

Incidental lesions in appendectomy specimens: Rare or rarely sampled?

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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, Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, 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. In this study, it was evaluated whether there was a difference between the two groups concerning 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 six 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 ($p=0.013$). Concerning 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 the 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 mostly arises from fecaliths and lymphoid

hyperplasia; however, unusual factors may sometimes lead to acute appendicitis. Although there are no findings in the 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].



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Different approaches are applied in the microscopic examination of appendectomy specimens in different centers. 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, Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, 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 three sections with two transverse sections from the surgical margin (resected edge) and mid appendix and one 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 this study. Patients who were below 18 years of age, patients with known appendix cancer, and those who underwent an incidental appendectomy in another surgical operation were excluded from this study. 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 two 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

Highlight key points

- During the microscopic examination of the specimens after appendectomy operations performed due to acute appendicitis, pathologists may encounter some incidental and unusual lesions.
- Multiple and dense sampling of appendectomy specimens increases the likelihood of detecting unusual lesions of the appendix.

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 concerning 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, six patients had a malignant unusual pathological diagnosis. Of these patients, three had low-grade mucinous neoplasia (LGMN), one had sessile serrated adenoma (SSA), two had a neuroendocrine tumor. In Group 2, which multiple and dense sampling examinations were performed, six low-grade mucinous neoplasia, five sessile serrated adenomas, two neuroendocrine tumors, three granulomatous appendicitis, three diverticulitis perforations, one endometriosis, one *Ascaris lumbricoides*, 13 malignant and eight benign unusual pathological diagnoses were made (Table 1, Fig. 1). All unusual lesions, in-

TABLE 1. Distribution of pathological diagnosis of appendectomy specimens

Pathological diagnosis	Group 1 %	Group 2 %	p
Negative appendectomy	9.8	10.1	
Positive appendectomy	89.1	86.3	
Acute appendicitis	19.9	28.2	>0.05 ^a
Phlegmonous appendicitis	38.9	37.9	
Gangrenous appendicitis	29.1	17.7	
Perforated appendicitis	12	16.1	
Other unusual pathological findings	1	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.

cluding 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 mostly arises from lumi-

nal obstruction. Obstructions in the lumen cause continued mucous secretion, leading to pathophysiological changes, such as increased intraluminal pressure, lymphatic drainage 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 may 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 [10]. SSAs may mimic acute

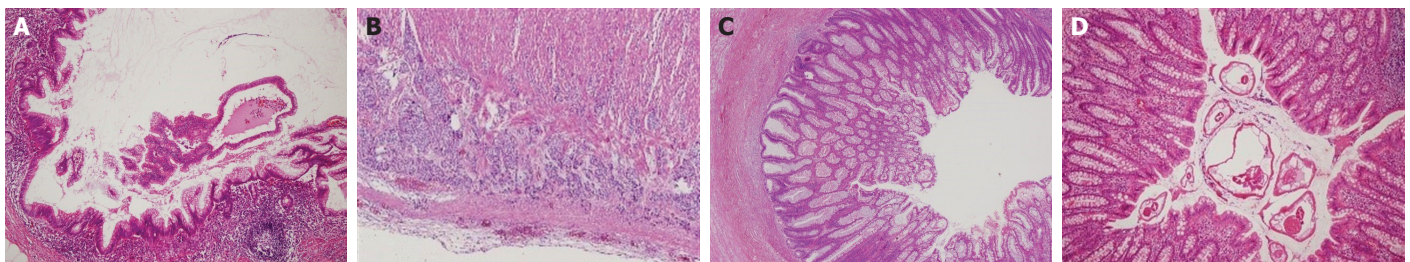


FIGURE 1. (A) Low-grade mucinous neoplasm of appendix, x100, H&E. (B) Neuroendocrine tumor of appendix, x100, H&E. (C) Sessile serrated adenoma of the appendix, x40, H&E. (D) *Ascaris lumbricoides* eggs in the appendix lumen, x100, H&E.

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 [16, 17]. It may be associated with systemic inflammatory diseases, such as Crohn's disease and sarcoidosis. Definitive diagnosis can be made after long-term follow-up and further examinations. In our study, no granulomatous appendicitis was found in Group 1, whereas it was found in three patients in Group 2.

Appendiceal diverticulosis was reported rarely, with an incidence between 0.004% and 2.1% [3, 18, 19]. Increased intraluminal pressure due to fecaliths, proximal tumors, excessive luminal mucus secretion is the main factors for the appendiceal diverticulum formation. 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 three 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, 20, 21].

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 the 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 for 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. Matthysens et al. [22] 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. 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 the 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 the literature. Therefore, to our knowledge, our study is the first report in the literature on this subject. However, the retrospective nature of our study and given that the data were obtained from a single-center are the limitations of this study.

Conclusion

The data we obtained from this study shows that multiple cross-sectional examinations 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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