

Unusual Histopathologic Findings in Appendectomy Specimens: A Retrospective Analysis

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Background: Appendicitis is one of the most common acute conditions of the abdomen. Although, lymphoid hyperplasia and fecalith are the most common etiologic factors, some unusual factors including intestinal worms and tumors have been identified.

Objectives: The aim of this study was to investigate the incidence and implications of unusual histopathologic findings among appendectomy specimens from patients with clinical impression of acute appendicitis.

Patients and Methods: The clinicopathological data of 2757 patients who had undergone appendectomy for presumed acute appendicitis from January 2006 to November 2013 were retrospectively assessed. According to microscopic findings, the patients were classified into six groups: appendix vermiformis, suppurative appendicitis, phlegmonous appendicitis, gangrenous appendicitis, perforated appendicitis, and unusual histopathologic findings.

Results: A total of 2757 appendectomies were performed to treat patients with suspected acute appendicitis. The mean age of patients was 25.4 ± 11.8 years (range, 5-86) and 69.7% were male. There were 1608 suppurative appendicitis (58.3%), 855 appendix vermiform (31%), 99 gangrenous appendicitis (3.6%), 19 perforated appendicitis (0.7%), 19 phlegmonous appendicitis (0.7%), and 157 patients with unusual histopathologic findings (5.7%). The unusual histopathologic findings (n = 157) were contained fibrous obliterated appendix (80.2%), carcinoid tumor (7%), mucocele (3.8%), *Enterobius vermicularis* (3.8%), B-cell non-Hodgkin's lymphoma (B-NHL) (1.9%), eosinophilic infiltration (1.2%), and granulomatous infiltration (1.9%). Histopathologic findings of appendectomy specimens revealed 14 malignancies among 157 unusual findings (8.9%; 0.5% of all appendectomies) including carcinoid tumor (n = 11) and B-NHL (n = 3).

Conclusions: Although unusual pathologic findings in appendectomy specimens are rare, histopathologic assessment will allow early diagnosis of many unusual diseases. Thus, even when the macroscopic appearance of appendectomy specimens is normal, all specimens should be subjected for routine histopathologic examination.

Keywords: Appendectomy; Appendicitis; Pathology

1. Background

Appendicitis is one of the most common acute conditions of the abdomen and appendectomy is one of the most frequently performed emergency surgeries (1). Epidemiologic studies have shown that the incidence of acute appendicitis roughly parallels that of lymphoid development, with the peak incidence between ten and 30 years of age (2, 3). The male to female ratio of acute appendicitis is about equal up to puberty, but at puberty and thereafter, the male to female ratio increases to 2:1 (2, 4). The most important etiologic factor of acute appendicitis is development of luminal obstruction although lymphoid hyperplasia is the most common factor in patients younger than 20 years old and fecalith is the most common factor in the elderly. In addition, some unusual etiologic factors including intestinal worms and tumors (malignant or benign) have been identified (1, 2, 5-7). These conditions are rarely associated with clinical manifestation; they are recognized either during an operation or pathological examination of appendectomy specimens (1-7).

2. Objectives

The aim of this study was to investigate the incidence and implications of unusual histopathologic findings among appendectomy specimens from patients with clinical impression of acute appendicitis.

3. Patients and Methods

Hospital records of 2757 patients who had undergone surgery for presumed acute appendicitis between 2006 and 2013 at Be'sat Educational and Research Hospital in Tehran, Iran, were studied retrospectively with special reference to age, sex, operation report, and histopathologic findings. Patients with incidental appendectomy during the course of an operation for an illness other than appendicitis including gynecological or colorectal cancer surgery, or trauma surgery were excluded from the study. According to microscopic findings in pathology report, the patients were classified into one of the following six groups including: appendix vermiformis,

suppurative appendicitis, phlegmonous appendicitis, gangrenous appendicitis, perforated appendicitis, and unusual histopathologic findings.

Two experienced pathologists independently reevaluated slides of patients in the “unusual histopathologic findings” group. The results were analyzed using simple percentage and presented clearly to reflect the type of pathology involved.

4. Results

4.1. General Characteristics of Patients Who Undergone Appendectomy

Totally, 2757 appendectomies were performed to treat suspected acute appendicitis. The mean age of patients was 25.4 ± 11.8 years (range, 5-86). Overall, the majority of patients (87.8%) were ≤ 40 and 1.5% were ≥ 61 years old. The male to female ratio was 2.3:1.0 (males, 69.7%). According to histopathologic reports, there were 1608 suppurative appendicitis (58.3%), 855 appendix vermiform (31%), 99 gangrenous appendicitis (3.6%), 19 perforated appendicitis (0.7%), 19 phlegmonous appendicitis (0.7%), and 157 patients (5.7%) with unusual histopathologic findings. Clinical and histopathologic characteristics of patients are summarized in Table 1. There was an age tendency towards patients ≤ 40 years old in the vermi-

Table 1. Clinicopathologic Characteristics of the 2757 Patients Who had Undergone Appendectomy^a

Patient Characteristics	Results
Gender	
Male	1921 (69.7%)
Female	836 (30.3%)
Total	2757
Mean age, y	
Overall	25.4 ± 11.8
Male	24.9 ± 10.9
Female	26.6 ± 13.4
Distribution of patients based on age range	
≤ 10	103 (3.7%)
11-20	1037 (37.6%)
21-30	975 (35.4%)
31-40	305 (11.1%)
41-50	217 (7.9%)
51-60	79 (2.9%)
61-70	13 (0.5%)
≥ 71	28 (1%)
Histopathologic findings	
Suppurative appendicitis	1608 (58.3%)
Appendix vermiformis	855 (31%)
Perforated appendicitis	19 (0.7%)
Gangrenous appendicitis	99 (3.6%)
Phlegmonous appendicitis	19 (0.7%)
Unusual histopathologic findings	157 (5.7%)

^a Data are presented as No. (%) and mean \pm SD.

form appendix (normal appendix) group (94.1% of the 855 patients). Of all performed appendectomies, 157 specimen revealed abnormal histopathologic diagnoses (5.7%). The mean age of this group of patients was 35.7 ± 16.5 years and the male to female ratio was 1:1.1. The mean age of men and women with abnormal histopathologic diagnoses were 38.5 ± 18.5 (range, 10-76) and 33.2 ± 14.2 years (range, 18-79), respectively.

4.2. General Characteristics of Patients with Unusual Histopathologic Findings in Appendectomy Specimens

The unusual histopathologic findings (n = 157) were fibrous obliterated appendix (n = 126; 80.2%), carcinoid tumor (n = 11; 7%), mucocele (n = 6; 3.8%), *E. vermicularis* (n = 6; 3.8%), B-NHL (n = 3; 1.9%), eosinophilic infiltration (n = 2; 1.2%), and granulomatous infiltration (n = 3; 1.9%). Clinicopathologic feature of 157 patients with unusual histopathologic findings are summarized in Table 2. Among 157 patients with unusual histopathologic findings, 127 showed no evidence of inflammatory cells infiltration and the remaining 30 patients showed varying degrees of infiltration.

Histopathologic findings of appendectomy specimens revealed 14 malignancies among 157 unusual findings (8.9%; 0.5% of all studied appendectomies) including carcinoid tumor (n = 11) and B-NHL (n = 3). All of the

Table 2. Characteristics of 157 Patients With Unusual Histopathologic Findings^a

Patient Characteristics	Results
Gender	
Male	75 (47.8%)
Female	82 (52.2%)
Total	157
Mean age, y	
Overall	35.7 ± 16.5
Male	38.5 ± 18.5
Female	33.2 ± 14.2
Histopathologic findings	
Fibrous obliteration	126 (80.2%)
<i>Enterobius vermicularis</i>	6 (3.8%)
Eosinophilic infiltration	2 (3.8%)
Carcinoid tumor	11 (7%)
Granulomatous inflammation	3 (1.9%)
Mucocele	6 (3.8%)
Non-Hodgkin's lymphoma (B cell)	3 (1.9%)
Distribution of patients based on age range, y	
≤ 10	3 (1.9%)
11-20	28 (17.8%)
21-30	41 (26.1%)
31-40	25 (15.9%)
41-50	44 (28%)
51-60	3 (1.9%)
61-70	13 (8.3%)
≥ 71	3 (1.9%)

^a Data are presented as No (%) and mean \pm SD.

Table 3. Detailed Characteristics of the Patients With Appendicular Malignancy^a

No.	Age, y	Sex	Primary Tumor Type	Tumor Size, mm	Parietal Spread	Surgical Approach
1	10	M	B-NHL	≈15 ^b	Muscularis propria	Appendectomy
2	23	M	B-NHL	70	Mesoappendix	Appendectomy
3	24	F	B-NHL	30	Mesoappendix	Appendectomy
4	39	F	Carcinoid	11	Mesoappendix	Appendectomy
5	21	F	Carcinoid	8	Submucosa	Appendectomy
6	28	F	Carcinoid	10	Mesoappendix	Appendectomy
7	27	F	Carcinoid	8	Mesoappendix	Appendectomy
8	33	M	Carcinoid	6	Muscularis propria	Appendectomy
9	53	F	Carcinoid	6	Submucosa	Appendectomy
10	41	M	Carcinoid	5	Mesoappendix	Appendectomy
11	22	F	Carcinoid	13	Mesoappendix	Appendectomy
12	43	F	Carcinoid	9	Submucosa	Appendectomy
13	11	F	Carcinoid	5	Mesoappendix	Appendectomy
14	24	M	Carcinoid	10	Muscularis propria	Appendectomy

^a Abbreviation: B-NHL, Non-Hodgkin's Lymphoma.

^b Exact size was not found.

patients with carcinoid tumor were only treated with appendectomy and the tumor diameters of these cases ranged from 5 to 13 mm. The patients with B-NHL were referred to the oncology center for further treatment. Detailed characteristics of patients with appendicular malignancy are summarized in Table 3.

5. Discussion

Acute appendicitis is the most common surgical emergency and obstruction of the appendiceal lumen seems to be essential for developing appendicitis. Although fecalith and lymphoid hyperplasia are the usual causes of the obstruction, some unusual factors were also reported (2, 8, 9). Appendiceal tumors, which have been reported in less than 3% of all appendectomy specimens, are rarely associated with clinical manifestations. They are frequently recognized either during an operation or the pathological examination (2, 10, 11). Benign tumors of the appendix consist of tubular adenoma, villous adenomas, leiomyoma, neuromas, and lipomas. Malignant tumors of the appendix include carcinoids, goblet cell carcinoids, lymphomas, primary adenocarcinomas, and mucinous cystadenocarcinomas (2, 10, 11). The most common appendiceal malignant lesion is carcinoid tumor which comprises about 60% of all appendiceal tumors, but are found in only 0.3% to 2.27% of appendectomies specimens; malignancy and metastasis of these tumors are very rare and are seen only in tumors that exceed 1 cm. Therefore, simple appendectomy is considered sufficient management for these tumors and right hemicolectomy is recommended for tumor ≥ 2 cm (12-14). In our study, the incidence of appendiceal carcinoid was 0.39%, which was similar to other studies.

All patients in our study had signs and symptoms of acute appendicitis and diagnosis was made after appendectomy and histopathologic examination. Female preponderance, location in the tip of appendix, and size of less than 1 cm

in our study were also similar to other reports (2, 12-14). The most common mucinous epithelial neoplasm of the appendix is mucocele. In this condition, mucoid material accumulates in the intraluminal region of the appendix causing obstructive dilation of the organ. The overall incidence of this condition in the literatures ranges from 0.2% to 0.7%. Currently, four histopathologic types of appendiceal mucocele are recognized including (in order of incidence) mucinous cystadenoma, mucosal hyperplasia, mucinous cystadenocarcinoma, and retention cyst (1-3, 8-11, 15-18). Appendectomy is the standard of care for mucinous cystadenoma, whereas a cystadenocarcinoma requires a right hemicolectomy and consequent chemotherapy (1, 15, 16). In our patient series, the incidence of appendiceal mucocele (0.2%) was also in accordance with previous reports.

The gastrointestinal tract is the most common site for extranodal lymphomas and accounts for 30% to 43% of all extranodal cases. The stomach is the most commonly involved organ followed by the small intestine, colon, and esophagus (19). The incidence of primary appendiceal lymphoma is extremely low and has been estimated at 0.015% to 0.05% (19-22).

Cases of appendiceal lymphoma most often occur in young adults ageing 20 to 40 years. Most of the cases presents with symptoms of acute appendicitis and are found during histopathologic examination (19). In our patient series, the incidence of appendiceal lymphoma (0.1%) was higher than previous reports (20-22). The incidence of neurogenic appendicopathy (fibrous obliteration) is estimated at 30%, although this condition is described as fibrous obliteration, recent studies show that the occlusive proliferation is predominantly neurogenic. Differential diagnosis of appendicitis relatively depends upon a patient's history, symptoms, and findings of laboratory and physical examination (1, 23-25). In the current patient series, the incidence of fibrous obliteration was 4.5%, which was lower than the previous reports (23-25).

Enterobius vermicularis, also known as pinworm or oxy-

uris, is a widespread parasitic infection. It is estimated that up to 200 million people are infested with *E. vermicularis* worldwide. The association of pinworm infection and appendicitis was first made in the late 19th century. While the reported incidence of pinworm in appendectomy specimens of patients suspected for appendicitis ranged from 0.02% to 41.8%, the reported rates of inflammation in infected specimen with pinworm ranged from 13% to 37% (1, 26-29). *Enterobius vermicularis* was found in six cases (0.2%) in the present study and one of them had acute appendicitis on histopathologic examination, which is in accordance with the previous studies (1). Granulomatous appendicitis (GA) is a rare condition that is discovered incidentally in patients with suspected acute appendicitis during histopathologic studies. The incidence ranged from 1.3% to 2.3% in underdeveloped countries and from 0.14% to 0.03% in western countries (1, 30, 31). Various infectious and noninfectious diseases including *Yersinia* spp., *Mycobacterium tuberculosis*, *Schistosoma* spp., Crohn's disease, and sarcoidosis have been mentioned as causative factor in GA (1, 29-32). The incidence rate of GA in this study was 0.8% that was lower than other reports (1, 25, 30, 31).

In summary and with considering the overall case reports and case series in the literature, although fecalith and lymphoid hyperplasia are the usual causes of acute appendicitis, some unusual factors such as parasites and tumors may also lead to appendicitis. Thus, even when the macroscopic appearance of appendix is normal, histopathologic assessment of specimens will allow early diagnosis of many unusual diseases that may require further surgery and treatment.

Authors' Contributions

Katayoun Ziari and Kamyab Alizadeh developed the original idea and the protocol, abstracted and analyzed data, wrote the manuscript, and are guarantor.

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