LUMEN ET VIRTUS

A case report on appendix mucocele: A rare pathology

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ABSTRACT

Introduction: The vermiform appendix is a cylindrical muscular structure originating near the junction of the cecum and ileum, with an average of 9 cm. Therefore, it may be the site of the development of neoplastic processes, which may or may not involve the production of mucus, as in the case of appendicular mucocele (AM), a rare disease that causes obstructive dilation of the appendix due to the intraluminal accumulation of mucin. Patients with MA are largely asymptomatic or may present with vague and nonspecific manifestations. Due to its rarity and atypical clinical characteristic, MA is very difficult to diagnose correctly. Early surgical resection is the recommended treatment for all AM to exclude mucinous neoplasia and prevent spontaneous rapture in the future. Discussion: Mucinous appendix neoplasms are classified into a spectrum from benign to malignant based on certain characteristics during histological examination. Appendicular neoplasms may snatch and mucin may leak into the peritoneal cavity. The term pseudomyxoma peritoneal (PMP) is used to describe a diffuse spread that includes abundant mucin production rather than mucin deposits near the appendix. Surgical resection of the appendicular mucocele is the preferred treatment. Conclusion: Appetite mucocele is a rare condition, and therefore, they are often found incidentally, as many patients are asymptomatic or have nonspecific symptoms. Surgical resection of the appendicular mucocele is the treatment preferred by specialists, with ultrasound and computed tomography being the tests of choice for diagnosis.

Keywords: Appendix Mucocele, Pseudomyxoma, Peritoneal, Treatment.

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INTRODUCTION

The vermiform appendix is a cylindrical muscular structure originating near the junction of the cecum and ileum, averaging 9 cm (5–35 cm) in size. As it is a more mobile viscera, it can adopt several positions, the most common being the retrocecal position (CONSTANTIN et al., 2023). Although the appendix has often been called a vestigial organ, this interpretation is changing, as it serves as an immune tissue in the gut that is also able to regulate the gut microbiome (KILLINGER and LABRIE, 2019). In addition, it appears to be involved in immune function, serving in the maturation of B lymphocytes and immunoglobulin A production, and in endocrine function by excreting amines and hormones in the 2–3 mL of mucus secreted daily (CONSTANTIN et al., 2023).

However, throughout life, the appendix can be the site of various pathologies, being categorized into inflammatory pathologies (acute appendicitis), pathologies related to congenital anomalies of the appendix and other related diseases and tumors of the appendix. However, only acute appendicitis has specific symptoms (abdominal pain descending to the right lower quadrant, nausea, vomiting, and anorexia), and the rest of the pathologies have similar symptoms or no specific symptoms (CONSTANTIN et al., 2023).

Histologically, the appendicular wall is composed of serosa, subserosa, external muscular tunic, submucosa, an internal muscular layer, mucosa, lamina propria, and epithelium, with the mucosal layer being the most prominent secretory layer of the appendix. In view of this, the vermiform appendix may be the site of the development of neoplastic processes, which may or may not involve the production of mucus, as in the case of appendicular mucocele, a rare disease that causes obstructive dilation of the appendix due to intraluminal accumulation of mucin (CONSTANTIN et al., 2023) (WANG et al., 2021).

Appendix mucocele (AM) is a descriptive and morphological term given to an obstructive and distended appearance of the appendix due to intraluminal accumulation of mucosal substance, regardless of the pathology which may be non-neoplastic and neoplastic (SINGH, 2020). MA are rare, being detected in only 0.1-0.7% of appendicular specimens and 8-10% of all appendicular tumors. They typically occur in patients between the ages of 50 and 60 years and are more common in women. They are often found incidentally, as many patients are asymptomatic or have nonspecific symptoms (SANTOS et al., 2022) (WANG et al., 2021).

MA can be caused by these four etiologies: retention cysts, mucosal hyperplasia, cystadenomas, and cystadenocarcinomas (SINGH and HUDA, 2022). The first group consists of a simple retention cyst secondary to proximal occlusion of the appendix, such as a fecalite or scar tissue from previous inflammation, or in rare cases due to endometriosis. With increasing pressure, degenerative changes in the appendicular mucosa develop consecutively. This type of mucocele is usually smaller than 2cm in diameter. The second group, called mucosal hyperplasia, has the same

characteristics as hyperplastic polyps of the colon (FAURE et al., 2014). Mucinous cystadenoma is the most prevalent type of benign neoplasm affecting the appendix. It is estimated to occur in approximately 0.6% of all appendectomy specimens. It is often associated with abdominal pain, which is the most common presenting symptom (KHAN et al., 2023). Finally, the fourth group encompasses malignant mucinous cystadenocarcinomas, characterized by glandular stromal invasion and/or tumor cells in peritoneal implants and has a higher perforation rate, which can lead to the development of pseudomyxoma peritoneal (PMP), being its worst complication (WANG et al., 2021) (FAURE et al., 2014). Other complications of appendicular mucocele include intestinal bleeding/obstruction, melena, and pyonephrosis (SAAD et al., 2018).

The World Health Organization has even classified MA into neoplastic and non-neoplastic (OYEH et al., 2024). According to the WHO pathological classification, updated in 2019, neoplastic causes of a mucocele include serrated lesions/polyps, low-grade appendicular mucinous neoplasms (LAMNs), high-grade appendicular mucinous neoplasms (HAMNs), and mucinous adenocarcinomas. Serrated lesions/polyps are mucosal polyps characterized by a stellate or sawtooth-shaped crypt lumen. These lesions include hyperplastic polyps and sessile serrated lesions, with or without dysplasia. A lesion that grows beyond the mucosa, with pushing edges, is classified as either a LAMN or a HAMN. A LAMN has low-grade cytologic atypia and features such as mucosal muscle loss, submucosal fibrosis, appendix rupture, and mucin or cells outside the appendix. A HAMN has all the architectural features of a LAMN, but has high-grade cytological atypia. Although differentiating between benign and malignant causes of an appendix mucocele is relevant to prognosis, making this preoperative distinction remains a challenge (SANTOS et al., 2022).

Patients with MA are largely asymptomatic or may present with vague and nonspecific manifestations (SINGH, 2020). The most common symptom is pain in the right lower quadrant. Therefore, they can clinically and radiologically mimic an adnexal mass or acute/subacute inflammation of the appendix (SANTOS et al., 2022). In women, MA can often mimic a pathology with a palpable pelvic mass and poses a challenge for preoperative diagnosis during imaging or even at the time of surgery. Nausea, vomiting, changes in bowel habits, gastrointestinal bleeding, genitourinary symptoms may be the initial presentation. MA can also result in intussusception and bowel obstruction (SINGH, 2020). The lack of distinct clinical features can lead to the misidentification of this condition as acute appendicitis, resulting in incorrect treatment. Therefore, it is imperative to correctly diagnose these two pathologies before surgery to ensure appropriate surgical treatment (KHAN et al., 2023).

Due to its rarity and atypical clinical feature, MA is very difficult to diagnose correctly, resulting in misdiagnosis or late diagnosis. This increases the possibility of spontaneous rapture or delayed or inappropriate treatment (SINGH, 2020). It is difficult to make an appropriate preoperative

diagnosis due to the nonspecific clinical presentation of appendicular mucocele (WANG et al., 2021). In general, conditions such as appendicitis, periappendicular abscess, diverticulitis, inflammatory bowel disease, mesenteric ischemia, lymphocele, peritoneal inclusion cyst, pyelonephritis, urolithiasis, cystitis, inguinal hernia, and appendicular neoplasms (carcinoid, adenocarcinoma, lipoma, fibroma, leiomyoma) should be excluded. In addition, uterine fibroids, adenomyosis, pelvic inflammatory disease, tubo-ovarian abscess, hydrosalpinx, ruptured ovarian cyst, and endometriosis should be excluded in women, while benign prostatic hypertrophy should be excluded in men preoperatively (OYEH et al., 2024). In recent years, with the improvement of diagnostic techniques and the accumulation of clinical experience, the preoperative diagnosis rate has been improved (WANG et al., 2021).

Most AM is detected incidentally during surgery, colonoscopy of unrelated conditions, at the time of pathological examination of a dissected specimen of the appendix, and during imaging. When an appendicular mucucele is demonstrated on imaging, a colonoscopy may be indicated to examine in more detail other appendicular lesions, colonic lesions, and also to see if the cecum is also involved, indicating local invasion of an adenocarcinoma. In approximately 13%-42% of patients with appendicular neoplasia, a synchronous colonic lesion is present (SINGH, 2020). Colonoscopy usually reveals a smooth, ball-shaped mound in the hole of the appendix, moving in and out with breathing motion. The appendicular orifice is in the center of the mound, which is known as the "volcano sign" (WANG et al., 2021). Probing with the biopsy forceps may reveal firm or soft consistency, with a gentle central indentation called the "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 (SINGH, 2020).

Classification of appendicular mucocele is essential to make an accurate diagnosis and determine the appropriate treatment approach (KHAN et al., 2023). Abdominal ultrasound is used as a first-line diagnostic method in any patient presenting with abdominal pain. An appendix mucocele appears as an ovoid or pear-shaped cystic mass in the lower right quadrant, where the appendix is usually located. Although the well-known "onion skin" appearance (inner concentric echogenic layers of mucin) is considered typical, the internal ecotexture of appendix mucoceles varies. Dystrophic mural calcifications can produce acoustic shadowing, a feature that is seen in less than half of all cases (SANTOS et al., 2022). CT is the most commonly used preoperative diagnostic method. The characteristic is a well-encapsulated, round, thin-walled cystic mass filled with slightly attenuated material in the right lower abdomen, and up to 50% of cases show mural calcification. The wall thickness of the appendix is less than 6 mm, with no periappendicular inflammation usually, which is useful for distinguishing mucocele from acute appendicitis (WANG et al., 2021). Some articles in the literature have reported appendicular mucinous cystadenoma coexisting with

appendicular carcinoid tumors; therefore, colonoscopy is sometimes mandatory to rule out associated colon tumors. Endoscopy with targeted appendix biopsy is useful in preoperative diagnosis, but it is quite difficult due to the narrowness of the appendicular lumen (KHAN et al., 2023). Preoperative diagnosis is difficult even with the use of abdominal ultrasound or computed tomography. Histopathological examination of the dissected specimen is necessary for a definitive diagnosis aiming at a correct and appropriate treatment for each case (SINGH, 2020).

Early surgical resection is the recommended treatment for all AM to exclude mucinous neoplasia and prevent spontaneous rapture in the future. There is no consensus on the ideal surgical procedure. Standard appendectomy is the initial procedure (SINGH, 2020). Frozen section of the base of the intraoperative appendix may help distinguish mucocele from other mucinous neoplasms. In the case of simple mucocele less than 2 cm in diameter, an appendectomy with removal of all fat and lymph nodes in the mesoapendic is warranted (SINGH and HUDA, 2022). Appendectomy for simple mucocele, hyperplastic mucocele, and mucinous cystadenoma has a 90%-100% survival rate at 5 years, and is the ideal treatment for patients with a histological diagnosis of benign mucocele (WANG et al., 2021). However, in the case of a positive margin at the base, positive periappendicular lymph nodes, or an appendicular base dilated more than 2 cm, right hemicolectomy or ileoecectomy is the best choice (SINGH and HUDA, 2022).

Therefore, the extent of surgery depends on several factors and should be guided by pathological diagnosis. Tumor size, location, mucin content, cecum and ileum involvement, lymph node involvement, margin status, and final pathology report need to be considered. In addition, the coexisting ovarian or colonic tumor should also be considered in decision-making and exploration of the abdomen should be done (SINGH, 2020). If the histological diagnosis is cystadenocarcinoma, appendectomy combined with right colectomy should be performed. However, the disadvantages of surgical procedures include a high degree of trauma, high cost, and possible serious complications caused by the rupture of the mucocele. For non-neoplastic appendicular mucocele, colonoscopy can replace traditional surgery to achieve good therapeutic effects by thoroughly flushing the mucus. For neoplastic appendicular mucocele, surgical resection increases the risk of implantation metastasis caused by mucocele rupture if the intraluminal pressure of the appendix is high. However, colonoscopy can relieve pressure on the appendicular lumen by flushing out mucus, thereby reducing the risk of rupture caused by subsequent surgery (WANG et al., 2021).

When there is a high-grade tumor, invasive adenocarcinoma or goblet cell tumor and/or those with a mucin-containing epithelial cell outside the appendix are at increased risk of nodal involvement and subsequent development of PMP (SINGH and HUDA, 2022). Perforation of an appendix mucocele can occur spontaneously or intraoperatively. This can lead to the spread of mucin, epithelial cells, or both, throughout the peritoneal cavity, resulting in pseudomyxoma

peritoneal (PMP), which can cause fatal complications. Therefore, diagnostic imaging and immediate surgical treatment are crucial (SANTOS et al., 2022).

On CT scans of patients with PMP, the following features are usually seen: mucinous ascites (which can become large in volume, with or without septa); peritoneal soft tissue implants; "omental agglomeration"; and ovarian involvement. Mucinous implants manifest as low-attenuation nodules that may contain gross calcifications. Indentations on the surface of solid abdominal organs, such as the liver, are quite typical and represent a mass effect characteristic of mucinous implants (SANTOS et al., 2022). These patients should be treated as patients with established PMP and considered for right hemicolectomy with prophylactic regional peritonectomy (right parietal), omentectomy, and intraperitoneal chemotherapy (SINGH and HUDA, 2022).

There is an ongoing debate about the appropriateness of open surgery in relation to the laparoscopic approach. The chances of snatching are lower in the open approach due to the more careful and meticulous handling that keeps it intact. Palpation of the tumor and choice of optimal resection are possible during surgery (SINGH, 2020). However, surgical intervention, whether open surgery or laparoscopic surgery, is necessary for the treatment of appendicular mucocele. And this choice depends on whether or not the appendicular mucocele is perforated, involvement of the base of the appendix, and the presence of mesoapendic and ileocolic lymph nodes (OYEH et al., 2024). Patients with low-grade epithelial malignancies without any evidence of mucin or epithelial cells other than the appendix have a very low risk of developing PMP. A colonoscopy should be done to exclude any associated colonic epithelial lesions and patients should be kept under postoperative surveillance for at least 5 years. Surveillance may include clinical review, annual abdominopelvic CT scan, and appendix-related tumor markers (CEA, CA 199, CA 125) (SINGH and HUDA, 2022).

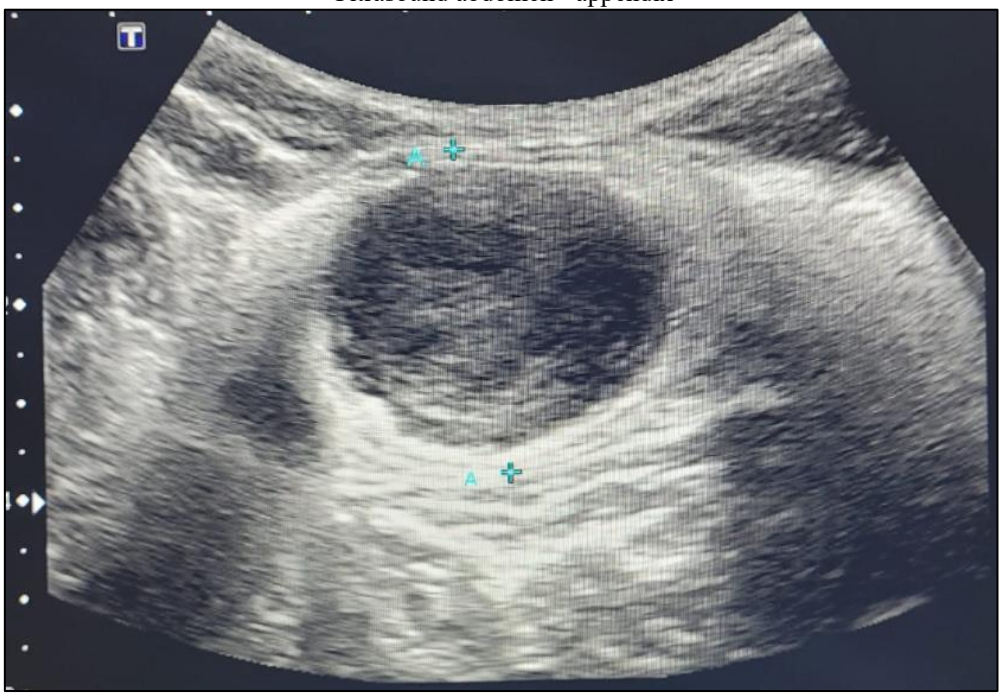
Therefore, in terms of tumor markers, Carcinoembryonic Antigen (CEA), CA19-9 and CA-125 are the tumor markers for follow-up, whose elevation can announce the recurrence of the disease (OYEH et al., 2024). These markers are not specific, but need to be measured after diagnosis of MA and routinely repeated to monitor disease progression, as well as follow-up, as available evidence suggests that their elevated level correlates with advanced tumor stage in most patients (SINGH, 2020).

CASE DESCRIPTION

Patient A.R.P.J, male, 29 years old, without comorbidities. She sought care complaining of abdominal pain, of varying duration. On physical examination, the abdomen was uncomfortable on palpation and palpable alteration in the right iliac fossa. Ultrasound of the total abdomen was performed, which showed focal hyperechogenicity with imprecise boundaries in the right hepatic lobe, which may correspond to focal steatosis, and an elongated and hypoechoic tubeliform image

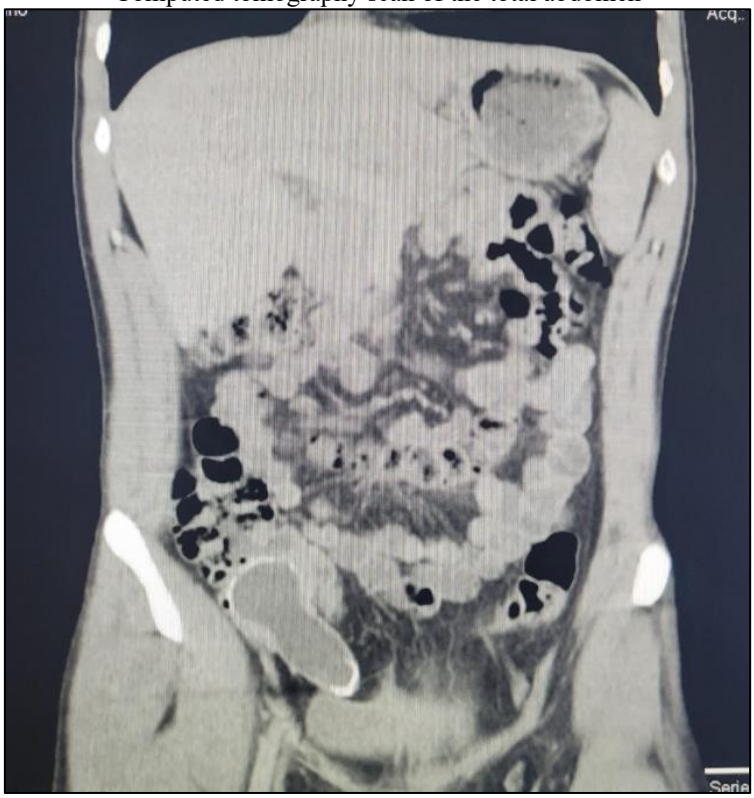
with a thick wall, in close contact with the lateral margin of the cecum, which may correspond to distension/mucocele of the appendix. For a diagnostic complementation, computed tomography was requested, which showed a well-circumscribed, low-attenuation, tubuliform expansive formation contiguous to the base of the cecum, measuring approximately 76x33x37 mm in its longest axes, and curvilinear calcifications were observed in its walls. The image ends in "blind background". The patient was diagnosed with appendix mucocele and referred for surgery. Partial colectomy (typflectomy + appendectomy) was performed without colostomy and the specimen was sent to the anatomopathological examination, where it came back negative for neoplasia. The patient remained with pain on palpation the day after surgery, and was discharged on the second day, without intercurrences.

Ultrasound abdomen - appendix



Images provided by Dr. Fernando Pereira de Almeida, Santa Casa de Misericórdia de Presidente Prudente.

Computed tomography scan of the total abdomen



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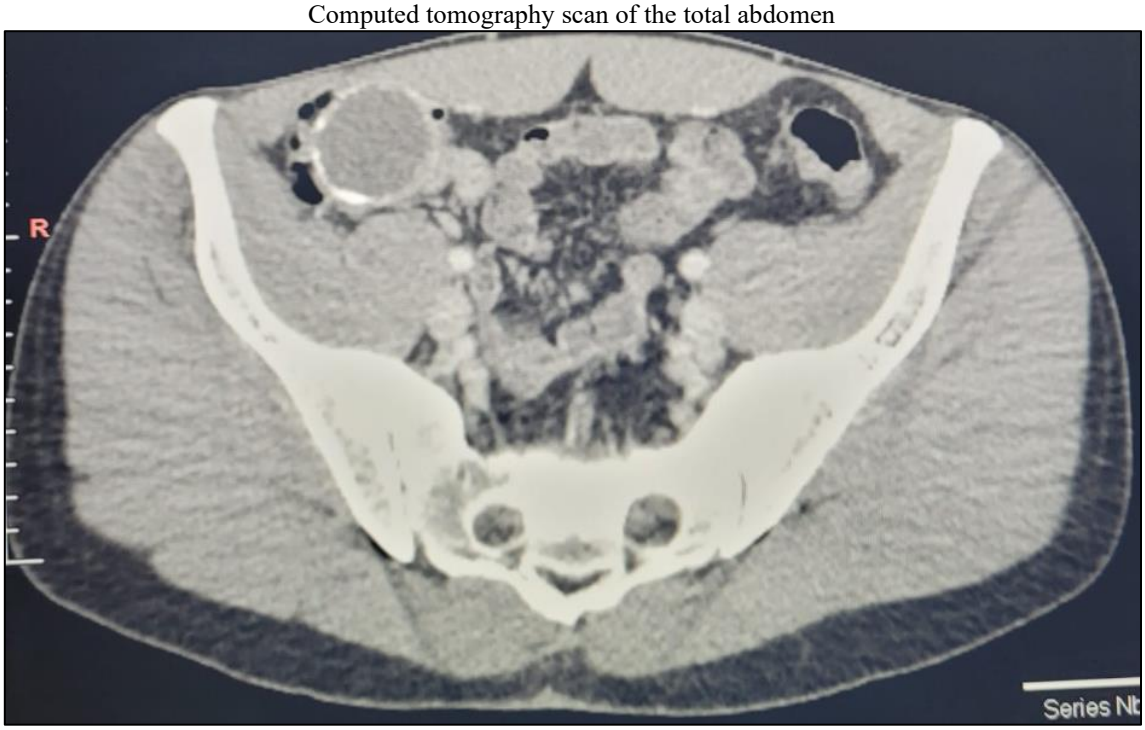

Images provided by Dr. Fernando Pereira de Almeida, Santa Casa de Misericórdia de Presidente Prudente.

DISCUSSION

Appendix tumors have an epithelial or mesenchymal origin and, according to the WHO, are categorized into several types: hyperplastic polyps, sessile serrated lesions without dysplasia, serrated lesions with dysplasia, NOS adenocarcinomas (not otherwise specified), undifferentiated

carcinoma NOS, goblet cell adenocarcinomas (GCAs), neuroendocrine tumors, and mucinous neoplasms of the appendix. (CONSTANTIN, et al., 2023). According to the Peritoneal Surface Oncology Group International (PSOGI) in 2012, there are two categories of appendicular mucinous lesions: non-neoplastic (involving the simple mucocele, retention cysts, inflammatory or obstructive mucocele) and neoplastic (involving serrated polyps with or without dysplasia and mucinous neoplasms) (SINGH, 2020). In the case reported, the patient is in non-neoplastic mucinous neoplasms, since his pathological examination was negative for neoplasms.

As there are no reliable criteria to exclude malignant lesions on imaging tests, histopathological examination of the appendix sample after surgery is necessary to make a definitive diagnosis (SINGH, 2020). Mucinous neoplasms of the appendix are classified into a spectrum of benign to malignant based on certain characteristics during histological examination. At the benign end of the spectrum, there is mucinous cystadenoma with no risk of recurrence. At the malignant end of the spectrum is mucinous adenocarcinoma with a very low survival rate and a high rate of metastases to the lymph nodes and liver (LOUIS and FELTER, 2014). In the patient in the case, there was no malignancy. The clinical presentation is delayed, atypical, often with a vague pain in the lower abdomen or palpable nodule mimicking appendicitis (as in the patient in this report) or tubo-ovarian mass in the woman (SINGH, 2020).

An endoscopic ultrasound (EUS) can detect the cystic nature of MA. It is also useful to exclude other submucosal lesions such as lipomas, neuroendocrine tumors, lymphangiomas, and stromal invasion of mucinous adenocarcinoma. For patients with an appendicular mucinous lesion incidentally detected on colonoscopy, a CT scan of the abdomen needs to be done for further confirmation of the diagnosis and to exclude other lesions such as coexisting ovarian mucinous tumor, which is seen in approximately 27% of cases. Despite extensive imaging workup, the correct diagnosis of MA may remain elusive. The reported incidence of preoperative diagnosis for chronic setting is 15%-29% and in acute setting it is even lower (7.5%). AM has the potential for malignant transformation and coexistence with other malignancies. The selection of appropriate operative procedures and to avoid complications of rapture during surgery and resulting PMP necessitate correct preoperative diagnosis. Misdiagnosis can delay surgical intervention and can lead to spontaneous rapture (SINGH, 2020). In this case, a computed tomography scan was of great relevance for the diagnostic confirmation of appendix mucocele, thus demonstrating the importance of such an examination.

Appendicular neoplasms may snatch and mucin may leak into the peritoneal cavity. The term pseudomyxoma peritoneal (PMP) is used to describe a diffuse spread that includes abundant mucin production rather than mucin deposits near the appendix. It is considered a malignant condition and its prognosis is determined by the level of cellularity within the mucin. If the lesion has ruptured and

the rupture is isolated, a right hemicolectomy may be performed followed by complete peritoneal lavage. Findings of peritoneal cavity leakage should be documented and the patient should be transferred to a specialized center for further treatment according to the final pathology report. For non-neoplastic mucinous lesion, no further treatment is required after appendectomy, even if it is ruptured. The prognosis depends on histology and the presence and extent of peritoneal spread and invasion that determine recurrence. After appendectomy, the 5-year survival rate for simple ROM is 91-100%, but reduces to 25% for malignant ROM (SINGH, 2020). In several studies, MRI has been shown to have a higher sensitivity than CT for the detection of PMP-related implants (84% vs. 54%) (SANTOS et al., 2022).

Surgical resection of the appendicular mucocele is the preferred treatment, and selecting which surgical method to use is critical. The best surgical approach to deal with appendix mucocele is controversial, and laparotomy has been recommended by many authors to prevent mucocele rupture. However, laparoscopic surgery provides the advantages of good exposure and evaluation of the entire abdominal cavity, as well as faster recovery avoiding a large incision and a better cosmetic result. If a laparoscopic approach is adopted, intraoperative care should be taken not to cause spillage of contents leading to the formation of pseudomyxoma peritoneal. Because in the presence of pseudomyxoma peritoneal, an aggressive surgical attitude is required, which includes right hemicolectomy, omentectomy, removal of all peritoneal mucin masses, and intraperitoneal chemotherapy (KHAN et al., 2023). In the case reported here, the surgery of choice was partial colectomy without colostomy. The patient was discharged from the hospital two days later without complications.

METHODOLOGY

From a medical case that occurred at the Santa Casa da Misericórdia de Presidente Prudente, together with his medical record, information was collected to carry out this case report. In addition, a search for information was carried out in databases.

CONCLUSION

Allergy mucocele is a rare condition, and because of this, they are often found incidentally, as many patients are asymptomatic or have nonspecific symptoms. Surgical resection of the appendicular mucocele is the treatment preferred by specialists, with ultrasound and computed tomography being the tests of choice for diagnosis.

CONFLICT OF INTEREST

The authors agree that there was no conflict of interest during this case report.

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