

Usual and Unusual Pathologies of Appendicitis: A Retrospective Analysis of 385 Patients

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Received : 04 March 2021
Accepted : 24 April 2021

ABSTRACT

Purpose: Appendectomy is the most common abdominal surgery performed worldwide. In this report, we evaluated the results of pathological examinations of acute appendicitis specimens.

Methods: We performed a retrospective analysis of patients operated on for acute appendicitis at our surgical department from 2009 to 2017. Data on age, gender, and pathological diagnostic parameters were analyzed.

Results: A total of 385 patients (168 women [43.6%] and 217 men [56.4%]), were classified into acute appendicitis (Group 1), normal appendix (Group 2), and unusual pathological findings (Group 3) groups. The patients undergoing appendectomy were mostly in the 21–30 (n = 136, 35.3%) and 31–40 years (n = 118, 30.6%) age groups. The negative appendectomy rate was 4.4% in Group 2, and the proportion of women (70.6%) was significantly higher in that group than the other groups (p < 0.05). In total, 24 (6.2%) patients had unexpected findings. Among the appendix tumors (n = 12 [3.1%]) in our series, low-grade mucinous neoplasm (n = 6, 1.6%) was the most common, followed by a well-differentiated neuroendocrine tumor (n = 3, 0.8%).

Conclusion: Although unusual pathological findings are rare during appendectomy, all appendectomy specimens should be sent for routine histopathological examination. The abnormal incidental findings of 24 cases in this series had a significant impact on management. Patients with rare abnormalities should be treated according to the results of their pathological reports.

Keywords: Appendicitis, appendectomy, appendix, histopathology

Apendisitinin Olağan ve Olağandışı Patolojileri: 385 Hastanın Retrospektif Analizi

ÖZET

Amaç: Apendektomi, dünya çapında en yaygın olarak uygulanan abdominal ameliyattır. Bu çalışmada, akut apandisit piyeslerinin, patolojik inceleme sonuçlarını değerlendirdik.

Yöntemler: Cerrahi bölümümüzde 2009-2017 yılları arasında akut apandisit nedeniyle ameliyat edilen hastaların retrospektif bir analizini gerçekleştirdik. Yaş, cinsiyet ve patolojik tanı parametrelerine ilişkin veriler analiz edildi.

Bulgular: Toplam 385 hasta (168 kadın [% 43.6] ve 217 erkek [% 56.4]), akut apandisit (Grup 1), normal apendiks (Grup 2) ve olağandışı patolojik bulgular (Grup 3) grupları olarak sınıflandırıldı. Apendektomi yapılan hastalar en çok 21-30 (n = 136, % 35,3) ve 31-40 yaş (n = 118, % 30,6) yaş grubundaydı. Negatif apendektomi oranı Grup 2'de % 4,4 idi ve bu grupta kadınların oranı (% 70,6) diğer gruplara göre anlamlı olarak yüksekti (p < 0,05). Toplamda 24 (% 6,2) hastada beklenmedik patolojik bulgulara rastlandı. Serimizdeki apendiks tümörleri (n = 12 [% 3,1]) arasında, düşük dereceli müsinöz neoplazm (n = 6, % 1,6) en yaygın olanıydı, bunu iyi diferansiyel nöroendokrin tümör (n = 3, % 0,8) takip etti.

Sonuç: Apendektomi sırasında olağan dışı patolojik bulgular nadir olmakla birlikte, tüm apendektomi örnekleri rutin histopatolojik incelemeye gönderilmelidir. Bu serideki 24 vakanın anormal tesadüfi bulguları, hastaların tedavi yönetimi üzerinde önemli bir etkiye sahipti. Olağan dışı patolojik tanı alan hastalar, patoloji raporlarının sonuçlarına göre doğru tedavi şansını yakalarlar.

Anahtar Kelimeler: Apandisit, apendektomi, apendiks, histopatoloji

Acute appendicitis is the most common abdominal emergency encountered in general surgery services worldwide (1,2). The overall lifetime risk of this disease is approximately 7% (8.6% in men and 6.7% in women) (3,4). Luminal obstruction is the most common etiology of acute appendicitis (5). Obstruction of the lumen causes mucosal secretions to accumulate and increases intraluminal pressure, which disrupts venous and lymphatic drainage; in turn, this leads to necrosis and perforation.

Epidemiological studies have shown that the incidence of acute appendicitis peaks between the ages of 10 and 30 years, in parallel with the development of the lymphoid system in humans (6). Although fecaliths and lymphoid hyperplasia are the most common causes of this clinicopathological condition, some rare conditions can result in appendix obstruction. Endometriosis (7,8), diverticulitis (9), foreign body obliteration (10), neurofibroma (4), enterobiasis (11), tuberculosis (12), amebiasis (12), actinomycosis (1,13), and schistosomiasis (12), as well as appendix malignancies such as neuroendocrine tumor (carcinoid) (1,14), hyperplastic polyp (15), mucocele (1,6), mucinous cystadenoma (2), adenocarcinoma (6), mucinous cystadenocarcinoma (1), gastrointestinal stromal tumor (2), and lymphoma (2), are known to cause acute appendicitis.

In this report, we evaluated the histopathological results of patients who underwent appendectomy for acute appendicitis, to determine the frequency of unexpected appendicitis pathologies. We also discuss the value of routine pathological examinations.

Material and Methods

The demographic data and pathology reports of patients with a diagnosis of acute appendicitis who underwent an appendectomy in the surgical department of Acıbadem Bakırköy Hospital, between January 2009 and January, 2017, were obtained from the electronic registry system of the hospital and analyzed retrospectively. Patient age, gender, and histopathological diagnoses were recorded. Cases of appendectomy in conjunction with pelvic surgery, and pediatric (aged < 14 years) appendicitis cases, were excluded. All cases in our study were completed laparoscopically. The histopathological examination results of all cases were evaluated in the pathology department of our hospital. Patients were informed of the details of the laparoscopic appendectomy, and written informed consent was obtained prior to the operation. The study was approved by the local ethics committee of İstanbul Gelişim University and met all necessary governmental criteria.

The patients were assigned to acute appendicitis (Group 1), normal appendix (Group 2), and unusual pathological findings (Group 3) groups according to the results of the pathology report. Histopathological findings were examined according to age and gender. Cases without microscopic evidence of inflammation or fibrosis in the appendix were considered normal (negative appendectomy).

Statistical Analysis

Statistical analyses were performed using SPSS software (ver. 20.0 for Windows; IBM Corp., Armonk, NY). The data were analyzed using the Chi-square test and one-sample t-test. Results with a p-value <0.05 were considered statistically significant.

Results

In total, 385 patients (168 women [43.6%] and 217 men [56.4%]; gender ratio, 1:1.29) who met the inclusion criteria were included in this study. The mean age of the study group was 33.2 ± 11.6 years (range: 14–85 years). Most of the patients (~65.9%) undergoing appendectomy were aged 21–30 (n = 136, 35.3%) or 31–40 years (n = 118, 30.6%) (Table 1).

The majority of Group 1 patients exhibited acute appendicitis, based on the pathological examination (n = 344, 89.4%), Group 2 had a low rate of inflammation of the appendix (n = 17, [4.4%]), and some patients in Group 3 showed unusual pathological findings (n = 24, [6.2%]).

The unusual findings were as follows: fibrous obliteration, n = 2; appendicular diverticulitis, n = 3; endometriosis, n = 3; foreign body reaction, n = 1; actinomycosis, n = 1; granulomatous inflammation, n = 2; well-differentiated neuroendocrine tumor (carcinoid), n = 3; hyperplastic polyp, n = 2; mucinous cystadenoma (mucocele, n = 1; and low-grade mucinous neoplasm, n = 6 (Table 2). The average age of Groups 1–3 was 32.88, 32.29, and 37.91 years, respectively, compared to 33.17 years for all of the appendectomy patients in our study (p > 0.05).

Acute appendicitis and unusual findings were more common in males. Group 1 contained 57% males and 43% females, and Group 3 contained 66.7% males and 33.3% females; there were no significant difference in gender ratio between these groups (p=0.239), Group 2 contained a higher proportion of females (70.6%) than the other two groups (p <0.05) (Table 3).

Table 1. Distribution of the Incidence of the Groups According to Patient Age.

		Age groups							Total
		14-20	21-30	31-40	41-50	51-60	61-70	71-84	
Group 1 (Acute appendicitis)	n	41	123	104	47	20	7	2	344
	%	11,90%	35,80%	30,20%	13,70%	5,80%	2,00%	0,60%	100,00%
Group 2 (Negative appendicitis)	n	2	7	6	1	1	0	0	17
	%	11,80%	41,20%	35,30%	5,90%	5,90%	0,00%	0,00%	100,00%
Group 3 (Unusual findings)	n	1	6	8	4	4	1	0	24
	%	4,20%	25,00%	33,30%	16,70%	16,70%	4,20%	0,00%	100,00%
Total	n	44	136	118	52	25	8	2	385
	%	11,40%	35,30%	30,60%	13,50%	6,50%	2,10%	0,50%	100,00%

Table 2. Histopathological Diagnoses Encountered in the Appendectomy Specimens.

Histopathological Diagnosis	n	percentage
Acute appendicitis (Group 1)	344	89,4%
Normal appendix (Group 2)	17	4,4%
Unusual pathological findings (Group 3)	24	6,2%
Fibrous obliteration	2	0,5%
Appendicular diverticulitis	3	0,8%
Endometriosis	3	0,8%
Foreign body reaction	1	0,25%
Actinomycosis	1	0,25%
Granulomatous inflammation	2	0,5%
Neuroendocrine tumor, well differentiated (carcinoid)	3	0,8%
Hyperplastic polyp	2	0,5%
Mucinous cystadenoma (mucocele)	1	0,25%
Low-grade mucinous neoplasm	6	1,55%
Total	385	100%

Table 3. Gender Distribution of Patients in Groups.

		Gender		Total	p-value
		Male	Female		
Group 1	n	196	148	344	
	%	57,00%	43,00%		
Group 2	n	5	12	17	0,047
	%	29,40%	70,60%		
Group 3	n	16	8	24	
	%	66,70%	33,30%		
Total	n	217	168	385	
	%	56,40%	43,60%		

p=0,047

Perforated appendicitis was found in 22 (6.4%) of the 344 patients in Group 1 diagnosed with acute appendicitis. Although the frequency of perforation in male patients (n = 14, 6.5%) was higher than in female patients (n = 8, 4.8%), there was no significant difference gender difference in the perforation rate in any group (p> 0.05) (Table 4).

Table 4. Gender Distribution in Subgroups of Acute Appendicitis.

Acute Appendicitis		Gender		Total	p-value
		Male	Female		
Catarrhal	n	72	61	133	
	%	54,10%	45,90%		
Phlegmonous	n	97	70	167	
	%	58,10%	41,90%		
Gangrenous	n	13	9	22	
	%	59,10%	40,90%		
Perforated	n	14	8	22	0,811
	%	63,60%	36,40%		
Total	n	196	148	344	
	%	57,00%	43,00%		

p=0,811

Acute appendicitis and negative appendicitis were most common in the 21–30 years age group, while unusual appendiceal pathologies were most common in the 31–40 years age group (Table 1). The average age of patients with perforation (37.73 years) was higher than the average age of Group 1 (32.88 years), but the difference was not significant (p = 0.120).

Of the 385 patients who underwent appendectomy, 24 (6.2%) (8 women and 16 men) had unusual findings. Of the appendix tumors (n = 12, 3.1%) in our series, low-grade mucinous neoplasm (n = 6, 1.6%) was the most common type, followed by a well-differentiated neuroendocrine tumor (carcinoid) (n=3, 0.8%).

Discussion

Although acute appendicitis can occur at any age, it is most common in the second and third decades of life (16). In our series, patients who underwent appendectomy with a diagnosis of acute appendicitis were mostly in the second (35.3%) and third (30.6%) decades of life.

While the rate of acute appendicitis is higher in men, women are more likely to undergo a negative appendectomy (3). The difficulty of differential diagnosis of acute appendicitis in women may be associated with the high rate of negative appendectomy (3,6). In our study, the rate of negative appendectomy was significantly higher in women (70,6%) ($p < 0.05$). Diseases encountered in women during the premenopausal period, such as dysmenorrhea, ovarian torsion, ectopic pregnancy, and pelvic inflammatory disease, complicate the differential diagnosis (16). Negative appendectomy rates of 15–25% have been reported (17). It has been suggested that negative appendectomy may reflect subclinical appendicitis, and that symptoms normally resolve after surgery (15).

In recent years, a general decrease in the rate of negative appendectomy has been reported in association with more frequent use of preoperative imaging modalities, such as computed tomography (CT), especially in pediatric patients (18). While some have argued that routine preoperative imaging can reduce the rate of negative appendectomy, others disagree (19,20). In our series, in addition to physical examination and laboratory tests for the diagnosis of acute appendicitis, ultrasonography (US) examinations were performed for each patient. If the diagnosis was unclear, CT was performed, and approximately 45% of our cases were evaluated with CT. The rate of negative appendectomy in our series was 4.4%, and was highest in women in the second and third decades of life. Our low negative appendectomy rate may be due to the use of adequate radiological methods during diagnosis.

Perforation of an inflamed appendix is another undesirable outcome of inadequate management of acute abdomen. The rate of perforated appendicitis (6.4%) in our study was consistent with previous studies (3,18).

After appendectomy for acute appendicitis, unexpected and rare diseases are sometimes diagnosed. Previous studies have shown that the frequency of unexpected diagnoses, such as parasitic and granulomatous diseases, is lower in western compared to eastern countries (4, 21). Fungal infection, parasites, yersinia pseudotuberculosis, mycobacterium tuberculosis, actinomyces infection, Crohn's disease, foreign body reactions, and sarcoidosis can all cause granulomatous appendicitis. In our series, in agreement with previous reports, the rates of unexpected diagnoses such as actinomycosis (0.25%), foreign body reactions (0.25%), and granulomatous inflammation (0.5%) were relatively low. Patients diagnosed with granulomatous inflammation were referred to the gastroenterology department for further examination. Our patient, who was diagnosed with actinomycosis, was treated with appropriate antibiotherapy for 6 months after surgery.

Fibrous obliteration is also known as neurogenic appendicopathy and appendiceal neuroma. Hyperplasia due to neurogenic proliferation in the appendix lumen results in acute appendicitis (22). In previous studies, the incidence of appendiceal neuroma was reported as 0.2–4.5% (4). In our appendectomy series, the prevalence of fibrous obliteration was 0.5%.

Appendicular diverticulitis is a very rare cause of acute appendicitis during pathological examinations (0.004–2.1%) (9). Given the difficulty of preoperative diagnosis, appendicular diverticulitis is only revealed by postoperative histopathological examinations. In our study, three patients (0.8%) were diagnosed with appendicular diverticulitis histopathologically.

Although intestinal endometriosis is common in the rectum and sigmoid colon, it is uncommon in the appendix and rarely causes acute appendicitis. Hormonotherapy is required for postoperative follow-up (4).

Among our patients unexpectedly diagnosed with appendicitis, hyperplastic polyps were detected in two cases. The clinical significance of hyperplastic polyps

remains unclear, but there is very minimal malignant potential (15).

Mucinous cystadenoma (mucocele) is a rare (0.2–0.7%) appendix pathology (6). Appendix mucoceles can have a malignant or benign cause, and it is important that the mucocele be resected without rupture during surgery. Otherwise, the spread of mucinous tumor cells from the appendix to the abdomen may cause pseudomyxoma peritonei. In our case with mucocele, which was the cause of acute phlegmonous appendicitis, perforation did not occur during surgery. In the postoperative period, she was referred to the gastroenterology department to be evaluated for colon-ovarian malignancy.

After appendectomy, appendix tumors are found in less than 3% of cases (2). The most common appendix tumors are carcinoid tumors and mucinous neoplasms. In our series, in agreement with previous reports (0.3–0.9%) (17), three neuroendocrine tumors (carcinoid) related to appendicitis were detected. None of the three patients initially diagnosed with acute appendicitis showed symptoms of carcinoid syndrome, or were diagnosed with an appendicular tumor on preoperative abdominal tomography. If carcinoid tumors are smaller than 1 cm, appendectomy is sufficient regardless of whether there is mesoappendix invasion. Right hemicolectomy is recommended in cases with tumor greater than 2 cm in size (1,2). Right hemicolectomy was performed in one of our cases for this reason, as well as due to deep invasion in the mesoappendix. Appendectomy was sufficient in the other two patients. The prevalence of appendix mucinous neoplasms after appendectomy was approximately 0.2–0.4% (1). In our series, low-grade mucinous neoplasm was detected in six patients (1.6%); in five of the patients, the tumor was located distally in the appendix; in the remaining cases, it was located in the middle part. Appendectomy was considered an adequate treatment, as dysplastic epithelium was not observed at the surgical margins.

Whether routine histopathological examination of all removed appendectomy specimens is necessary remains controversial. While some centers send all resected appendixes for histopathological examination, others only examine specimens that appear macroscopically abnormal (15).

Khan et al. reported that routine histopathological examination results did not have a positive effect on the treatment outcome in their pediatric patient series. Cases should be evaluated on an individual basis in terms of cost-effectiveness (23). In their study, Matthyssens et al. suggested that routine pathological examination is unnecessary because of the rarity of abnormal pathologies in cases of acute appendicitis, and that examining selected cases based on the macroscopic findings of the surgery would be appropriate (24).

Rare pathologies found during pathological examinations may affect the treatment strategy. Long-term additional antibiotic treatment may be considered in rare infectious diseases. In addition, gastroenterology, gynecology, and oncology consultations may be required, as well as advanced surgical interventions such as right colectomy and ileocolic resection.

Conclusion

While the incidence of abnormal pathological findings is low, routine histopathological examination is expensive and constitutes a major part of the workload of pathologists. The main purpose of routine histopathological examination after appendectomy is to achieve a definitive diagnosis while considering incidental findings during the operation. The pathology report is a medico-legal document that can improve the quality of outcomes by informing surgical decision-making.

Appropriate radiological imaging methods shorten the time to diagnosis of inflammatory appendicitis, and reduce the frequency of both perforated appendicitis and negative appendectomy. However, they are not always sufficient for the diagnosis of abnormal appendix pathology, and even intraoperative macroscopic diagnosis may not be possible despite the advantages for laparoscopic surgery.

The unexpected diagnoses detected by chance in 24 cases in our series had a significant impact on treatment management; serious pathological diagnoses could be overlooked, which would affect the treatment for some patients if samples are not sent for routine histopathological analysis. Therefore, all appendectomy specimens should be subjected to histopathological examination.

References

1. Limaiem F, Arfa N, Marsaoui L, Bouraoui S, Lahmar A, Mzabi S. Unexpected Histopathological Findings in Appendectomy Specimens: a Retrospective Study of 1627 Cases. *Indian J Surg.* 2015;77: 1285-90. DOI:10.1007/s12262-015-1278-8.
2. Akbulut S, Tas M, Sogutcu N, et al. Unusual histopathological findings in appendectomy specimens: a retrospective analysis and literature review. *World J Gastroenterol.* 2011;17: 1961-70. DOI: 10.3748/wjg.v17.i15.1961.
3. Elfaedy O, Benkhadoura M, Elshaikhy A, Elgazwi K. Impact of routine histopathological examination of appendectomy specimens on patient management: a study of 4012 appendectomy specimens. *Turk J Surg.* 2019;35: 196-201. DOI: 10.5578/turksurg.4253.
4. Dincel O, Göksu M, Türk BA, Pehlivanoğlu B, İslser S. Incidental Findings in Routine Histopathological Examination of Appendectomy Specimens; Retrospective Analysis of 1970 Patients. *Indian J Surg.* 2018;80 :48-53. DOI: 10.1007/s12262-016-1557-z.
5. Addiss DG, Shaffer N, Fowler BS, Tauxe RV. The epidemiology of appendicitis and appendectomy in the United States. *Am J Epidemiol.* 1990;132: 910-25. DOI: 10.1093/oxfordjournals.aje.a115734.
6. Unver N, Coban G, Arıcı DS, et al. Unusual Histopathological Findings in Appendectomy Specimens: A Retrospective Analysis of 2047 Cases. *Int J Surg Pathol.* 2019;27: 142-6. DOI: 10.1177/1066896918784650.
7. Tumay V, Ozturk E, Ozturk H, Yilmazlar T. Appendiceal endometriosis mimicking acute appendicitis. *Acta Chir Belg.* 2006;106: 712-3. DOI: 10.1080/00015458.2006.11679989.
8. Faucheron JL, Pasquier D, Voirin D. Endometriosis of the vermiform appendix as an exceptional cause of acute perforated appendicitis during pregnancy. *Colorectal Dis.* 2008;10: 518-9. DOI: 10.1111/j.1463-1318.2007.01428.x.
9. Yardimci AH, Bektas CT, Pasaoglu E, et al. Retrospective study of 24 cases of acute appendiceal diverticulitis: CT findings and pathological correlations. *Jpn J Radiol.* 2017;35: 225-32. DOI: 10.1007/s11604-017-0625-z.
10. Klingler PJ, Seelig MH, DeVault KR, et al. foreign bodies within the appendix: A 100-year review of the literature. *Dig Dis.* 1998;16: 308-14. DOI: doi: 10.1159/000016880.
11. Yildirim S, Nursal TZ, Tarim A, Kayaselcuk F, Noyan T. A rare cause of acute appendicitis: parasitic infection. *Scand J Infect Dis.* 2005;37: 757-9. DOI: 10.1080/00365540510012161.
12. Chamisa I. A clinicopathological review of 324 appendices removed for acute appendicitis in Durban, South Africa: a retrospective analysis. *Ann R Coll Surg Engl.* 2009;91: 688-92. DOI:10.1308/00358 8409X12486167521677.
13. Nissotakis C, Sakorafas GH, Koureta T, Revelos K, Kassaras G, Peros G. Actinomycosis of the appendix: diagnostic and therapeutic considerations. *Int J Infect Dis.* 2008;12: 562-4. DOI: 10.1016/j.ijid.2007.12.015.
14. Shapiro R, Eldar S, Sadot E, Venturero M, Papa MZ, Zippel DB. The significance of occult carcinoids in the era of laparoscopic appendectomies. *Surg Endosc.* 2010;24: 2197-9. DOI: 10.1007/s00464-010-0926-0.
15. Jones AE, Phillips AW, Jarvis JR, Sargen K. The value of routine histopathological examination of appendectomy specimens. *BMC Surg.* 2007;7: 17. DOI: 10.1186/1471-2482-7-17.
16. Rabah R. Pathology of the appendix in children: an institutional experience and review of the literature. *Pediatr Radiol.* 2007;37: 15-20. DOI: 10.1007/s00247-006-0288-x.
17. Ma KW, Chia NH, Yeung HW, Cheung MT. If not appendicitis, then what else can it be? A retrospective review of 1492 appendectomies. *Hong Kong Med J.* 2010;16: 12-7.
18. Charfi S, Sellami A, Affes A, Yaïch K, Mzali R, Boudawara TS. Histopathological findings in appendectomy specimens: a study of 24,697 cases. *Int J Colorectal Dis.* 2014;29: 1009-12. DOI: 10.1007/s00384-014-1934-7.
19. Khairy G. Acute appendicitis: is removal of a normal appendix still existing and can we reduce its rate? *Saudi J Gastroenterol.* 2009;15: 167-70. DOI: 10.4103/1319-3767.51367.
20. Chiang DT, Tan EI, Birks D. 'To have...or not to have'. Should computed tomography and ultrasonography be implemented as a routine work-up for patients with suspected acute appendicitis in a regional hospital? *Ann R Coll Surg Engl.* 2008;90: 17-21. DOI: 10.1308/003588408X242259.
21. Bastiaenen VP, Allema WM, Klaver CEL, et al. Routine histopathologic examination of the appendix after appendectomy for presumed appendicitis: Is it really necessary? A systematic review and meta-analysis. *Surgery.* 2020;168: 305-12. DOI: 10.1016/j.surg.2020.03.032.
22. Patel AV, Friedman M, MacDermott RP. Crohn's disease patient with right lower quadrant abdominal pain for 20 years due to an appendiceal neuroma (Fibrous obliteration of the appendix). *Inflamm Bowel Dis.* 2010;16: 1093-4. DOI: 10.1002/ibd.21143.
23. Khan RA, Ghani I, Chana RS. Routine histopathological examination of appendectomy specimens in children: is there any rationale? *Pediatr Surg Int.* 2011;27: 1313-5. DOI: 10.1007/s00383-011-2926-0.
24. Matthyssens LE, Ziol M, Barrat C, Champault GG. Routine surgical pathology in general surgery. *Br J Surg.* 2006;93: 362-8. DOI: 10.1002/bjs.5268.