Landen S, Bertrand C, Maddern GJ, Herman D, Pourbaix A, De Neve A, *et al.* Appendiceal mucoceles and pseudomyxoma peritonei. *Surg Gynecol Obstet* 1992;175:401.
6. Furman MJ, Cahan M, Cohen P, Lambert LA. Increases risk of mucinous neoplasm of the appendix in adults undergoing interval appendectomy. *JAMA Surg* 2013;148:703-6.
7. Z Teke, IC Eray, E Aydin, AB Ortlek. Appendiceal intussusceptions caused by mucinous cystadenoma presenting as acute appendicitis. *Ann R Coll Surg Engl* 2020;102:e1-4
8. Ali Toffaha, Walid El Ansari, Ammar Aleter. What you see might not be what you get: Discrepancies between intraoperative findings and preoperative diagnosis of ovarian tumor. Appendicular mucocele presenting as an adnexial mass- Case report and review of literature. *Int J Surg Case Rep*.2020;75:543-9.
9. Aleter A, El Ansari W. Incidental appendiceal mucinous neoplasm mimicking a left adnexial mass: A case report. *Int J Surg Case Rep* 2020;74:132-5.
10. Abdulaziz OA, Mohammed YA, Morshed A, Shoukry A. Low grade appendiceal mucinous neoplasm mimicking an ovarian cyst: A case report. *Int J Surg Case Rep* 2020;70:145-8.
11. Sun P, Jiang F, Sun H, Zhao X, Ma J, Li C, *et al.* Minimally invasive surgery for appendiceal intussusceptions caused by mucocele of appendix: Case report and review of the literature. *J Gastrointest Oncol* 2020;11:102-7.
12. Smeenk RM, Van Velthuisen ML, Verwaal VJ, Zoetmulder FA. Appendiceal neoplasms and pseudomyxoma peritonei: A population based study. *Eur J Surg Oncol* 2008;34:196-201.
13. Carr NJ, Cecil TD, Mohamed F, Sobin LH, Sugarbaker PH, Moreno SG, *et al.* A consensus for classification and pathological reporting of pseudomyxoma peritonei and associated appendiceal neoplasia: The results of the Peritoneal Surface Oncology Group International (PSOGI) modified Delphi process. *Am J Surg Pathol* 2016;40:14.
14. Carr NJ, Bibeau F, Bradley RF, Dartigues P, Feakins RM, Geisinger KR, *et al.* The histopathological classification, diagnosis and differential diagnosis of mucinous appendiceal neoplasm, appendiceal adenocarcinomas and pseudomyxoma peritonei. *Histopathology* 2017;71:847-58.
15. Misdraji J, Carr NJ, Pai RK. Appendiceal serrated lesions and polyps. In: WHO Classification of Tumours: Digestive System Tumours, 5th ed, WHO Classification of Tumour Editorial Board (Ed), IARC,2019.p. 141.
16. Misdraji J, Carr NJ, Pai RK. Appendiceal mucinous neoplasm. In: WHO Classification of Tumours: Digestive System Tumours, 5th ed, WHO Classification of Tumour Editorial Board (Ed), IARC,2019.p. 141-4.
17. Kameda T, Kawai F, Taniguchi N, Omoto K, Kobori Y, Arakawa K. Evaluation of whether the ultrasonographic onion skin sign is specific for the diagnosis of an appendiceal mucocele. *J Med Ultrason* (2001) 2014;41:439-43.
18. Kwak HD, Ju JK. A prospective study of discrepancy between clinical and pathological diagnosis of appendiceal mucinous neoplasm. *Ann Surg Treat Res* 2020;98:124-9.
19. Sagebiel TL, Mohamed A, Matamoros A, Taggart MW, Doamekpor F, Raghav KP, *et al.* Utility of appendiceal calcifications detected on computed tomography as a predictor for an underlying appendiceal epithelial neoplasm. *Ann Surg Oncol* 2017;24:3667-72.
20. Wang H, Chen YQ, Wei R, Wang QB, Song B, Wang CY, *et al.* Appendiceal mucocele: A diagnostic dilemma in differentiating malignant from benign lesions with CT. *AJR Am J Roentgenol* 2013;201:W590-5.
21. Zissin R, Gayer G, Kots E, Apter S, Peri M, Shapiro-Feinberg M. Imaging of mucocele of the appendix with emphasis on the CT findings: A report of 10 cases. *Clin Radiol* 1999;54:826-32.
22. Rohani P, Scotti SD, Shen P, Stewart JH, Russell GB, Cromer M, *et al.* Use of FDG-PET imaging for patients with disseminated cancer of the appendix. *Am Surg* 2010;76:1338-44.
23. Zanati SA, Martin JA, Baker JP, Streutker CJ, Marcon NE. Colonoscopic diagnosis of mucocele of the appendix. *Gastrointest Endosc* 2005;62:452-6.
24. Nakagawa T. Colonoscopic diagnosis of mucocele of the appendix. *Gastrointest Endosc* 1993;39:733-4.
25. Trivedi AN, Levine EA, Mishra G. Adenocarcinoma of the appendix is rarely detected by colonoscopy. *J Gastrointest Surg* 2009;13:668-75.
26. Uradomo LT, Darwin PE. Evaluation of subepithelial abnormalities of the appendix by endoscopic ultrasound. *Diagn Ther Endosc* 2009;2009:295379.
27. Shiihara M, Ohki T, Yamamoto M. Preoperative diagnosis and surgical approach of appendiceal mucinous cystadenoma: Usefulness of volcano sign. *Case Rep Gastroenterol* 2017;11:539-44.
28. Bennet GL, Tanpitukpongse TP, Macari M, Cho KC, Babb JS. CT diagnosis of mucocele of the appendix in patients with acute appendicitis. *Am J Roentgenol* 2009;192:W103-10.
29. Carmignani CP, Hampton R, Sugarbaker CE, Chang D, Sugarbaker PH. Utility of CEA and CA 19-9 tumor markers in diagnosis and prognostic assessment of mucinous epithelial cancers of the appendix. *J Surg Oncol* 2004;87:162-6.
30. Van Ruth S, Hart AA, Bonfrer JM, Verwaal VJ, Zoetmulder FA.

- Prognostic value of baseline and serial carcinoembryonic antigen and carbohydrate antigen 19.9 measurements in patients with pseudomyxoma peritonei treated with cytoreduction and hyperthermic intraperitoneal chemotherapy. *Ann Surg Oncol* 2002;9:961-7.
31. Baratti D, Kusamura S, Martinetti A, Seregini E, Laterza B, Oliva DG, *et al.* Prognostic value of circulating tumor markers in patients with pseudomyxoma peritonei treated with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. *Ann Surg Oncol* 2007;14:2300-8.
 32. Chua TC, Chong CH, Liauw W, Zhao J, Morris DL. Inflammatory markers in blood and serum tumor markers predict survival in patients with epithelial appendiceal neoplasms undergoing surgical cytoreduction and intraperitoneal chemotherapy. *Ann Surg* 2012;256:342-9.
 33. Stocchi L, Wolff BG, Larson DR, Harrington JR. Surgical treatment of appendiceal mucocele. *Arch Surg* 2003;138:585-90.
 34. Demetrashvili Z, Chkhaidze M, Khutsishvili K, Topchishvili G, Javakhishvili T, Pipia I, *et al.* Mucocele of the appendix: Case report and review of literature. *Int Surg* 2012;97:266-9.
 35. Glasgow SC, Gaertner W, Stewart D, Davids J, Alavi K, Paquette IM, *et al.* The American Society of Colon and Rectal Surgeons, Clinical Practice Guidelines for the management of appendiceal neoplasms. *Dis Colon Rectum* 2019;62:1425-38.
 36. Dhage-Ivatury S, Sugarbaker PH. Update on the surgical approach to mucocele of the appendix. *J Am Coll Surg* 2002;202:680-4.
 37. Palanivelu C, Rangarajan M, John SJ, Senthilkumar K, Annapoorni S. Laparoscopic right hemicolectomy for mucocele due to a low-grade appendiceal mucinous neoplasm. *JSL* 2008;12:194-7.
 38. Park KJ, Choi HJ, Kim SH. Laparoscopic approach to mucocele of appendiceal mucinous cystadenoma: Feasibility and short-term outcomes in 24 consecutive cases. *Surg Endosc* 2015;29:3179-83.
 39. Loungnarath R, Causeret S, Bossard N, Faheez M, Sayag-Neaujard AC, Brigand C, *et al.* Cytoreductive surgery with intraperitoneal chemohyperthermia for the treatment of pseudomyxoma peritonei: A prospective study. *Dis Colon Rectum* 2005;48:1372-9.
 40. Pai RK, Beck AH, Norton JA, Longacre TA. Appendiceal mucinous neoplasms: Clinicopathologic study of 116 cases with analysis of factors predicting recurrence. *Am J Surg Pathol* 2009;33:1425-39.
 41. Misdraji J, Yantiss RK, Graeme-Cook FM, Balis UJ, Young RH. Appendiceal mucinous neoplasms: A clinicopathologic analysis of 107 cases. *Am J Surg Pathol* 2003;27:1089-103.