ORIGINAL ARTICLE

Clinicopathological analysis of patients operated for appendiceal mucocele

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ABSTRACT

BACKGROUND: The term mucocele refers to the dilatation of the appendix due to mucus, and it is an uncommon disorder with an estimated incidence of 0.2%–0.3% of all appendectomies performed and 8%–10% of all appendiceal tumors. It is often asymptomatic, but may manifest appendicitis-like symptoms.

METHODS: Twenty-six patients (14 females and 12 males) were operated on due to mucocele of the appendix. Sixteen patients exhibiting the characteristics of clinically acute appendicitis required an emergency operation. Appendectomy was performed on 14 patients, and right hemicolectomy was carried out on 2 patients. Of the remaining 10 patients who received surgery under elective conditions, 4 underwent a right hemicolectomy and 6 underwent an appendectomy.

RESULTS: The patients' age ranged from 27 to 81 years. Sixteen open and 4 laparoscopic appendectomies were performed. An incidental appendiceal mucocele was identified in 2 patients who had undergone colonoscopy. According to the histopathological examination, the incidence rate of mucosal hyperplasia, mucinous cystadenoma, and mucinous cystadenocarcinoma was found to be 23.1%, 61.4%, and 15.5%, respectively.

CONCLUSION: In patients with long-term pain in the right lower quadrant of the abdomen, appendiceal mucocele should be considered, and the results of radiological imaging tests should be carefully analyzed before surgery.

Keywords: Appendectomy; appendiceal neoplasms; mucocele.

INTRODUCTION

Appendiceal mucocele is an obstructive dilatation of the appendix caused by the intraluminal accumulation of mucoid material.[1] Appendiceal mucocele is a disease with an incidence estimated at 0.2%–0.3% of all appendectomies performed and 8%–10% of all appendiceal tumors.[2] It was first described by Rokitansky in 1842.[3] Mucocele of the appendix can be categorized in four histological types, including retention cyst, mucosal hyperplasia, mucinous cystadenoma, and mucinous cystadenocarcinoma.[4,5] The affected patients are usually above the age of 50 years.[6] Clinical signs include abdominal pain in the right lower quadrant, a palpable mass, colicky pain in case of obstruction or intussusception, gastrointestinal bleeding and anemia, genitourinary symptoms or acute abdomen, and sepsis in case of spontaneous rupture of the cyst. However, since these symptoms are nonspecific or absent, the disease is usually detected incidentally by radiological, sonographic, or endoscopic intervention.[7–9] The worse complication is pseudomyxoma peritonei characterized by peritoneal dissemination caused by the iatrogenic or spontaneous rupture of the mucocele.[10,11]

The recommended treatment for appendiceal mucocele is surgery, and the surgical procedure must be performed according to the examination of the tumor (size, presence of local or diffuse mucus collection throughout the peritoneum, or ruptured appendix or safety margins) and its histology. A simple appendectomy is postulated in benign processes, and cecal resection or right ileal colectomy is suggested when there is involvement of adjacent intestinal segments, regional lymphadenopathy, peritoneal pseudomyxoma, or malignancy.[12] Despite the higher risk of the rupture involved, laparoscopic surgery can be safely performed.[13,14]

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MATERIALS AND METHODS

This study is a retrospective evaluation of 26 patients who were diagnosed with appendiceal mucocele and underwent surgery in the General Surgery Clinic of Haydarpaşa Numune Education and Research Hospital between 2006 and 2014. Based on the literature, a histopathological analysis was performed to determine the treatment options by taking into consideration the patients' gender, age, clinical findings, and results of the biochemical and diagnostic tests.

RESULTS

Mucocele was identified in 26 (0.31%) of the 8,347 appendectomy cases. The age of the patients ranged from 27 to 81 years (mean: 55.35±12.96 years), and 14 (53.8%) were females. Sixteen patients (61.5%) reported pain in the right lower quadrant of the abdomen that had started less than 72 h earlier and they exhibited the clinical symptoms of acute appendicitis. These patients were admitted for emergency surgery. The symptoms of the remaining 10 patients (38.5%) included a mass lesion in the right lower quadrant, chronic pain, anemia, and weight loss. An abdominal ultrasonography (USG) was performed in 23 patients (88%), while a computed tomography (CT) was required for 12 patients (69.2%–46%). USG showed a dilated tubular structure in the right iliac fossa, and CT revealed a long tubular structure distended with hypodense material with or without calcification in the wall of the appendix, together with mass effect in six cases. Two of the colonoscopy patients (13%) were referred for CT upon the appearance of the cecum around the appendiceal orifice (also known as volcano sign). Mucocele was identified in two patients. In one of these two patients, a histopathological diagnosis of sigmoid cancer was made, and therefore, a left hemicolectomy and appendectomy were simultaneously performed on this patient. This patient was identified as having mucosal hyperplasia. In the other patient, mucinous cystadenoma was identified following a right hemicolectomy.

Appendectomies were performed on 20 patients (76.8%) (14 emergency and 6 elective), which included 16 (75%) open and 4 (25%) laparoscopic surgeries. The histological results were benign in all 20 patients with appendectomy. Six patients (23.2%) underwent a right ileocolectomy, of which two surgeries were emergency and four were elective. Mucinous cystadenocarcinoma was identified in four patients and mucinous adenoma in two patients. Table 1 shows the type of operations and the results of the histopathological evaluation. In two patients who underwent a right hemicolectomy, acellular mucin extravasation was observed in the mesoappendix. The histopathological examination revealed very few histiocytes and macrophages without signs of dysplasia. These patients were included in the follow-up program; however, they did not require further surgery. The analysis of tumor markers in the preoperative period showed that three patients (11.5%) had high levels of carcinoembryonic antigen (CEA). During surgery, cystadenocarcinoma was detected in two of these patients. After the surgery, 22 patients were followed up for an average of 21.82±12.50 months, and no mortality was observed.

DISCUSSION

Patients with mucocele of the appendix can exhibit confusing symptoms and may even be asymptomatic. The literature reports a very low prevalence of mucocele in appendectomy patients, and the majority of studies have been based on case reports. One of the most comprehensive series of cases was that of Stocchi et al.[15] who investigated 135 patients over a 24-year period. Another study was conducted by Lozano et al.[2] with 31 cases.

The incidence of mucocele predominates in the age range of 50–69 years, although it can be diagnosed at any age.[16] In a series of 31 appendiceal mucocele cases, García Lozano et al.[2] reported the mean age of the patients to be 62.1 years. In our study, the mean age of 25 of the 26 patients was found to be within the range reported in the literature. However, a female patient aged 27 years who was suspected to have appendicitis was included in the study, and after surgery, she was diagnosed with mucinous hyperplasia.

Regarding gender distribution, discrepancies have been reported in the literature.[10] Some studies describe a female predominance,[17] whereas others report a similar incidence in males and females.[2,16] In our study, the female-to-male ratio was 14:12.

Acute or chronic pain in the right iliac fossa is the most fre-

Table 1. Type of operations and the results of the histopathological evaluation

	Type of operation		Pathology		
	Appendectomy	Right Hemicolectomy	Mucosal Hyperplasia	Mucinous Adenocarcinoma	Mucinous Cystadenocarcinoma
Emergency	4	2	5	10	1
Elective	16	4	1	6	3
Total	20 (76.8%)	6 (23.2%)	6 (23.1%)	16 (61.5%)	4 (15.4%)

quent symptom, appearing sometimes as a mass in the physical examination.[8,9,18] The symptoms of malignant mucocele cases were linked to weight loss, deterioration of general health, and the presence of intra-abdominal masses, whereas benign mucoceles were more related to acute pain in the right iliac fossa.[2] In our study, 61.5% of patients (n=16) exhibited the characteristics of acute appendicitis. Mucinous cystadenocarcinoma was identified in one patient who underwent a right hemicolectomy. Of the 10 patients (38.5%) who exhibited symptoms of a mass lesion in the right lower quadrant of the abdomen, anemia, and weight loss and underwent elective surgery, 3 (30%) were found to have malignant mucoceles.

The advancements in diagnostic methods primarily related to ultrasound and abdominal CT have led to an increase in the possible preoperative diagnosis of the mucocele.[2] Depending on the composition of the mucus, the ultrasound can reveal cysts with variable echogenicity. Multiple echogenicity foci can reveal multiple echogenic layers in a dilated appendix giving the appearance of onion skin concentric layers that may be pathognomonic for the mucocele.[19] In a USG examination, an appendix with a diameter of ≥15 mm is determined as the threshold for mucocele diagnosis with a sensitivity of 83% and a specificity of 92%.[20] In a CT scan, the appearance of cystic masses well circumscribed with low attenuation is indicative of mucocele; furthermore, curvilinear mural calcifications can be observed about 50% of the time that are highly suggestive of mucocele.[21,22] The appearance of enhancing nodules in the mucocele wall suggests a diagnosis of cystadenocarcinoma.[23] To rule out the association of colorectal neoplasm, a colonoscopy is recommended in all patients in whom there is a suspicion of an appendiceal mucocele.[9]

Colonoscopic findings include the "volcano sign" in which the appendiceal orifice is observed in the center of a firm mound covered by normal mucosa or a yellowish, lipoma-like submucosal mass[24] Mucosal biopsies are often normal;[9] however, in our study, the mucocele was an incidental finding during the colonoscopy of two patients.

Blood tests also contribute to the diagnosis of the mucocele, wherein elevated levels of CEA can be seen in malign cystadenocarcinomas.[15] In the current study, cystadenocarcinoma was observed in two of the three patients with elevated preoperative CEA levels. Elevated CEA levels with cystadenoma rarity may be explained by the fact that routine CEA tests are not usually requested for patients with cystadenoma, although this antigen is often produced by neoplasms of the colon.[25] The remaining one patient with elevated CEA levels was diagnosed with sigmoid cancer and appendiceal mucocele hyperplasia.

Shimizu and Oshimo reported elevated preoperative CEA levels in patients with mucinous cystadenoma of the appendix.[26,27] It should be remembered that 11%–20% of patients with colonic cancer are accompanied by an appendiceal mucocele, and in malignant cases, tumors in solid organs such as the kidneys and lungs should be investigated. Postoperative follow-up should be carefully performed,[28] and furthermore, tumor markers such as alpha-fetoprotein (AFP), CEA, and CA19-9 should be determined during the preoperative evaluation.

The mucinous neoplasms of the appendix are classified into the following four pathological entities according to the characteristics of the epithelium: retention cyst, mucosal hyperplasia, mucinous cystadenoma, and mucinous cystadenocarcinoma.[3] A simple retention cyst determined by the intraluminal accumulation of mucoid material is rarely greater than 2 cm. Mucosal hyperplasia, a mild dilatation, constitutes 5%–25% of mucoceles. In the current study, this percentage was found to be 23.1. Mucinous cystadenoma is characterized by a dilatation of the lumen by up to 6 cm with low-grade dysplasia. Mucinous cystadenomas are the most common form, accounting for 63%–84% of cases. In our study, mucinous cystadenoma was identified in 61.4% of the patients.[4,29] Mucinous cystadenoma is at the benign end of the spectrum with no risk of recurrence.

Mucinous cystadenocarcinoma with stromal invasion and intraperitoneal spread is similar to that of ovarian mucinous cystadenocarcinoma. Malign mucinous cystadenocarcinoma represents 11%–20% of all cases of mucosal cases. In our study, 15.4% of the patients presented with malign mucinous cystadenocarcinoma.

Pseudomyxoma peritonei is the formation of peritoneal implants containing mucin due to the perforation of a lesion and the subsequent entry of the contents into the peritoneal cavity. Pseudomyxoma peritonei can occur during appendectomy due to the perforation of the mucocele of the appendix or other conditions such as mucinous cystadenoma and mucinous cystadenocarcinoma. The most common symptom is acute or chronic pain in the right lower quadrant of the abdomen.[30] The ruptured primary mass and the mucinous cells spreading along the peritoneal surfaces can be benign or malign. However, in both cases, the disease is progressive. Pseudomyxoma peritonei usually develops as a complication of ovarian and appendiceal masses. Current treatment strategies range from careful continuous observation to extensive cytoreductive surgery alone or with hyperthermic intraoperative peritoneal chemotherapy (HIPEC) or early postoperative intraperitoneal chemotherapy (EPIC).[31] In our study, none of the patients developed diffuse pseudomyxoma peritonei. Mucin extravasation in the periappendiceal mesoappendix was detected in two patients who had undergone a right hemicolectomy; however, the histopathological examination did not reveal dysplasia and no problems were reported during the follow-up. Mucoceles are treated surgically, and the preoperative diagnosis aids in the planning of careful mobilization and resection to prevent peritoneal contamination. There is a consensus that appendectomy is sufficient to treat benign mucoceles of the appendix that have not ruptured.[32,33]

A right hemicolectomy is frequently performed if a malignant cause is suspected based on imaging or the analysis of an intraoperative frozen section.[34] In the current study, the diagnosis of mucinous cystadenocarcinoma was confirmed in the frozen sections of four of six patients who underwent a right hemicolectomy, and the remaining two patients exhibited a large malignant mucocele forming adhesion on the intestinal segments. The histopathological examination confirmed the diagnosis of mucinous cystadenoma. The choice of open or laparoscopic surgery is controversial in patients with mucocele of the appendix.[31,35] If the mucocele is large and resection will be difficult, open laparotomy is the best option. In laparoscopic surgery, it is important to prevent rupture and peritoneal mucus contamination, and the appendix should be removed using an endobag. Among the six appendectomies performed laparoscopically, we did not observe any intra-abdominal mucus contamination.

In conclusion, mucocele is a rare tumor of the appendix, which can be characterized as benign or malign. In addition to presenting with clinically acute appendicitis, this tumor can cause several nonspecific symptoms. Ultrasound and CT can be useful in preoperative diagnosis. Mucoceles can also be incidentally detected during a colonoscopy. They can be accompanied by solid organ tumors, in particular, colon cancer. The surgical treatment of mucoceles is an open or laparoscopic appendectomy. Other viable treatment options include cecal resection and right hemicolectomy. The most dreadful complication is pseudomyxoma peritonei, and therefore, surgeons should be careful to prevent the rupture of the appendix and avoid peritoneal mucus contamination.

Conflict of interest: None declared.

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ORİJİNAL ÇALIŞMA - *ÖZET*

Appendiks mukoseli nedeni ile ameliyat edilen hastaların klinik ve patolojik analizi

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AMAÇ: Mukosel apendiksin mukus tarafından tıkanması sonrası genişlemesini tanımlar. Nadir bir bozukluktur. Çoğu zaman semptomsuz olmakla beraber apandisit kliniğine sebep olabilir. Tüm apendektomilerin %0.2–0.3 ve apandiks tümörlerinin %8–10'unda görülür.
GEREÇ VE YÖNTEM: Yirmi altı hasta (14 kadın–12 erkek) apandiks mukoseli nedeni ile ameliyat edildi. On altı hasta klasik apandisit bulguları ile acil şartlarda ameliyat edildi. Acil ameliyat edilenlerin 14'üne apendektomi, ikisine sağ hemikolektomi uygulandı. Elektif hastaların altısına apendektomi dördüne sağ hemikolektomi uygulandı.
BULGULAR: Hastaların yaşı 27–81 arasında idi. On altı hastaya açık, dört hastaya laparoskopik apendektomi uygulandı. Histopatolojik sonuçlara göre mukozal hiperplazi %23.1, müsinöz kistadenom %61.4 ve müsinöz kistadenokarsinom %15.5 oranında tespit edildi.
TARTIŞMA: Uzun süre sağ alt kadran ağrısı ile görülen hastalarda apandiks mukoseli ayırıcı tanıda düşünülmelidir. Ameliyat öncesi radyolojik değerlendirme doğru cerrahi tedavi için gereklidir.
Anahtar sözcükler: Apandiks tümörleri; apendektomi; mukosel.

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