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The Role of Clinical, Radiologic and Laboratory Markers in Distinguishing an Appendiceal Mucocele from Acute Appendicitis

Apendiks Mukoselini Akut Apandisitten Ayırmada Klinik, Radyolojik ve Laboratuvar Belirteçlerin Rolü

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Abstract

Aim: This study aims to assist the surgical treatment plan by increasing the rate of correct preoperative diagnoses through comparing the clinical, radiological, and laboratory findings of appendiceal mucocele (AM) and acute appendicitis (AA) before surgery.

Material and Method: The study included 63 patients with a histopathologic diagnosis of AM and AA among 4867 patients who underwent appendectomy with the diagnosis of acute appendicitis in the general surgery clinic between 2009 and 2020. The patients were separated into two groups: those with AM (21 patients) and those with AA (42 patients). Age, gender, physical examination (PE), Alvarado appendicitis score, ultrasonography (USG), computed tomography (CT), laboratory, preoperative diagnosis, intraoperative diagnosis, and pathological diagnosis results of both groups were compared.

Results: PE, abdominal pain, nausea, vomiting, fever symptoms, and Alvarado score were found to be significant between the two groups ($p<0.05$). In addition, WBC, NE, LYM %, and CRP were found to be high in group 2 ($p<0.05$), while there was no difference in radiological diagnosis (USG/CT) between the two groups ($p<0.05$). However, the appendix diameter was larger in group 1 ($p<0.05$). Patients with AM in 80% preoperatively, and 52% intraoperatively were operated on with a provisional diagnosis of AA. The second surgery was performed in Group 1 with a rate of 9.5% (2/21).

Conclusion: In our study, patients with AM who underwent surgery with a diagnosis of AA were found to differ in radiological, clinical, and laboratory findings from patients with AA.

Keywords: Appendiceal mucocele, acute appendicitis, differential diagnosis

Öz

Amaç: Bu çalışmanın amacı; cerrahi öncesi apendiks mukoseli(AM) ile akut apandisit(AA)'i klinik, radyolojik ve laboratuvar sonuçlarını karşılaştırıp ameliyat öncesi doğru tanı oranımızı artırarak cerrahi tedavi planına yardımcı olmaktır.

Gereç ve Yöntem: Çalışmaya 2009-2020 yılları arasında genel cerrahi kliniğinde akut apandisit tanısıyla apendektomi yapılan 4867 hastadan histopatolojik olarak AM ve AA tanısı alan 63 hasta dahil edildi. Hastalar AM'li olanlar (21 hasta) olmak üzere iki gruba ayrıldı. ve AA'lı olanlar (42 hasta). Her iki grubun yaş, cinsiyet, fizik muayene (PE), Alvarado apandisit skoru, ultrasonografi (USG), bilgisayarlı tomografi (BT), laboratuvar, preoperatif tanı, intraoperatif tanı ve patolojik tanı sonuçları karşılaştırıldı.

Bulgular: PE, karın ağrısı, bulantı, kusma, ateş semptomları ve Alvarado skoru iki grup arasında anlamlı bulundu ($p<0,05$). Ayrıca grup 2'de WBC, NE, LYM % ve CRP yüksek bulunurken ($p<0,05$), radyolojik tanı (USG/BT) açısından iki grup arasında fark yoktu ($p<0,05$). Ancak apendiks çapı grup 1'de daha büyüktü ($p<0,05$). AM'li hastaların %80'i ameliyat öncesi, %52'si ameliyat sırasında geçici AA tanısıyla ameliyat edildi. İkinci ameliyat ise %9,5 (2/21) oranında Grup 1'de yapıldı.

Sonuç: Çalışmamızda AA tanısıyla ameliyat edilen AM'li hastaların radyolojik, klinik ve laboratuvar bulgularının AA'lı hastalardan farklı olduğu görüldü.

Anahtar Kelimeler: Apendiks mukosel, akut apandisit, ayırıcı tanı

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INTRODUCTION

Appendiceal mucocele (AM) is a cystic disease caused by dilating the appendiceal lumen with mucopurulent fluid. It is a very rare and pathological condition of appendicitis, usually benign but sometimes malignant. It occurs due to complete or almost complete obstruction of the appendiceal lumen for many reasons, especially inflammation and defecation.[1] Acute appendicitis is the most commonly performed emergency abdominal surgery.[2] A negative appendectomy is performed in about 28% of these operations. In about 0.2% and 0.3% of patients operated on with a diagnosis of acute appendicitis (AA), the pathologic diagnosis is appendiceal mucocele.[2,3] While it is often found incidentally without causing symptoms, it sometimes produces an acute abdominal finding. Mucosal hyperplasia, mucinous cystadenoma, and mucinous cystadenocarcinoma are the four pathologic subgroups of AM retention cyst.[4] Mucinous cystadenoma is the most common of these pathological subgroups. Although AM generally occurs in all age groups and both genders, it is more common in women after the 5th decade. Although there is no common consensus on the surgical treatment option, appendectomy or right hemicolectomy is usually performed.[4] Despite the intensive use of radiological imaging equipment, it is unfortunately not possible in most cases to establish a definitive diagnosis before surgery.[5] Patients are usually operated on with a preliminary diagnosis of AA. Sometimes, patients are diagnosed by chance before surgery. Their complaints are mostly similar to AA. It can result in a second surgery and pseudomyxoma if misdiagnosed and treated. A correct preoperative diagnosis is very important to avoid such complications. For this purpose, the clinical prediction score, the Alvarado appendicitis score, ultrasonography (USG), and computed tomography (CT) should be used intensively.[6,7] Moreover, synchronous tumors, especially gastrointestinal tumors, may also occur in patients with AM.[8]

This study aims to compare the clinical, radiological, and laboratory results of AM and AA before surgery and support the surgical treatment plan by increasing our rate of correct diagnosis before surgery.

MATERIAL AND METHOD

The study was conducted as a retrospective case-control study in the General Surgery Clinic of Hospital between 2009-2020. The study comprised AM patients with histopathological diagnosis among 4867 appendectomy patients. The study included twice as many patients with similar demographic features and histopathological diagnosis of acute appendicitis as the control group. The study was conducted in compliance with the Declaration of Helsinki, after approval by the Ethics Committee on 24.12.2020 under the number 2020/78.

The list of all appendectomy patients included in the study was obtained from our hospital's computerized electronic records system. In these patients, pathological diagnoses such as appendiceal lymphoma, neuroendocrine tumor of the appendix, adenocarcinoma of the appendix, granulomatous appendicitis, appendiceal mucocele were reached histopathologically, except AA. Patients with a diagnosis of non-AM and non-AA were excluded from the study. A total of 63 patients, 21 of whom were diagnosed with AM and 42 patients with AA as a control group, were included in the study. The patients' diagnoses were re-examined one by one in the pathology laboratory by an expert pathologist, and their diagnoses were confirmed following the new histopathological classification.

Patients who did not meet the criteria of our study, who were under 18 years of age, who were over 80 years of age, who had a laparoscopic appendectomy, and who had previously been diagnosed with colon and gastrointestinal stromal tumors were excluded from the study. Patients over 18 and under 80 years of age with open appendectomy diagnosed histopathologically with AM and AA were included in the study.

The Alvarado scoring system was used to evaluate the physical examination findings of the study's patients. In all patients, a diagnostic abdominal USG was performed. Diagnostic abdominal CT was additionally performed in patients in whom physical examination and abdominal USG failed to establish a definitive diagnosis.

The age and gender of patients who met study criteria and were enrolled in the study were recorded from their electronic files. The patients' physical examination, Alvarado appendicitis scores, USG, CT, laboratory results, and preoperative, intraoperative, and pathologic diagnoses were recorded individually. The recorded results were compared between the two groups.

Statistical Analysis

In the statistical analysis of the data, the SPSS 23.0 package software was used. Continuous measurements were summarized as mean, standard deviation, and minimum-maximum; categorical measurements were summarized as numbers and percentages. The conformity of the variables with the normal distribution was examined using the Shapiro-Wilk test. The Mann-Whitney U test was used for parameters that did not conform to the normal distribution, and independent Student t-tests were used for parameters that did conform to the normal distribution. The statistical significance level was taken as $p<0.05$ for all tests.

RESULTS

63 patients from 4867 appendectomies performed in our clinic for 10 years participated in the study. Group 1 consisted of 21 (0.04%) AM patients, and group 2 consisted of 42 AA control group patients. The gender distribution was similar in the groups (p:0.859). The mean age was 50 years for AM and 45 years for AA (p:0.285). 47% of AM patients were male, and 53% were female. 88% (56/63) of the operated patients were operated on urgently and 12% (7/63) electively. The number of patients who underwent urgent surgery was higher in the AA group than in the AM group (p:0.002). All from group

2 presented to the clinic with abdominal pain. Nausea (95% vs 83.3 p<0.001) and vomiting (95% vs 47.6% p:0.003) were more common in AA than AM. Fever AA was more frequent (9.5% vs. 42.9%, p:0.007). Other physical examination findings were not significant between the two groups (p>0.05) (**Table 1**). The Alvarado score was significantly higher in the AA group than in the AM group (p<0.001) (**Table 2**).

While 100% (21/21) USG and 47.6% (10/21) CT were performed radiologically in AM patients, (42/42) USG was performed in AA patients (100%) and CT in (17/42) (40.5%) patients. Radiological diagnosis of AM was 14.2% (3/21) and AA was diagnosed preoperatively in 92.8% (39/42) (p<0.05) . Pre-diagnosis of the AM group was rectal Ca in 4.7% (1/21), uterine myoma in 4.7% (1/21), intra-abdominal abscess in 4.7% (1/21), plastron appendicitis in 4.7% (1/21), and AA in 66% (14/21) of patients. Intraoperatively, AM has been diagnosed in 61.9% (13/21) cases, AA in 38% (8/21) cases and 4.7% (1/21) rectal Ca and 4.7% (1/21) uterine tumors were diagnosed together. In the control group, perforated appendicitis was diagnosed radiologically in 4.7% (2/42) of patients and ileus in 2.3% (1/42) (**Table 1**).

Table 1. Demographic and clinical data

	Group 1 Patients with Appendiceal Mucocele (n=21)	Group 2 Patients with Acute Appendicitis (n=42)	p
	n (%)	n (%)	
Gender			
Male	10 (47.6)	21 (50.0)	
Female	11 (52.4)	21 (50.0)	
Age (t)	50.3±17.1	45.76±15.2	0.879
Admission			
Emergency	15 (71.4)	41 (97.6)	0.002
Elective	6 (28.6)	1 (2.4)	
Physical Examination (Abdomen)			
Abdominal pain (+)	17 (81.0)	42 (100.0)	0.010
Nausea (+)	7 (33.3)	35 (83.3)	<0.001
Vomiting (+)	2 (9.5)	20 (47.6)	0.003
Constipation (+)	7 (33.3)	10 (23.8)	0.422
Diarrhea (+)	0 (0.0)	4 (9.5)	0.144
Fever (+)	2 (9.5)	18 (42.9)	0.007
Rebound and defense (+)	0 (0.0)	1 (2.4)	>0.05
Tenderness in the right lower quadrant (+)	2 (9.5)	9 (24.4)	>0.05
Mass in the right lower quadrant (+)	4 (19.0)	0 (0.0)	>0.05
Bottom right rebound (+)	0 (0.0)	31 (73.8)	<0.05
Rebound/defense in all quadrants (+)	0 (0.0)	1 (2.4)	<0.05
Radiological Diagnosis			
USG (+)	21 (100)	42 (100)	0.086
CT (+)	10 (47.6)	17 (40.5)	0.589
Surgical Method			
Open appendectomy (+)	21 (100)	42 (100)	
Secondary operation (+)	2 (9.5)	0 (0.0)	<0.05

* p<0.05, (t)=Independent Student's t-test, chi-square, and Fisher's exact test

Table 2: Alvarado score ratios between Group1 (AM) and Group2 (AA)

	Group1 (AM) (n=21) score (%)	Group2 (AA) (n=42) score (%)	p
Symptoms			
Abdominal pain (+)	17 (81.0)	42 (100.0)	0.010
Anorexia (+)	7 (33.3)	35 (83.3)	<0.001
Vomiting (+)	2 (9.5)	20 (47.6)	0.003
Clinical Findings			
Tenderness in the right lower quadrant (+)	4 (9.5)	18 (24.4)	>0.05
Bottom right rebound (+)	0 (0.0)	4 (9.5)	0.144
Fever (+)	2 (9.5)	18 (42.9)	0.007
Laboratory Results			
Increase in the number of leukocytes (+)	12 (35)	72 (85)	0.001
Left shift in neurophile (+)	6 (35)	33 (78.5)	0.001
Total Score	50	242	0.001

* p<0.05, (t)=Independent Student's t-test, chi-square, and Fisher's exact test

The mean appendix diameter was larger in AM (2 vs. 1 p < 0.001), and its size was larger in AA (6.6 vs. 7.1 cm). White blood cell count (10.8 vs. 15 p:0.001), neutrophil count (7.79 vs. 11.8 p:0.001), and CRP (9.6 vs. 55.5 p:0.001) were higher in AA, as shown in **Table 3**.

Table 3. Laboratory parameters

	Group 1 Patients with Appendiceal Mucocele (n=21)	Group 2 Patients with Acute Appendicitis (n=42)	p
	n (%)	n (%)	
Diameter (u) (USG/CT)	2 (1-7)	1 (0.5-2)	<0.001
Dimension (u) (USG/CT)	6.6±1.9	7.1±1.5	0.299
WBC (t)	10.8±4.8	15.0±4.4	0.001
EOS% (u)	0.55 (0-2.56)	0.64 (0-5.47)	0.759
NE (t)	7.79±4.7	11.8±4.3	0.001
LYM% (t)	22.7±13.9	15.6±7.1	0.010
BAS% (u)	0.4 (0.03-1.86)	0.32 (0-5.5)	0.321
CRP (u)	9.6 (0.3-367.01)	55.5 (2-436)	0.001
Hematuria (+)	7 (33.3)	10 (23.8)	0.422

* p<0.05, (t)=Independent Student t-test, (u)= Mann-Whitney u test, chi-square test

100%(42/42), one of which was perforated, were diagnosed intraoperatively as AA. All of these cases were histologically diagnosed as AA. 11.9% (5/42) of them were perforated. Open appendectomy was performed in all (**Table 2**). The rate of preoperative diagnosis of acute appendicitis in patients in group AM (81% vs. 97.6% p<0.05) was found in 52% of patients in group AM with intraoperative appendicitis mucocele. **Table 4** shows the intraoperative and postoperative variables.

Table 4. Preoperative and pathological variables

Diagnosis	Group 1 Patients with Appendiceal Mucocele (n=21)	Group 2 Patients with Acute Appendicitis (n=42)	p
	n (%)	n (%)	
Preoperative diagnosis			
Appendiceal mucocele	2 (9.5)	0 (0.0)	>0.05
Acute appendicitis	17 (81.0)	41 (97.6)	<0.05
Acute abdomen	0 (0.0)	1 (2.4)	>0.05
Rectum Ca	1 (4.8)	0 (0.0)	>0.05
Uterine tumor	1 (4.8)	0 (0.0)	>0.05
Pathological diagnosis			
No	0 (0.0)	42 (100.0)	<0.001
Mucinous adenocarcinoma (high-grade dysplasia)	2 (9.5)	0 (0.0)	<0.001
Low Mucinous cystadenoma (low-grade dysplasia)	14 (66.7)	0 (0.0)	<0.001
Mucocele, mucosal hyperplasia	2 (9.5)	0 (0.0)	<0.001
Mucocele, retention cyst	3 (14.3)	0 (0.0)	<0.001

* p<0.05, chi-square and Fisher's exact test

Histologically, 57.1% (12/21) of patients were diagnosed with low-grade appendiceal mucinous neoplasm (LAMN), 9.5% (2/21) with high-grade appendiceal mucinous neoplasm (HAMN), 14.2% (3/21) with mucocele retention cyst, and 9.5% (2/21) with mucocele mucosal hyperplasia. There was one case each of rectal Ca, uterine leiomyoma, and pseudomyxoma peritonei, synchronous with these diagnoses(**Table 4**). All operations (100%) were open, and the second operation was right hemicolectomy with a rate of 9.5% (2/21) (p<0.05) (**Table 1**).

DISCUSSION

In this study, when we compared AM patients' radiological, laboratory, and clinical data with those of patients who underwent appendectomy mainly because of AA, AM patients were found to have different findings than AA patients, and most of these data were statistically significant.

In their study, Akbaş et al. noted that the rate of correct diagnosis could increase by evaluating the preoperative radiological, physical examination, history, and laboratory data of the patients to be taken with the preliminary diagnosis of AA.[9] Beyrouti et al. reported that the clinical picture of AM patients overlapped by approximately 73% with the clinical findings of AA in their study.[10] Another study reported that many diseases of appendicitis, especially AM, can clinically and radiologically mimic acute appendicitis.[11] Sökücü and Balık (2010) noted that the signs and symptoms of AM patients are similar to those of AA, but sometimes they were diagnosed incidentally during an operation performed for another reason without symptoms .[12] Our two AM patients were also diagnosed during abdominal surgery, which was performed for a different reason.

In our study, the mean age and female gender were higher in the AM group than in the AA group, but this was not statistically significant. A study conducted in China found that the average age of patients with AM was generally high and that both groups were equally distributed in terms of gender. [13] Another study found that patients with AM were more common in women and older age, whereas patients with AA were more common in younger and older men.[14]

Preoperatively, all patients in group 2 had symptoms of abdominal pain, whereas only 81% of patients in group 1 had abdominal pain. Other clinical findings, nausea, vomiting, and fever, were statistically significant between the two groups. As a result of clinical studies, it was found that clinical symptoms were more likely to be observed in the AM patient group.[12,15] Another study found that patients with AA generally present to the clinic with symptoms of abdominal pain, nausea, vomiting, and fever.[16] Our study is compatible with the literature in this regard. In our study, the abdomen's physical examination (PE) was normal in 71% of the AM group, whereas 28.6% had pathologic findings. However, abdominal PE findings were pathological in 100% of the AA group. Senturk et al. discovered in their study that the clinical findings of AM patients, which differ from our results, are similar to the clinical findings of AA.[17] However, another study reported that only 50% of AM symptoms and clinical findings were similar to AA symptoms.[18] In recent years, the Alvarado appendicitis score has been applied to reduce the rate of negative appendectomies and increase the preoperative rate of correct diagnosis of acute appendicitis, and it has been reported to have a sensitivity of 54% to 70% in many scientific studies.[19,20] On the other hand, it has been reported that the Alvarado score alone is important but inadequate for a correct preoperative diagnosis. Therefore, radiologic diagnostic tools such as USG and, when appropriate, CT should be used to increase the rate of correct diagnosis. [21,22] Our study is compatible with the literature in this aspect.

Our study found no statistically significant difference between the two groups in the radiological evaluation of the patients' preoperative diagnosis. In most patients in the AM group, a radiological diagnosis of AA could not be established. The diagnosis was confirmed radiologically in the majority of AA patients. The literature indicates that the primary diagnosis in AM patients is radiologically low and is more likely to be established intraoperatively or histologically.[23,24] In our study, the correct diagnosis of AM patients was mostly established intraoperatively or histologically following the literature.

In many studies, it has been found that the diameter of the appendix can be an essential indication for preoperative diagnosis because the diameter of the appendix is larger in AM patients than in AA patients.[25,26] The appendix diameter of AM patients was found to be larger than that of AA patients in our study. Furthermore, Saylan et al. reported in their study that although the blood parameters between the two groups were not statistically significant, the number of patients with

erythrocytes in the urine was significantly higher in the AM group.[27] In our study, the values of blood parameters WBC, NE, LYM %, and CRP were statistically significantly higher in the group AA than in the group of AM patients, while hematuria was not statistically significantly higher in the AM group.

In all patients, the open surgical method was preferred. Right hemicolectomy was performed in the second surgery because of the pathologic diagnosis of mucinous cystadenocarcinoma in two patients in the AM group and the pathologic diagnosis of local pseudomyxoma peritonei in one of these patients. In clinical studies, open or laparoscopic appendectomy carefully performed to avoid AM pseudomyxoma peritonei is recommended, whereas cecal resection or right hemicolectomy is recommended if the diagnosis is cystadenocarcinoma.[27] On the other hand, it was observed in many studies that open surgery was recommended to AM patients instead of laparoscopy.[12]

The limitation of our study might be that it is a single-center retrospective study. Another limiting factor is that no intraoperative frozen section examination was performed in suspicious cases. Its strength is that it is the first study to compare AM and AA with preoperative radiological, clinical, and laboratory data.

CONCLUSION

In this study, it was found that radiological, clinical, and laboratory data differed among AM patients who were operated on with a diagnosis of AA and some of whom required surgery for the second time. This may contribute to the treatment plan to be applied by increasing the preoperative differential diagnosis rate for two different emergency surgical conditions of the same organ by noting the differences. However, there is a need for studies that include more patients and compare prospective AM with AA.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Niğde Ömer Halisdemir University Ethics Committee (Date: 24.12.2020, Decision No: 2020/78).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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