Clinical outcomes and pathologic results following identification of appendicitis

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ABSTRACT

Aims: Acute appendicitis (AA) is one of the most frequent clinical pathologies for urgent surgery in children We aimed to investigate the occurrence and distribution of pathological findings in appendectomy specimens from patients initially diagnosed with AA.

Methods: The demographic information and histopathological findings of patients who underwent appendectomy at our center between 2011 and 2021 were retrospectively analyzed.

Results: A total of 259 patients were included in the study. The patients were aged 38-212 months (mean 143±39), with 180 (69.5%) male patients. Based on the histopathological results, 63 (24.3%) patienst had lymphoid hyperplasia (LH), 109 (42.1%) AA, 11 (4.2%) suppurative appendicitis (SA), 46 (17.8%) phlegmonous appendicitis (PA), and 30 (11.6%) gangrenous/necrotizing appendicitis (GA). Twenty (31.7%) patients with LH and 16 patients (53.3%) with GA had an invisible appendix on ultrasound. The leukocyte count and appendix diameter were significantly lower in LH than in the other groups (for all comparisons, p<0.001). CRP level was significantly higher in the complicated groups (GA, PA, SA) than the LH and AA groups. The appendix diameter was significantly higher in the GA group than in the PA group (p=0.049). We found a positive correlation between appendix diameter (AD) and preopertaive leukocyte count, and the duration of hospitalization in days (r=0.265, p=<0.001; r=0243, p=0.001). On the other hand, there was no correlation between appendix diameter and CRP. The binary logistic regression analyses showed that high appendix diameter was a risk factor fo CA (OR:0.206, CI: 95%, 1.061-1.422, p= 0.006).

Conclusion: The high rate of complicated cases (33.5%) we found in our study shows that appendicitis can still be complicated. Additionally, the conclusion has been drawn that even in serious cases such as GA, ultrasonography (US) may overlook appendicitis at a high rate. Finally new diagnostic methods should be developed for cases that do not require surgical intervention, such as LH and eosinophilic gastrointestinal pathologies (colitis).

Keywords: Pathology, acute appendicitis, suppurative appendicitis, phlegmonous appendicitis, gangrenous/necrotizing appendicitis.

INTRODUCTION

Acute appendicitis (AA) is one of the most frequent clinical pathologies for urgent surgery in children.[1] The prevailing pathogenesis involves an initial phase characterized by blockage of the appendicular lumen. The resulting obstruction leads to increased mucus secretion, bacterial growth, luminal distension, and elevated intraluminal pressure.[2,3] The subsequent stage occurs when bacteria can penetrate the luminal wall, inducing transmural inflammation or suppurative appendicitis. During this stage, the inflammation extends to the parietal peritoneum and other surrounding structures, known as periappendicitis. Ultimately, intramural venous and arterial thromboses develop in the later stages, resulting in gangrenous appendicitis.[4,5] Ultrasonography (US) is a widely utilized technique for diagnosing acute appendicitis. The specific criteria identifying the appendix is a fluid-filled, non-compressible, blind-ended tubular structure with a diameter of greater than 6 mm.[6,7]

Accordingly, the presence of edema and polymorphonuclear leukocytes along the mucosa, submucosa, or throughout the entire wall of the appendix was considered as AA; the presence of necrosis in the appendix wall and/or the surgeon indicating the observation of purulent material inside the abdomen and/or a perforation in the appendix wall was considered as complicated appendicitis (CA)[8]; reactive follicular hyperplasia was considered as lymphoid hyperplasia (LH). A phlegmonous appendicitis (PA) is characterized as an inflammatory tumor composed of the inflamed appendix, its neighboring viscera, and the greater omentum and a suppurative appendicitis (SA) represents an advanced stage of appendicitis that develops when bacteria and inflammatory fluid, accumulated in the appendix lumen, obstruct the lymphatic and venous drainage.[9,10] So, when the appendix is obstructed, it first leads to acute appendicitis; if the treatment is delayed, it progresses to phlegmonous appendicitis as inflammation increases. Subsequently, if the appendix wall undergoes ischemia, it becomes partially gangrenous in some areas. If still left untreated, perforation occurs from the gangrenous portions.[11]

The histopathological features of a removed appendix, particularly in children, significantly impacts patient management. To address this, we aimed to investigate the occurrence and distribution of pathological findings in appendectomy specimens from patients initially diagnosed with acute appendicitis.

METHODS

The ethics committee approval of the study was obtained from the Kırıkkale University Clinical Research Ethics Committee (Date:28.02.2024, Decision No: 2024.02.30). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The demographic information and histopathological findings of patients who underwent appendectomy at Kırıkkale University Hospital between 2011 and 2021 were extracted from the hospital's electronic record system and retrospectively analyzed. The patients presented to the pediatric emergency department and the pediatric gastroenterology outpatient clinic with complaints of abdominal pain at the time of admission. Clinical and demographic features were documented, encompassing patient age and gender, clinic, time of appendicitis, type of appendectomy, ultrasonographic and/or tomographic findings, preoperative serum CRP, hemoglobin, leukocyte count, and postoperative histopathological diagnosis.

For the patients included in the study, appendectomy was performed either through an open or laparoscopic technique based on the individual preference of the surgeon. The precise diagnosis of operated patients was confirmed histopathologically.

Statistical Analysis

The normality of the data distribution was assessed using the Kolmogorov-Smirnov test. Differences between the groups in terms of continuous variables in two and three groups were evaluated using the Student's t-test, and when appropriate ANOVA test was employed. Differences in

proportions were evaluated using the chi-square test. Correlations between parameters were assessed using Pearson/Spearman correlation tests. Regression analysis was used to assess the relationship between appendix radius and related parameters. A p-value of less than 0.05 was considered statistically significant. Statistical Package for Social Science (SPSS) version 21.0 (SPSS, Chicago, IL, USA) was used for all statistical analyses.

RESULTS

A total of 259 patients were included in the study. The patients were aged 38-212 months (mean 143±39), with 180 (69.5%) male patients. The laparoscopic surgery technique was used in 98 (37.8%) interventions and the classical approach in 161 (62.2%) interventions. The postoperative hospitalization duration in days was statistically shorter in patients who underwent laparoscopy (3.0±1.1 vs 3.6±1.5 days, p<0.001). Ultrasonography was performed in all patients. In 59 (22.8%) patients the appendix was invisible in US. The mean appendix diameter (AD) was 8.3±2.1mm. Out of these patients, CT was performed in 9 patients. In 7 (2.7%) patients the appendix was retrocecal. Twenty-five (9.6%) patients also had perforation.

The seasonal distribution was as follows: 72 (27.8%) patients presented in spring, 56 (21.6%) in summer, 60 (23.2%) in autumn, and 71 (27.4%) in winter. As a significant observation; 36.5% of the LH patient group were diagnosed in winter.

Based on the histopathological results, 63 (24.3%) patiensr had LH, 109 (42.1%) AA, 11 (4.2%) SA, 46 (17.8%) phlegmonous appendicitis (PA), and 30 (11.6%) gangrenous/necrotizing appendicitis (GA). So 33.5% of the patients had CA. Twenty (31.7%) patients with LH and 16 patients (53.3%) with GA had an invisible appendix on US report. So, we divided the patient in to 3 groups according to the pathology specimens: LH, AA, CA (Table 1).

Table 1. Comparison of pathologic groups in mean of demographic, clinical and laboratory parameters

Variable	Lymphoid hyperplasia n=63	Acute appendicitis n=109	Complicated appendicitis n=87	P-value	Post Hoc analysis A=between LH and AA B=between LH and CA C=between AA and CA
Gender (female) n (%)	22 (34.9)	27 (24.8)	29 (33.3)	0.293	
Mean age (month)	114±39	143±38	141±42	0.862	
Mean leukocyte count /μl	10548±5109	15728±4687	15858±4763	<0.001	**A=<0.001** **B=<0.001** C=0.99
Mean hemoglobin (g/dl)	13.1±1.3	13.4±1.2	13.1±1.2	0.266	
Mean CRP (mg/L)	14.9±3.6	34.8±5.6	61.7±8.9	<0.001	A=0.145 **B=0<0.001** **C=0.011**
Mean appendix diameter	6.8±1.5	8.5±1.8	8.9±2.4	<0.001	**A=<0.001** **B=<0.001** C=0.736
Mean days of postoperative hospitalization	2.9± 0.8	3.4± 1.3	3.8± 1.7	<0.001	**A=0.019** **B=0.001** **C=0.047**
Patients hospitalized for more than 3 days n (%)	11 (17.5)	32 (29.6)	43 (49.4%)	<0.001	A=0.077 **B=<0.001** **C=0.005**
Operation type (Laparoscopic)	29 (46)	40 (37)	28 (32.2)	0.222	

A comparison of histopathological groups with respect to mean LH, AA and CA revealed no significant difference regarding sex, age, and hemoglobin level. The leukocyte count and AD were significantly lower in LH than in the other groups (for all comparisons, p<0.001). CRP level was significantly higher in the CA group than the LH and AA groups. There was a significant difference between the three groups with respect to the mean postoperative hospitalization duration (PHD) (p<0.001). The percentage of patients with CA who were hospitalized for more than 3 days was significantly higher in the CA group than the LH and AA groups (<0.001 and 0.005, respectively). There was no significant difference between the groups regarding the operation type (p=0.222).

A comparison of the complicated pathology groups revealed that there was no significant difference between sex, age, leukocyte count, Hb, and CRP level. The AD was significantly higher in the GA group than in the PA group (p=0.049). The mean hospitalization duration in days was significantly greater in the GA group than the PA and SA groups (for both comparisons, p<0.001). The percentage of patients with GA who were hospitalized for more than 3 days was significantly higher than the PA and SA groups (80% vs 37% and 18.2%, respectively, p<0.001) There was no difference between the groups regarding the operation type (p=0.349) (Table 2).

Table 2. Comparison of complicated appendicits pathologic groups in mean of demographic, clinical and laboratory parameters

Variable	Phlegmonous n=46	Gangrenous/ necrotic n=30	Suppurative n=11	P-value	Post Hoc analysis A=between PL and GN B=between PL and SPP C=between GN and SPP
Gender (female) n (%)	17 (37)	10 (33.3)	2 (18.2)	0.495	
Mean age (month)	148±42	129±42	142±37	0.158	
Mean hemoglobin (g/dl)	15022±4648	16585±5116	17427±3903	0.181	
Mean hemoglobin (g/dl)	13.2±1.3	12.8±1.2	13.5±0.6	0.200	
Mean CRP (mg/L)	50.9±10.9	89.3±19.5	40.0±12.6	0.098	
Mean appendix diameter	8.3±1.9	10.1±3.2	9.6±2.2	**0.040**	A=0.049 B=0.459 C=0.99
Mean postop hospitalization days	3.1± 1.3	5.2± 1.5	2.8± 1.0	**<0.001**	A<0.001 B=0.362 C<0.001
Patients hospitalized for more than 3 days n (%)	17(37)	24(80)	2(18.2)	**<0.001**	A=<0.001 B=0.235 C=<0.001
Operation type (Laparoscopic)	16(34.8)	7(23.3)	5(45.5)	0.349	

We found a positive correlation between AD and preopertaive leukocyte count, and the duration of hospitalization in days (r=0.265, p=<0.001; r=0243, p=0.001). On the other hand, there was no correlation between AD and CRP, age (Table 3). The binary logistic regression analyses showed that high AD was a risk factor fo CA (Odds ratio:0.206, Confidence interval: 95%, 1.061-1.422, p=0.006); however, high leukocyte and CRP levels were not risk factors for CA.

Table 3. Correlation coefficients between appendix diameter and the variables

Variables*	Appendix radius
Age	r=0.0.15, p=0.840
CRP	r= 0.080, p=0.313
Leukocyte	r= 0.265*,p=<0.001*

*p<0.05

DISCUSSION

In our study, we aimed to correlate the pathology data obtained after surgical diagnosis of appendicitis in children with clinical and laboratory findings.

Acute appendicitis is a prevalent cause for urgent abdominal surgery, and globally, appendectomy stands out as one of the most frequently performed surgical procedures.[12,13] The occurrence of AA closely mirrors that of lymphoid development, reaching its peak between the ages of 10 and 30 years. While there is an equal distribution of acute appendicitis cases between genders before puberty, the incidence in males starts to rise gradually during puberty. By the age of 15 to 25, the male-to-female ratio shifts to 2:1 in favor of men.[14,15] The lifetime prevalence of appendicitis is 9%, peaking between the ages of 10 and 14 years.[16] In our study group, the mean patient age was approximately 12 years (143 months), and there was a male predominance (69.5%), which were consistent with previous studies.[14,15]

The use of laparoscopy in pediatric cases offers not only diagnostic precision but also the benefits of minimally invasive techniques, contributing to overall improved outcomes and patient satisfaction.[17] In recent years, laparoscopic appendectomy has become a standard therapeutic procedure for acute appendicitis in many hospitals. Approximately 1/3 of patients underwent laparoscopic appendectomy in our study group. The postoperative hospital stay was also shorter in our laparoscopic group in our study.[18,19]

In this study, we found a positive correlation between leukocyte count and AD. Besides, a high leukocyte count was not found as a risk factor for CA, but high AD was. In addition, we found no correlation between AD and CRP. Moreover, a high CRP level was not a risk factor for CA. In our opinion these findings weaken the use of CRP in appendicitis. Likewise, Daldal et al.[20] also found that CRP was not useful in predicting AA, unlike leukoyte count.

The diagnosis of AA primarily relies on assessing the patient's symptoms, medical history, and the results of physical examination, and most importantly, the US examination. In a study by Abu-Yousef et al.[21] the sensitivity of US in diagnosing appendicitis was calculated as 80%. According to their findings, US accurately diagnosed two out of three cases reported with a pathological diagnosis of appendicitis. In another study, the sensitivity of US was determined to be 96.4%.[22] The accuracy rate of US was significantly high based on the decision made in accordance with the patient's clinical presentation. However, the appendix was invisible in US in our study group in nearly 1/3 of patients with LH and nearly half of the patients with GA. So, our result showed that an invisible appendix did not exlude the disease, even in its severe form (GA) like previous studies.[23]

In the US examination, the mean AD was 6.8±1.5 in LH group, which was significantly lower than the radius in AA and CA. An appendix diameter over 6 mm has been found to be significant in previous studies.[24,25] Previous studies found a positive AA rate of 88.4% in patients with an AD above 6 mm, which was statistically significant compared to the group with an AD below 6 mm.[20] In a study conducted by Xue, it was found that an appendix diameter of 6-8 mm, in particular, led to false-positive results.[26] This narrowed

the gray zone for distinguishing between appendicitis and lymphoid hyperplasia in the differential diagnosis. The diameter of the appendix appears to be the most crucial criterion in differentiating appendicitis from lymphoid hyperplasia.[6] This underscores the significance of the gray zone within the 6-7 mm diameter range. In patients with AA, the AD was found to be 8.5 mm. In cases of lymphoid hyperplasia, this measurement was even lower. In our opinion, when one suspects appendicitis, the revised radius diameter should be 8 mm. The less the diameter the more likely the pathology of LH.

The pelvic cavity is the most common location for the appendix, followed by a descending order of the intraperitoneal position (31-74%) and retrocecal position (26-65%), which are also prevalent.[27,28] In some cases, patients may exhibit atypical symptoms and physical findings, potentially causing a delay in diagnosis and increased complications. An atypical presentation could be associated with the appendix's position. For instance, an ascending retrocecal appendicitis, characterized by right upper abdominal pain, may be clinically indistinguishable from acute pathologies involving the gallbladder, liver, biliary tree, right kidney, and right urinary tract. Here, in our study, the rate of retrocecal appendicitis was relatively low (%2.7).

It is believed that the perforation of the appendix typically occurs within 24 to 36 hours after the symptom onset. Perforated appendicitis constitutes around 20-30% of cases in children aged 10-17 years with appendicitis, and it is more frequently observed in younger children.[29,30] We found a lower rate, which was 9.6%. The ease of patients reaching a doctor and the prompt availability of ultrasound facilities lead to such a relatively low perforation rate in our center. We found a higher perforation rate and appendix radius in gangrenous appendicitis than the flamenetous one, as expected. In GA, perforation occurs more frequently as a result of a focal abscess, large hemorrhagic ulceration, and gangrenous necrosis.[31]

Lymphoid hyperplasia appears to be a physiological response to inflammation rather than the primary cause of appendicitis. It has been linked to inflammatory conditions.[32] So, this explains the high rate of LH in winter in our study.

Limitations

Our study has several limitations. It is an observational study that outlines outcomes. Additionally, our data are constrained by what was available in the electronic medical records. Regarding pathology reports, as multiple pathologists conducted the reports, there may be some variability in the analysis and reporting of these specimens. Although the pathology results for each case were discussed and classified in consultation with a single pathologist during data collection, individual pathology specimens were not individually reviewed.

CONCLUSION

The high rate of complicated cases (33.5%) we found in our study shows that appendicitis can still be complicated. Additionally, the conclusion has been drawn that even in serious cases such as GA, US may overlook appendicitis at a high rate. As a result of our study, it has been revealed that leukocytosis is a significant determinant in the diagnosis of appendicitis compared to CRP. Furthermore, diagnostic ADs should be reevaluated for the diagnosis of appendicitis. New diagnostic methods should be developed for cases that do not require surgical intervention, such as LH and eosinophilic gastrointestinal pathologies (colitis).

ETHICAL DECLARATIONS

Ethics Committee Approval

The ethics committee approval of the study was obtained from the Kırıkkale University Clinical Researches Ethics Committee (Date: 28.02.2024, Decision No: 2024.02.30).

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.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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