

Appendiceal mucocele: a rare pathological entity but an important differential diagnosis

Abstract

This is the review of research articles on the topic of appendiceal mucocele at PubMed, searched by using the term "appendiceal mucocele" and "mucocele". Full texts and abstracts of 240 articles of all publications related to appendiceal mucocele from the year 2015 to 2000 were reviewed. Subsequently, the full text of 111 research articles was analyzed and summarized based on appendiceal mucocele incidence, malignancy incidence, clinical presentations, its complications, and management. An Appendiceal mucocele is the rare clinical entity that occurs in only 0.1–0.3% of all appendectomies. In females, it mimics as right adnexal mass or acute appendicitis commonly. Complications of appendiceal mucocele can be listed as torsion, intussusception, ureteral and intestinal obstruction, gastrointestinal bleeding, hematuria, and rupture resulting into pseudomyxoma peritonei but cases of infection, right inguinal hernia and mucinous cystadenocarcinoma leading to cutaneous fistula have been also reported. Patients with simple or benign neoplastic mucoceles have 5-year survival rates of 91–100%, whereas in malignant mucoceles, the 5-year survival rate is markedly reduced (25%) due to complications of pseudomyxoma peritonei due to rupture of mucocele. USG and CT scan are useful diagnostic tools. Surgery is the treatment of appendiceal mucocele and open surgery is preferred over the laparoscopic approach to prevent complications of pseudomyxoma peritonei after rupture. Careful use of laparoscopic graspers and absolute use of endobag during extraction are important maneuvers during laparoscopy. Dhage-Ivatury recently proposed an algorithm for surgical management of a mucocele depending on cytology, resection margins, and appendiceal nodes involvement. Therefore, it is important to consider appendiceal mucocele as a different diagnosis and diagnose it pre-operatively to prevent complications during surgery.

Keywords: Appendiceal mucocele, Malignancy, Pseudomyxoma peritonei, Rupture, Surgery, Laparoscopy

Abbreviations: AM, Appendiceal Mucocele; USG, Ultrasonography; CT, Computed Tomography

Introduction

Appendiceal mucocele (AM) is an obstructive dilatation of the appendix by the intraluminal accumulation of mucoïd material which has been recognized by Rokitansky in 1842 and was formally defined by Feren in 1876¹. Its clinical presentation can vary from the patient being asymptomatic in 50% cases of the patient exhibiting symptoms that mimic those in acute appendicitis or appendicular mass. Tenderness in the right iliac fossa with a palpable mass is two most common presenting symptoms but appendiceal mucocele can represent in different ways also (e.g. Nausea, vomiting, bowel habit change, abdominal lump or colicky pain)². In 50% cases, the appendiceal mucocele is an incidental finding at the time of surgery and recognition of the disease is important because of potential for associated malignancy and development of complication pseudomyxoma peritonei due to rupture during surgery³. The 5-year prognosis of malignant mucoceles can fall from 90% to 25% as a result of complications of pseudomyxoma peritonei⁴. Therefore, it is essential that clinicians are aware of the disease and diagnose it before surgery to prevent its complications. In this study review of the literature was done based on incidence, clinical presentation, complication, and management to understand the importance of awareness for appendiceal mucocele.

Method of review

PubMed was searched using the term "appendiceal mucocele" and "mucocele". This yielded 462 articles initially from the year

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Vidya Bharati

Department of Obstetrics and Gynecology, Duke University, USA

Correspondence: Vidya Bharati, Department of Obstetrics and Gynecology, Duke University, 910 Constitution Drive, Apt # 311, Durham, North Carolina, USA, 27705, Tel 919-908-4325; 919-973-3675, Email: vidyabharati15@gmail.com

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2015–2000. Full texts and abstracts of 240 articles of all publications appendiceal mucocele were reviewed and remaining articles were either not related or had not any details. Articles not in English were excluded. Subsequently, the full text of 111 research articles was analyzed and summarized based on appendiceal mucocele incidence, malignancy incidence, clinical presentation, its complications, and management.

Discussion

Incidence

Various articles had shown that appendiceal mucocele occurs in only 0.1–0.3% of all appendectomies with a higher incidence in females (4:1) and more cases presenting in patients above the age of 50^{4,5}. Although neoplasms occur in 0.5% of appendices, neoplastic transformation occurs in approximately 75% of AM and mucinous adenocarcinomas constitute 8% of all malignant neoplasms of the appendix with an estimated incidence of 0.2/100 000 population/year^{6,7}. This signifies the consideration of appendiceal mucocele as an important differential diagnosis of appendicular pathology, especially in women more than 50 years of age.

Clinical presentations

It is important to know that a quarter of patients are asymptomatic and the tumor is discovered incidentally, although the most common presentation is acute or chronic right lower quadrant pain (64%). An abdominal palpable mass can be found in 50% of cases, whereas, nausea, vomiting, low gastrointestinal bleeding or genitourinary symptoms may be present^{8–10}. In few patients, there have been reports

of weight loss, a change in bowel habit and bleeding per rectum, rectal pain. It had been reported for mimicking as right adnexal mass in females, acute appendicitis or urolithiasis commonly. Its association had been seen with endometriosis, endometrial carcinoma and malignant melanoma and ulcerative colitis¹¹⁻¹⁴. The literature has revealed five cases where appendiceal tumors appear specifically associated with infertility in women¹⁵. A wide variety of presentation of the disease and its association with different conditions signifies that clinicians should be aware of the appendiceal mucocele, especially when seeing a patient who presents with recurrent pain or a mass in the right iliac fossa.

Complications

Although neoplasms occur in 0.5% of appendices, neoplastic transformation occurs in approximately 75% of AM⁶. Besides of malignancy and pseudomyxoma peritonei, torsion, intussusception, ureteral and intestinal obstruction, gastrointestinal bleeding, hematuria, appendicular abscess, right inguinal hernia and mucinous cystadenocarcinoma leading to cutaneous fistula have been reported which signifies need of increase awareness for appendiceal mucocele for abdominal pathologies^{2,16-18}. It is also important to keep in mind that appendiceal mucinous neoplasms are associated with an increased incidence of other tumors. It is most frequently associated with colon and rectal cancers, followed by ovarian neoplasm (its association ranges from 2 to 24%)¹⁹. Cystadenocarcinoma constitutes 11-20 % of cases¹ and its metastasis is rare. It tends to remain in the peritoneal cavity, although few cases of retroperitoneal and pleural implantations, urinary bladder invasion, and development of cutaneous fistula have been reported²⁰⁻²³. Perforation (spontaneous or iatrogenic) is one of the most feared complications (occurs 20% of cystadenomas and 6% of mucinous cystadenocarcinomas) which leads to the peritoneal dissemination of appendiceal mucocele (known as pseudomyxoma peritonei)^{7,20}. Various complications of appendiceal mucocele especially its malignant potential and pseudomyxoma peritonei increase the importance of knowledge of diagnostic and management methods of appendiceal mucocele.

Prognosis

Patients with simple or benign neoplastic mucoceles have shown an excellent prognosis with 5-year survival rates of 91-100%, even in cases with an extension of mucus into the extra-appendiceal spaces but in malignant mucocele, the 5-year survival rate is markedly reduced (25%)¹.

Diagnosis

Recognition of appendiceal mucocele is important because of the potential for malignant transformation, to prevent rupture leading to the development of pseudomyxoma peritonei, and its association with colonic adenocarcinoma and ovarian tumors (21.4% and 27%, respectively). The wrong diagnosis may delay surgical intervention²⁴. Ultrasonography and CT scan are useful diagnostic methods. USG is the first-line diagnostic method for patients with acute abdominal pain. USG can be used to differentiate between mucocele and acute appendicitis. In the case of acute appendicitis, the outer diameter threshold of the appendix is 6 mm and 15 mm and more indicates the presence of a mucocele, with 83% sensitivity and 92% specificity²⁵. In some patients, multiple echogenic layers along the dilated appendix produce the appearance of "onion skin-like" circles and are pathognomonic for mucocele²⁶. CT can be used to discover the signs specific to mucocele with high accuracy: appendix lumen more than 1.3 cm, its cystic dilatation, and wall calcification²⁵. Typically, it demonstrates a hypoattenuated well-

encapsulated smooth or lobulated mass. More complex masses tend to be associated with cystadenocarcinomas and may demonstrate infiltration into adjacent structures. In benign mucoceles, CT will more likely to show displacement of bowel loops secondary to mass effect⁴. By colonoscopy, an elevation of the appendiceal orifice is seen and a yellowish mucous discharge would be visible from this orifice. Furthermore, synchronous and metachronous tumors of the colon can be identified²⁵. It may reveal a characteristic mass with a central crater from which mucoid material exudes. This is known as "volcano sign"¹. Currently, there is no specific tumor marker for the mucinous cystadenoma. Carcinoembryonic antigen (CEA) has been studied but its effectiveness is still questionable²⁷.

Management

Definitive management of an appendiceal mucocele is surgical resection⁴. However, there is continuous debate regarding the most appropriate approach and extent of resection required⁴. Different approaches of surgery had been described by different surgeons which signify importance of being aware of appendiceal mucocele as a differential diagnosis and diagnose it preoperatively for deciding surgical approach and preventing its surgical complications (mainly perforation). Although some surgeons prefer to use open surgery to prevent rupture of mucocele during surgery, the optimum approach should be chosen according to the experience of the surgical team in laparoscopy. Careful use of laparoscopic graspers and absolute use of endobag during extraction are important maneuvers during laparoscopy. In considering the extension of the surgical treatment, the base of the appendix should be carefully assessed during the operation. The presence of positive margins and difficulty to close the appendiceal stump necessitate more extensive surgery like cecectomy²⁸.

Dhage-Ivatury recently proposed an algorithm for surgical management of a mucocele²⁹. Patients should be referred for surgical removal, and in the case of a non- perforated mucocele (presenting with negative cytology, negative resection margins, with the absence of appendiceal nodes) a standard appendectomy should be performed, requiring no long-term follow-up. Since it is very important to prevent rupture or spilling of mucoid material, an open laparotomy or a conversion of a laparoscopic to a laparotomic procedure could be required. Also, according to Dhage-Ivatury and Sugarbaker, when a dysplastic mucocele has ruptured and mucinous carcinomatosis or pseudomixoma peritonei has been diagnosed, minimal surgery (including appendectomy with free margins, appendiceal lymphadenectomy and sampling of the ascites) should be performed with the goal of establishing a diagnosis; in addition, the authors suggest irrigating the surgical incisions to minimize neoplastic seeding. Following and on the basis of the pathological and cytological reports, patients should be referred to a specialized center for the further treatment and follow-up. Treatment may range from appendectomy to right colectomy and cytoreductive surgery, heated intraoperative intraperitoneal chemotherapy and early postoperative intraperitoneal chemotherapy, on the basis of the presence of neoplastic cells in the

1. Mucinous ascites,
2. Resections margins and/or
3. Appendiceal nodes.

Even though some controversies still exist regarding the clinical and histopathological definition of the pseudomixoma peritonei syndrome, this condition requires a multidisciplinary approach in a referral center, since these treatments are affected by a high morbidity

rate; 5-year survival rates have been reported ranging from 50–96%. Ronnet et al.²⁸ classified mucinous appendiceal neoplasms on the basis of prognosis as disseminated peritoneal adenomucinosis (least aggressive) and peritoneal mucinous adenocarcinoma (most aggressive)²⁸. According to Sugar baker, 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 years²⁹.

Conclusion

Appendiceal Mucocele is a rare pathological entity which has been recognized a long time ago by Rokitansky in 1842². It has a higher incidence in females mostly after 50 years of age. Many patients remain asymptomatic, are being diagnosed incidentally or had been reported as right lower quadrant abdominal pain, right adnexal mass and mimicking acute appendicitis or urolithiasis. Its association with various conditions like ovarian tumor, endometriosis, and infertility or ovarian tumor has been found. AM has various complications but malignancy and pseudomyxoma peritonei (due to rupture) are most fearful complications. USG and CT scan are important tools to diagnose and surgery is definitive management. Benign appendiceal mucocele has good prognosis while prognosis of malignant mucocele reduces significantly due to complications of pseudomyxoma peritonei. There is a continuous debate for the approach for surgery. Open surgery is preferred over the laparoscopy to prevent rupture during surgery. Therefore, it is important to consider appendiceal mucocele as a differential diagnosis which may remain asymptomatic and can be found incidentally, represent in various ways and can be associated with various conditions. Awareness of appendiceal mucocele as a differential diagnosis in various abdominal pathology can lead to increase in its preoperative diagnosis, prevent dreadful consequences of rupture (which can be reduced by careful surgery, if we will know the condition preoperatively) and improve its prognosis (which reduces significantly due to malignancy and pseudomyxoma peritonei).

Acknowledgments

None.

Conflicts of interest

None.

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