

APPENDICEAL MUCOCELE (Literature review)

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Introduction

Appendiceal mucocele (AM) is a rare entity that can present with a variety of clinical symptoms or occur as an incidental surgical finding. The incidence is 0.2%-0.4% of all appendectomied specimens and 8% of appendiceal tumors [1-5]. AM is a progressive dilatation of the appendix as a result of intraluminal accumulation of the mucoid substance [5,6]. It may be a benign or malignant process.

They can be asymptomatic and discovered incidentally in a radiological or endoscopic test or at laparotomy or laparoscopy performed for another reason [7-9]; thus over 50% of cases present with pain in right iliac fossa suggestive of acute appendicitis [1].

Preoperative diagnosis that distinguishes AM from acute appendicitis (AA) is essential for the best choice of surgical approach (open vs laparoscopic) to prevent peritoneal dissemination and perform the appropriate surgery [5,10].

Etiology and pathology

Around 10%–15% of mucocèles progress to pseudomyxoma peritonei, changing completely the outcome. Incorrect management may determine this progression [11].

The term “mucocele of the appendix” includes the histological diagnosis of simple mucocele or retention cyst, mucosal hyperplasia, mucinous cystadenoma, and mucinous cystadenocarcinoma, excluding all cases that were initially discovered as pseudomyxomaperitonei [12]. Notwithstanding, some authors have recently questioned this classification and terminology due to uncertain behavior [13].

Simple mucocèles or retention cysts are characterized by degenerative epithelial changes due to obstruction, usually caused by a fecalith, and distension of the appendix. Such a mucocele presents a plain epithelium, atrophy, and no proliferative changes. This type represents 20% of all mucocèles. Mucosal hyperplasia is histologically similar to a hyperplastic colon polyp, and this form of mucocele represents 20% of cases. Mucinous cystadenoma

is a neoplasm showing a tube-glandular or papillar pattern with important mucus production, presenting adenomatous epithelium, reminiscent of adenomatous colon polyps or villous adenomas. As described in the literature, this type represents 50% of mucocèles. Mucinous cystadenocarcinoma differs from cystadenoma, when glandular and stromal invasion is demonstrated; such lesions are similar to mucinous colonic tumors [1,2,11,14,15].

Pastor et al. [1] describe simple mucocele due to obstruction as a rare entity and suggest that its frequency is probably lower than estimated, because when a clear appendiceal neoplasm (cystadenoma or cystadenocarcinoma) is not observed, pathologists systematically diagnose simple mucocele.

Referring to gender distribution, there are discrepancies between different reports. Some studies describe female predominance [2,15], others show a similar incidence in men and women [11,16] and still others, show a higher frequency in men [1]. In age distribution the incidence is predominating in the 5th and 6th decades of life, although mucocele may be diagnosed at any age [11]. Acute appendicitis is a pathology predominating in patients under 30 years old, so that mucocele of the appendix must be taken into consideration in the differential diagnosis of a pain in right iliac fossa in a patient older than 35–40 years.

Simple mucocele and mucosal hyperplasia are usually smaller, not exceeding 2 cm in diameter, whereas cystadenomas and cystadenocarcinomas can reach up to 6 cm diameter [15,17].

Clinical features

Mucocele of the appendix can be discovered incidentally in radiological or endoscopic tests or at laparotomy or laparoscopy performed for other reason. Some authors report that up to 50% of the cases are incidental findings, but most of the published series, revealed that acute abdominal pain is the main clinical manifestation of mucocele [18]. Acute or chronic pain in right iliac fossa is the most frequent symptom, appearing sometimes as a mass at physical examination. Unusual manifestations are low gastrointestinal bleeding associated with intussusception of mucocele, intestinal obstruction, sepsis, or genitourinary symptoms [9,11,14,15].

Various authors have observed an association between mucocele of the appendix and other colorectal tumours, with a frequency around 20% [7]. These associations could be explained by the hypothesis that appendiceal tumors have the same nature as colonic ones, estimating an incidence

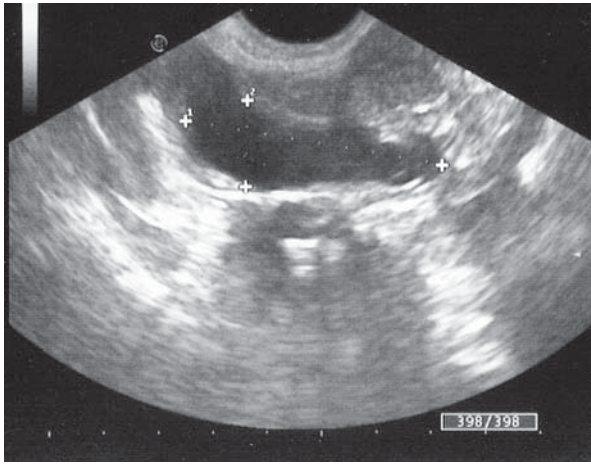


Fig. 1. USG showing markedly dilated appendix with hypoechoic content.



Fig. 2. CT demonstrating an appendiceal mucocele.

of colonic neoplasms 6 times higher than normal population [11]. Associations between mucocele and breast, ovarian, and kidney tumors have also been observed [19,20]. AM is nearly always present in women who are diagnosed with ovarian cystadenocarcinoma, and concomitant benign ovarian cystic tumor is also sometimes seen in association with AM [21-25]. This is why it is recommended to perform a complete colonic and ovarian examination intra and/or postoperatively, looking for abnormalities.

Imaging

Classically, preoperative diagnosis of mucocele has been considered as exceptional, but with the use of available diagnostic techniques that are more sensitive and specific than in the past, the number of cases diagnosed preoperatively has increased; ultrasound and CT scan have left barium enema in a second place as diagnostic test. Serrano et al., in a review of all published cases of mucocele in Spain up to 1989, note only a 15% rate of preoperative diagnosis [11].

USG, CT and colonoscopic examinations can facilitate preoperative diagnosis of AM [3,26-28]. Nevertheless, computed tomography and ultrasound findings are nonspecific and a differential diagnosis must be established with benign appendiceal neoplasms (leiomyoma, neuroma, fibroma, and lipoma) and other pathologies as mesenteric cysts, hydrosalpinx, carcinoid, lymphoma, bowel intussusception, endometriosis, and appendiceal adenocarcinoma, among others [8,29].

Ultrasound is the firstline diagnostic modality for patients with acute abdominal pain or mass. Different sonographic findings of AM and AA have been described [5,30,31]. Ultrasound shows cysts with variable echogenicity, depending of

the composition of the mucus (fig. 1). Multiple echogenic layers along a dilated appendix produce the appearance of “onion-skin” circles and may be pathognomonic for mucocele [32]. Appendix diameter 15 mm or more in USG examination has been determined as the threshold for AM diagnosis with a sensitivity of 83% and a specificity of 92% [5]. Outer diameter threshold for AA diagnosis has been established as 6 mm [33].

CT is also an effective diagnostic tool for AM. CT can determine the relation between lesion and the neighbouring organs, and help confirm the diagnosis [28,30,34,35]. Typical features of CT scan are cystic masses well circumscribed with low attenuation (fig. 2). Curvilinear mural calcifications are seen about 50% of the time and are very suggestive of mucocele [15,24,36]. Chiou et al. [37] note that enhancing nodules in the mucocele wall may suggest cystadenocarcinoma. Souei-Mhiri et al. report that ultrasound is useful to determine appendiceal abnormalities but does not allow a precise diagnosis; meanwhile, CT-scan is more specific in establishing the diagnosis of mucocele [38]. Barium enema may demonstrate a cecal filling defect or an ulceration [29].

Colonoscopy in patients with abdominal pain is a useful tool for determination of mucocele [4,39]. At endoscopy, the appearance of the appendiceal orifice at the center of the mound has been labeled as the “volcano sign,” moving in and out with respiration. An endosonographic probe can disclose the cystic nature of the mucocele and rule out solid lesions such as carcinoids, lipomas, and lymphangiomas. Stromal invasion may also be detected, which would predict the malignant character of mucocele [8,9,29,40].



Fig. 3. Skin fistula and implantation on the right flank (previously published, reprinted with permission) [44].

Complications and management

The spontaneous and surgery induced complications of AM include intestinal obstruction, intussusceptions [35,41], intestinal bleeding [20,26,42], fistula formation (fig. 3) [28,43-45], volvulus [46-48], compartment syndrome [49]. The worst complication is pseudomyxoma peritonei, characterized by peritoneal dissemination caused by iatrogenic or spontaneous rupture of the mucocele [10].

Cystadenomas and cystadenocarcinomas present an incidence of perforation around 20%, much lower in simple mucocele and mucosal hyperplasia. When the mucocele has ruptured, mucoid material can appear in the peritoneal cavity. This mucoid material may be acellular or can contain cells with different grades of dysplasia. An intact mucocele is considered to present no future risk for the patient, but once perforation occurs and epithelial cells escape into the peritoneal cavity, it becomes a potentially lethal entity [17]. Classically it has been thought that only cystadenocarcinomas might progress to pseudomyxoma peritonei, whereas the other histological types of mucocele were benign. Recently it has been observed some cases of pseudomyxoma peritonei originated from the other types of mucocele. Misdraji et al. [13] presented 3 cases of pseudomyxoma peritonei appearing as progression of low-grade mucinous appendiceal neoplasms whose only differential features were higher cellularity of the mucus and more cytological atypia, without reaching criteria to establish the diagnosis of mucinous cystadenocarcinoma. The higher incidence of perforation in cystadenocarcinomas would justify that most pseudomyxoma peritonei had this histological pattern.

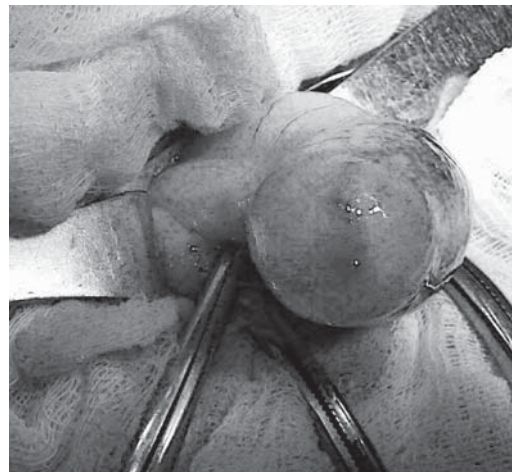


Fig. 4. Appendiceal mucocele which on histologic examination was confirmed to be mucinous cystadenoma (intraoperative view).

Appendectomy is the treatment of choice. Non-surgical management cannot be accepted, because apparently benign lesions can progress to mucinous cystadenocarcinoma, and the rupture of mucocele may determine the development of pseudomyxoma peritonei [15,20]. It is important to keep a mucocele intact during operation, to avoid dissemination of mucoid material into peritoneum.

The tissues should be handled carefully during surgery in order to avoid rupture of the mucocele. Thus, conventional surgery is preferred rather than laparoscopic approaches for the treatment [4,10,41,50] (fig. 4, 5). Laparoscopic approach has an increased risk of rupture and subsequent pseudomyxoma peritonei formation [4,10,50]. Moreno et al. [10] suggest conversion to an open appendectomy in case of mucocele when laparoscopic appendectomy is intended. This also allows the surgeon to explore the abdominal cavity, looking for the presence of mucoid fluid accumulations and mucin nodules in omentum and peritoneum. After leakage, the accumulations of mucoid material are most commonly found in the right retrohepatic space, deep in the pelvis and in the cul-de-sac created in the left paracolic space above the junction of sigmoid and descending colon (fig. 6), all anatomic sites difficult to explore at laparoscopy. If definitively laparoscopic appendectomy is performed, grasping the mucocele should be avoided, and an endobag must be used.

Few authors still recommend a minimally invasive approach in selected patients for this rare entity [46,51,52]. However, in these reports, laparoscopic approach has been adopted for a small number of patients. Thus, we need a large series to substantiate recommendations of laparoscopic approach.

A simple and thorough evaluation of these patients



Fig.5 Appendiceal mucocele which on histologic examination was confirmed to be mucinous cystadenocarcinoma (intra-operative view).

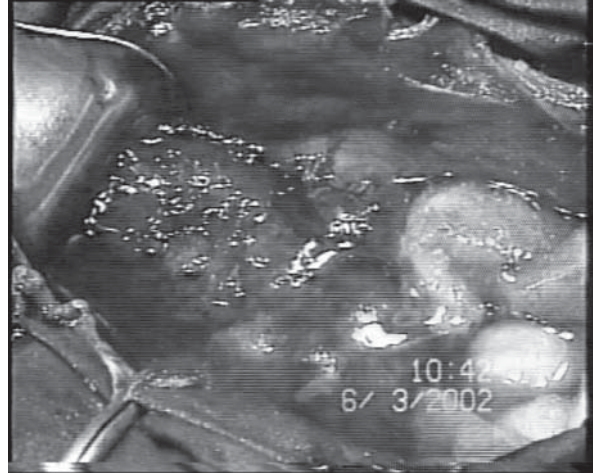


Fig. 6. Mucinous content in the peritoneal cavity in a patient with pseudomyxoma peritonei.

with a new algorithm has been suggested by Dhage-Ivatury and Sugarbaker [53]. Simple appendectomy is the choice of surgical treatment for patients with benign mucocele that has negative margins of resection without perforation. No long term follow-up is needed for these patients [4,46,50,53].

For patients with perforated mucocele, with positive margins of resection, positive cytology and positive appendiceal lymph nodes, right colectomy/cytoreductive surgery (CRS)/heated intraperitoneal chemotherapy (HIIC) and early postoperative intraperitoneal chemotherapy (EPIC) should be performed. Long term follow-up is obligatory for these patients [10,53-55].

Perforated mucocele with positive margins of resection, positive cytology, and negative appendiceal lymph nodes necessitate cecectomy/CRS/HIIC and EPIC. Long term follow-up is also obligatory for these patients [4,53,56].

Perforated mucocele with positive cytology but negative margins of resection and negative appendiceal lymph nodes should be treated with appendectomy/CRS/HIIC and EPIC [43,53].

The outcome of simple mucocele, mucosal hyperplasia, and mucinous cystadenoma after appendectomy is excellent, reaching 91% 10-year survival. Cystadenocarcinomas without peritoneal or adjacent organ involvement also show good outcome after surgical resection, but when they are at risk of progressing to pseudomyxoma peritonei, 5-year survival is 25%, with most deaths attributed to intestinal obstruction or renal failure [15].

In spite of an immediate good outcome of operation for mucocele, follow-up is recommended, because

there are cases of recurrences as pseudomyxoma peritonei and instances of metachronic colonic neoplasms [7,11]. Follow-up is recommended in all cases, even those with benign histology (simple mucocele, mucosal hyperplasia, and mucinous cystadenoma), because there are cases reported of development of pseudomyxoma peritonei with these histological types, although, obviously, less frequent [57].

Conclusions

Mucocele of the appendix is an unfrequent pathology, appearing usually in middle-aged patients, without gender preference. It should manifest clinically as pain or a mass in the right iliac fossa, similar to an acute appendicitis, although sometimes it is an incidental finding during a diagnostic test or at laparotomy or laparoscopy performed for another cause. In patients over 35–40 years of age, the incidence of mucocele increases, and therefore it should be included in the differential diagnosis of pain in right iliac fossa. Ultrasound and CT are helpful in the preoperative diagnosis, although their findings are nonspecific; CT seems to present higher accuracy than US, but the real difference must be confirmed by new studies. The treatment of choice is appendectomy, although in mucinous cystadenocarcinoma right hemicolectomy is needed.

The pathologist must do a careful study, looking for inadvertent perforations by the surgeon that may radically change the outcome for the patient. Followup of all patients is recommended, because of the risk of recurrence in the form of pseudomyxoma peritonei or colorectal neoplasms.

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Summary

The mucocele of the appendix is an uncommon disorder which is often asymptomatic but sometimes causes acute appendicitis-like symptoms. Sometimes, patients with mucocele can present with confusing symptoms. Preoperative suspicion and diagnosis of appendiceal mucocele are important. Ultrasonography and computed tomography are useful tools for the diagnosis of appendiceal mucocele. It may be also recognized by colonoscopy as a smooth submucosal lesion of the cecum. Optimal management of the mucocele could be achieved through accurate preoperative diagnosis. Preoperative diagnosis is a major component for minimizing intra-operative and post-operative complications.

Rezumat

Mucocele apendicular este o patologie rară, frecvent asimptomatică, dar care se manifestă uneori ca o apendicită. Uneori pacienții cu mucocele pot prezenta simptome confuze. Este important suspiciunea și confirmarea preoperatorie a diagnosticului. Metode utile în diagnosticul mucoceleului sunt ultrasonografia și tomografia computerizată. Mucoceleul poate fi identificat și la colonoscopie drept o leziune submucoasă a cecului. Managementul optimal al mucoceleului depinde de diagnosticul preoperator, care are un impact major pentru reducerea complicațiilor intra- și postoperatorii.

Резюме

Мукоцеле червеобразного отростка является редкой нозологией, зачастую бессимптомной, но проявляя иногда клинические симптомы острого аппендицита. Важным является предоперационный диагноз мукоцеле. Ультразвуковое исследование и компьютерная томография являются важными инструментами для диагностики мукоцеле. Колоноскопия также может выявить мукоцеле описываемый как гладкое подслизистое образование слепой кишки. Для выбора оптимальной тактики важна предоперационная диагностика мукоцеле. Правильный предоперационный диагноз способствует значительному снижению интра- и послеоперационных осложнений.