

Incidental lesions in appendectomy specimens; rare or rarely sampled?

 Nuray Kepil,¹  Sebnem Batur,¹  Ozan Akinci,²  Salih Pekmezci³

¹Department of Pathology, Istanbul University -Cerrahpasa, Cerrahpasa Faculty of Medicine, Istanbul, Turkey

²Department of General Surgery, Hakkari State Hospital, Hakkari, Turkey

³Department of General Surgery, Istanbul University -Cerrahpasa, Cerrahpasa Faculty of Medicine, Istanbul, Turkey

ABSTRACT

OBJECTIVE: During the microscopic examination of the specimens after appendectomy operations performed due to acute appendicitis, pathologists may encounter some incidental and unusual lesions. Appendectomy specimens are sampled as 3 sections/1 paraffin block in many centers. In this study, we aimed to evaluate whether multiple and dense sampling of appendix specimens has an impact on the incidence of incidental lesions of the appendix.

METHODS: This study is a retrospective study of 1154 patients who underwent appendectomy with presumed acute appendicitis at the Department of General Surgery, had histopathological evaluation between 2007–2011 and 2014–2018. Group 1 was made up of the patients whose appendix specimens were examined as 3 sections/1 paraffin block. Group 2 was made up of the patients whose appendix specimens were sampled completely. It was evaluated whether there was a difference between the two groups in terms of incidence of incidental benign and malign appendix lesions.

RESULTS: There were 579 patients in Group 1, 575 patients in Group 2, and the mean age of the groups was 26 and 28, respectively. Neither acute appendicitis findings nor any of the other unusual lesions were found in 57 specimens (9.8%) in Group 1 and 58 specimens (10.1%) in Group 2. Unusual pathological findings were detected in 6 specimens in Group 1 and 21 in Group 2. All unusual lesions, including benign and malignant, were significantly higher in Group 2 than in Group 1 ($p=0.013$). In terms of the incidence of malignant incidental lesions alone, there was no significant difference between the two groups ($p=0.136$).

CONCLUSION: Multiple and dense sampling of appendectomy specimens increases the likelihood of detecting unusual lesions of appendix.

Keywords: Acute appendicitis; incidental lesions; multiple and dense sampling.

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Acute appendicitis is one of the most common surgical emergencies worldwide, and appendectomy specimens are frequently encountered in pathology laboratories on a daily basis. Obstruction of the appendix lumen is the dominant factor in the etiology of acute appendicitis. Obstruction is mostly caused by fecaliths and lymphoid hyperplasia, however, unusual factors can sometimes

cause acute appendicitis. Although there are no findings in macroscopic examination, we may encounter some surprise lesions in microscopic evaluation. These lesions may include inflammatory processes with a specific etiology, as well as benign and malignant neoplasms [1–6].

Different approaches are applied in microscopic examination of appendectomy specimens in different cen-



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Correspondence: Dr. Nuray KEPIL. Istanbul Universitesi-Cerrahpasa, Cerrahpasa Tip Fakultesi, Patoloji Anabilim Dalı, Istanbul, Turkey.
Tel: +90 530 467 01 26 e-mail: nuraykepil@gmail.com

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ters. Some pathology centers perform sampling of appendix specimens with a single block while some centers perform multiple and dense sampling. This study aimed to evaluate whether multiple and dense sampling of appendix specimens had an impact on the incidence of incidental lesions of the appendix.

MATERIALS AND METHODS

This study is a retrospective study of 1154 patients who underwent appendectomy with presumed acute appendicitis at the Department of General Surgery, had histopathological evaluation between January 2007-January 2011 and January 2014-January 2018. Ethics committee approval was received (Approval no: 83045809). The patients' demographic, clinical and pathological data were obtained from the hospital's pathology and surgery reports. Group 1 was made up of the patients operated between 2007–2011 whose appendix specimens were examined as 3 sections/1 paraffin block. Sampling was performed by obtaining a total of 3 sections with 2 transverse sections from the surgical margin (resected edge) and mid appendix and 1 longitudinal section from the distal appendix. Group 2 was made up of the patients operated between 2014–2018 whose appendix specimens were sampled completely. The incidence of incidental benign and malignant appendiceal lesions was compared between the two groups.

Patients who were over 18 years of age and operated for acute appendicitis were included in the study. Patients who were below 18 years of age, patients with known appendix cancer, and those who underwent incidental appendectomy in another surgical operation were excluded. Patients diagnosed clinically and pathologically as acute appendicitis are considered as positive appendectomy, while patients who were clinically diagnosed and operated but had no featured of appendicitis pathologically are considered as negative appendectomy. All pathology preparations and pathology reports were retrospectively re-evaluated by 2 specialist pathologists. Patient confidentiality was maintained.

For statistical analysis; the Pearson chi-square, Trend chi-square, and Fisher tests were used to compare the categorical data where applicable. The Kolmogorov-Smirnov test was used for the measurements with a normal distribution. The Mann-Whitney U test was used to compare the measurements with non-normal distribution. The value of $p < 0.05$ was accepted to be statistically significant in all analyses. The analyses were performed using IBM® SPSS version 20.

RESULTS

There were 579 patients in Group 1 and 575 patients in Group 2, with a total number of 1154 appendectomy specimens evaluated in our study. The mean age of patients in Group 1 was 26, while it was 28 in Group 2, and the mean age of Group 1 was significantly lower than Group 2 ($p=0.014$). The male/female ratio was 371/206 in Group 1, while it was 358/217 in Group 2, and the gender distribution between the groups was similar ($p=0.473$).

The mean length of appendectomy specimens was 6.5 cm, with a mean appendix wall thickness of 0.3 cm in all cases.

The negative appendectomy rates in Group 1 and Group 2 were 9.8% ($n=57$) and 10.1% ($n=58$), respectively, and there was no significant difference between the groups in terms of negative and positive appendectomy rates ($p > 0.05$). Also, no significant trend pattern was observed in negative appendectomy rates over the years ($p=0.16$).

19 of 1154 specimens (1.64%) revealed appendix neoplasia. In Group 1, with 3 sections/1 paraffin block examination, a total of 6 patients had malignant unusual pathological diagnosis. Of these patients, 3 had low grade mucinous neoplasia (LGMN), 1 had sessile serrated adenoma (SSA), 2 had neuroendocrine tumor. In Group 2, which multiple and dense sampling examinations were performed, 6 low grade mucinous neoplasia, 5 sessile serrated adenomas, 2 neuroendocrine tumors, 3 granulomatous appendicitis, 3 diverticulitis perforations, 1 endometriosis, 1 ascaris lumbricoides, a total of 13 malignant and 8 benign unusual pathological diagnoses were made (Table 1, Fig. 1). All unusual lesions, including benign and malignant, were significantly higher in Group 2 compared to Group 1 ($p=0.013$). When patients with benign unusual pathologies were excluded, in groups 1 and 2, 6 and 13 patients had malignant unusual pathology, respectively. However, there was no significant difference between the two groups in terms of malignant unusual pathologies ($p=0.136$).

DISCUSSION

Appendectomy is one of the most common surgical operations worldwide, which is mostly caused by luminal obstruction. Obstructions in the lumen causes continued mucous secretion leading to pathophysiological changes such as increased intraluminal pressure, lymphatic drain-

TABLE 1. Distribution of pathological diagnosis of appendectomy specimens

Pathological diagnosis	Group 1		Group 2		p
	n	%	n	%	
Negative appendectomy	57	9.8	58	10.1	
Positive appendectomy	516	89.1	496	86.3	
Acute appendicitis	103	19.9	140	28.2	>0.05 ^a
Phlegmonous appendicitis	201	38.9	188	37.9	
Gangrenous appendicitis	150	29.1	88	17.7	
Perforated appendicitis	62	12	80	16.1	
Other unusual pathological findings	6	1	21	3.7	0.013^a
Only malign unusual pathological findings	6		13		0.136 ^b
Low-grade mucinous neoplasm	3		6		
Sessile serrated adenoma	1		5		
Neuroendocrine tumor	2		2		0.761 ^b
Granulomatous appendicitis	0		3		
Perforated diverticulitis	0		3		
Endometriosis	0		1		
Ascaris lumbricoides	0		1		

a: Pearson's chi-squared test; b: Fisher's exact test.

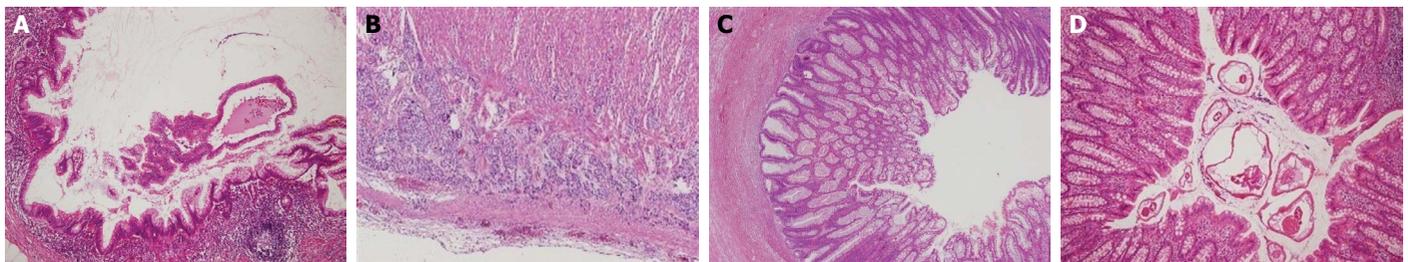


FIGURE 1. (A) Low grade mucinous neoplasia of appendix, x100, H&E. (B) Neuroendocrine tumor of appendix, x100, H&E. (C) Sessile serrated adenom of appendix, x40, H&E. (D) *Ascaris lumbricoides* eggs in the appendix lumen, x100, H&E.

age obstruction, and development of edema as a result of which the distension of the appendix increases and results in venous obstruction. These events lead to ischemia and necrosis on the appendix wall [7]. Fecaliths are the major causative factors for luminal obstruction of the appendix. Additionally, many other uncommon causes can result in luminal obstruction of the appendix. The most common abnormal pathological findings in appendectomy specimens are parasitic infestations (such as enterobiasis, ascariasis, taeniasis, schistosomiasis, amebiasis), endometriosis, granulomatous diseases, diverticulitis of the appendix, benign and malignant tumors (such as mesenchymal tumors, neuroendocrine tumors, lymphoma, gastrointestinal stromal tumors, low grade

mucinous neoplasia, tubular adenoma, villous adenoma, sessile serrated adenoma, adenocarcinoma) [1–6, 8–11].

Appendiceal tumors, which account for less than 3% of all appendectomy specimens, rarely present with clinical findings and are often identified during a surgical operation or pathological examination [1, 5, 12, 13]. Therefore, routine histopathological examination of appendectomy specimens is critical. Neuroendocrine tumors account for 60% of all appendiceal tumors originating in the appendix and are found in 0.3–2.27% of patients undergoing appendectomy [1, 14]. The rate of appendiceal neoplasia was found 1.64% in our study. Among these neoplasms, low grade mucinous neoplasms

were the most common ($n=9$, 0.77%). LGMNs are rare appendiceal tumors seen in less than 0.3% of appendectomy specimens [15]. In our study, the second most common malignant pathology was sessile serrated adenoma. Sessile serrated adenomas are generally asymptomatic and detected incidentally. They are mostly seen on the right side of the colon and rarely in the appendix [16]. SSAs may mimic acute appendicitis by increasing appendix diameter, and treated by surgical resection.

Granulomatous appendicitis is a rare condition with an incidence ranging from 0.31% to 1.04% in patients who are incidentally operated with a clinical presentation of acute appendicitis [17, 18]. It may be associated with systemic inflammatory diseases such as Crohn's disease and sarcoidosis. Definitive diagnosis can be made after a long-term follow-up and further examinations. In our study, no granulomatous appendicitis was found in Group 1, whereas it was found in 3 patients in Group 2.

Appendiceal diverticulosis was reported rarely, with an incidence between 0.004% and 2.1% [3, 19, 20]. Increased intraluminal pressure due to fecaliths, proximal tumors, excessive luminal mucus secretion are the main factors for the formation of appendiceal diverticulum. No further treatment besides appendectomy is needed. In our study, no diverticulitis was observed in any of the patients in Group 1, but perforated diverticulitis of the appendix was detected in 3 patients in Group 2.

Endometriosis is defined as the presence of endometrial tissue in ectopic locations outside the uterine cavity. Intestinal endometriosis accounts for approximately 10% of all women with endometriosis. It is mostly seen on the rectum and sigmoid colon, while rarely localized on the appendix. It is usually asymptomatic but may rarely cause acute appendicitis, perforation, and intussusception [9, 21, 22].

The histopathological examination of the appendix serves two purposes. First, it confirms the diagnosis of acute appendicitis. The second is to rule out malignancy. In the routine examination of appendectomy specimens, specimens are quickly fixed in formalin before the transport to the pathology laboratory. Specimens are evaluated after macroscopic examination, with one transverse section from the proximal surgical margin, one transverse section from the corpus, and one longitudinal section from the tip. In our study, we performed this routine pathological examination in Group 1. In Group 2, we examined the specimens by sampling completely. As a result of histopathological examination of

multiple and densely sampled materials, we observed that the incidence of unusual lesions increased statistically. We think this statistical difference is clinically significant. To give some examples, while appendectomy is curative in cases with benign tumors, additional surgery may be necessary in those with malignant tumors, based on the characteristics of the mass. Appendectomy is not sufficient therapy in parasitic diseases; in these cases, anti-parasitic treatment should be applied. Further laboratory, radiological or endoscopic examinations are needed for suspected systemic inflammatory diseases in patients with incidental granulomatous appendicitis.

Referral of appendectomy specimens for histopathological evaluation varies from center to center. Matthyssens et al. suggest that specimens should not be routinely submitted to pathology for examination unless encountered an obvious macroscopic abnormality during the operation as abnormal findings are rarely observed and pathological examination is costly [23]. However, since incidental appendiceal neoplasms have been shown to be more prevalent contrary to popular belief, it is clear that this practice has the potential to overlook significant pathologies that may affect patient management. This may bring about significant medical, social, ethical and legal problems. Although in present study, there was no statistically significant difference in the incidence of neoplastic lesions, we find it clinically important that there is a significant numerical difference.

We did not find any other study similar to ours in literature in English. Therefore, our study is the first report in the literature on this subject. However, the retrospective nature of our study and the fact that the data were obtained from single-center are the limitations of the study.

Conclusion

The data we obtained from this study shows that multiple cross-sectional examination of the appendectomy materials significantly increased the incidence of unusual lesions of the appendix, although the number of malignant cases did not increase. Therefore, we recommend multiple and dense sampling of appendectomy specimens.

Ethics Committee Approval: This study was approved by Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty Clinical Trials Ethics Committee (date: 07.04.2020, number: 83045809-604.01.02).

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