

Effect of Total Macroscopical Sampling of the Pediatric Appendectomy Specimen on Histopathological Diagnosis

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Abstract

Introduction: Acute appendicitis is considered the most common abdominal surgery in children. Pathological examination of the appendectomy specimen mainly is performed to document the presence or absence of inflammation and confirm the clinical diagnosis. If the diagnosis made by the pathologist is as 'no appendicitis', then clinical work up for other causes should be performed. Routine macroscopic evaluation of the appendectomy specimen consists of obtaining one section each from the base, body and the tip of the appendix and additional sections obtained from exuding or perforated areas. The aim of this study is to evaluate if the final pathological diagnosis would change when the appendectomy specimen is sampled totally.

Materials and Methods: In the present study, we performed conventional macroscopical sampling from the tip, body and base of the appendix and embedded these tissues in the first two cassettes, then the rest of appendix was completely sampled in additional two to five cassettes. The histopathological diagnosis of conventionally sampled tissues and the histopathological diagnosis of total macroscopical sampling were analyzed and compared.

Results: A total of 87 appendectomies were evaluated, of which 58.6 % were male, and the mean age was 11.7 (1 years-18 years). The initial histopathological diagnosis was changed in 14 (16%) cases. In 8 (9.2%) cases, the initial diagnosis of reactive lymphoid hyperplasia changed to

Keywords

- Acute appendicitis
- Macroscopical examination
- Pediatric
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acute focal appendicitis (early appendicitis). In 4 (4.6%) cases the initial diagnosis of acute suppurative appendicitis changed to acute suppurative and perforated appendicitis, and in 2 (2.2%) cases acute perforated appendicitis changed to acute perforated and gangrenous appendicitis.

Conclusion: Total macroscopical sampling of the appendectomy specimen in cases of negative appendicitis would improve the diagnosis and can document early appendicitis in pediatric cases.

Introduction

Appendectomy is considered the most common surgery performed in emergency services. The diagnosis is sometimes difficult for surgeons, because there are numerous conditions that mimic acute appendicitis. Acute appendicitis occurs in 7% to 12% of the general population, with the peak incidence in the 10 to 19 years of age.¹⁻⁵ Pathological examination of the appendectomy specimen mainly is performed to document the presence or absence of inflammation and confirm the clinical diagnosis. If the pathological diagnosis is negative for appendicitis, then clinical investigation for other potential causes should be carried out. The cases of negative appendectomy are associated with some risks and unnecessary costs to both patients and institutions and causes some dilemma in diagnosis.² In some of these negative appendectomy cases, the symptoms of the patient disappear post-operatively. Some authors suggested that there may be an early sub-clinical appendicitis in these cases.³

It has been shown that apparently normal appendices may show some clues of an inflammatory condition at histopathological evaluation.⁴ It is also reported

that normal appendices may have footprints of an inflammatory pathological reaction, which is only obvious at molecular level.³

In conventional macroscopical examination of the appendectomy specimen, one section is obtained from the base, body and the tip, and additional sections from exuding or perforated areas are also obtained. The aim of this study is to evaluate if the final histopathological diagnosis would change when the appendectomy specimen are totally sampled macroscopically. This is the first study which evaluates the correlation of histopathological diagnoses of the different macroscopical sampling methods.

Materials and Methods

A total of 87 patients who underwent the operation for appendicitis and had no other surgical pathological findings were included in this study. The patients were 51 males and 36 females with a mean age of 11.7 (1 years to 18 years). Appendectomy specimens were subjected to a routine protocol which consisted of immediate fixing in 10% buffered formaline solution before transport to the pathology laboratory.

Appendectomy specimens were macroscopically described, then according to the routine method were sectioned from the tip, body and the base and sampled in first two cassettes. For this routine macroscopical method, a 1-1.5 cm longitudinal slice from the tip along with a transverse section from the base were sampled in one cassette. Then the rest of the appendix was serially sectioned transversely at 3 mm intervals and slices from inflamed or perforated areas were sampled in a separate second cassette. Simultaneously, the rest of the appendiceal tissue slices, both transversely sectioned ones from the body and longitudinally sectioned one from the tip were totally sampled in additional 2 to 5 cassettes.

All the sections were examined by an expertised pathologist. Additional deeper sections from paraffin blocks were performed if there were artifacts related to microtomy, staining or mounting. The various stages of acute appendicitis were designated as acute focal, acute suppurative, gangrenous (phlegmonous), and perforative. The histopathological diagnosis of routine sampled sections and the diagnosis after total macroscopical sampling were noted and then compared.

Results

A total of 87 appendectomy cases were examined, of which 58.6 % were male, and the mean age was 11.7 (1 years-18 years). Clinical diagnosis were suspicious of acute appendicitis in all cases. Of the 87 patients, 85 (97.7%) had blunt right quadrant pain and 23 (26.4%) had fever. The mean (SD)

duration of symptoms was 34.3 (29.8) hours.

Macroscopical examination of the appendectomy specimens were normal or exhibited mild swelling with serosal erythematous and congested appearance in 25 (28.7%) of the cases. In rest of the cases varying degrees of serosal purulent exudate associated with erythema were evident. Mesoappendix and the base were also coated with a fibrinous or fibrinopurulent exudate in extensive inflamed cases. Partial or total obliteration of the lumen by pus and blood were evident. Nine (10.3%) cases showed a perforation focus and 14 (16%) showed fecalith, macroscopically. The perforation focus was characterized by dark coloured hemorrhagic area with irregular exudative surface and rupture. Macroscopically, focal necrosis of the appendiceal wall with mucosal sloughing was evident in 9 cases.

The histopathological diagnoses in all cases sampled by conventional method were as follows: 42 (48.3%) acute suppurative appendicitis (Figure 1), 15 (17.2%) acute perforated appendicitis, 5 (5.7%) acute gangrenous appendicitis (Figure 2), 6 (6.9%) acute perforated and gangrenous appendicitis, 4 (4.7%) focal acute appendicitis (Figure 3), and 15 (17.2%) reactive lymphoid hyperplasia. Two cases had infection with *enterobius vermicularis*. Associated histopathologic findings in appendicitis cases included vessels with thrombosis, vessels containing lymphocytes, lymphohistiocytic infiltration, varying degrees of fibrosis, and lymphoid follicles on the serosal surfaces.

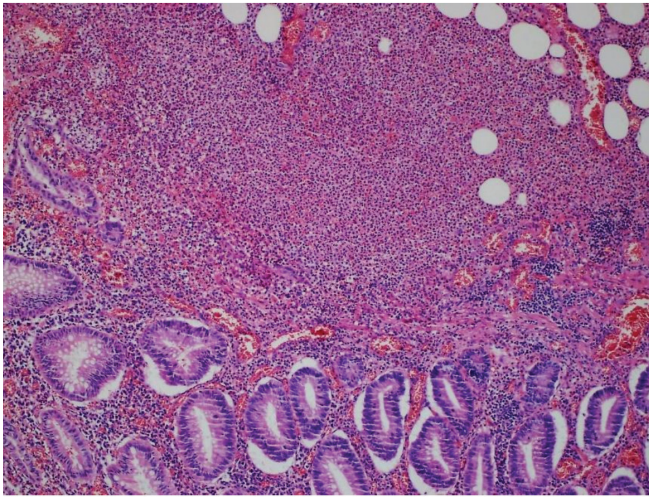


Figure 1: A case of acute suppurative appendicitis (H&E, X100).

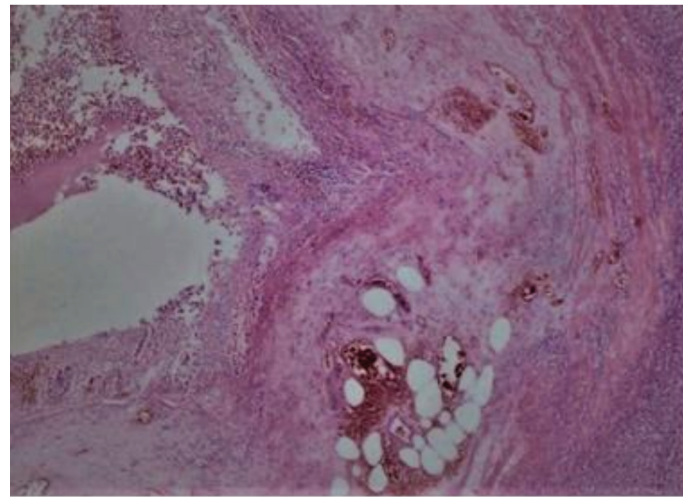


Figure 2: Acute gangrenous appendicitis (H&E, X40).

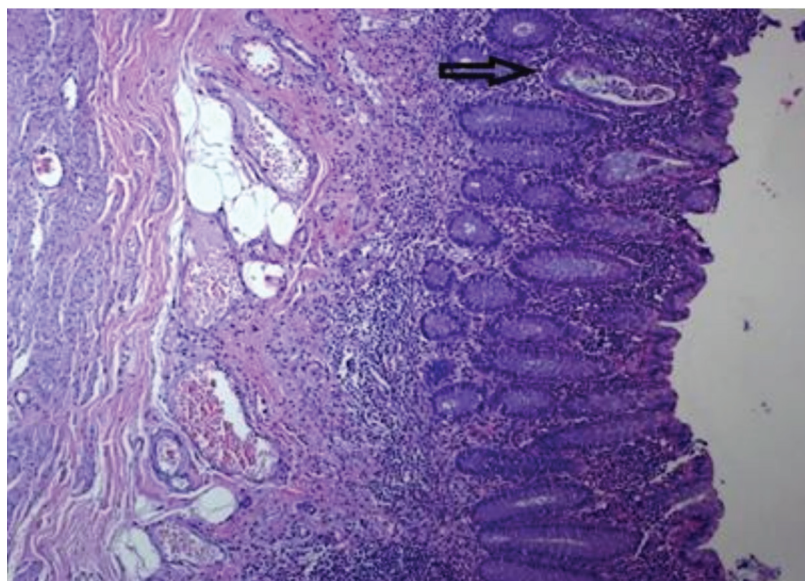


Figure 3: A case of acute focal appendicitis with small neutrophilic focus (black arrow) in the mucosa layer (H&E, X100).

After total macroscopical sampling, the initial diagnosis was changed in 14 (16%) cases. The initial diagnosis of reactive lymphoid hyperplasia changed

to acute focal appendicitis (early appendicitis) in 8 (9.2%) cases. In 4 (4.6%) cases the initial diagnosis of acute suppurative appendicitis changed to acute

suppurative and perforated appendicitis, and acute perforated appendicitis changed to acute perforated and gangrenous appendicitis in 2 (2.2%) cases.

Discussion

One of the most common surgical interventions and most frequent indications for acute abdominal surgery is acute appendicitis. The excision of the inflamed appendix reduces the risk of perforation, plastron formation, sepsis and also confirms the clinical diagnosis by histopathological examination. Nevertheless, this surgical procedure is considered somehow invasive, increasing the risks of morbidity and mortality to the patient, and also puts significant costs to the healthcare providers.¹

The most common etiology of acute appendicitis is obstruction of the appendiceal lumen. Some studies have revealed that the incidence of acute appendicitis correlates with lymphoid development and the peak incidence occurs between the ages of 10 and 30 years old. Lymphoid hyperplasia is the most common cause of luminal obstruction in patients under 20 years old, while fecalith plugs are the most common in the elderly.¹⁻⁵ Apart from fecal impactions and lymphoid hyperplasia, there are rare and unusual causes of appendiceal luminal obstruction; such as parasites, actinomycetes, radiocontrast agents, fruit pippins, endometriosis, tuberculosis, stromal and carcinoid tumors, lymphomas, adenomas, mucocoeles, dysplastic changes and carcinomas, eosinophilic granulomas and granulomatous diseases.^{6,7}

There are two purposes of histopathological examination of the appendectomy specimen.

First of all, the surgeon may be reassured of the diagnosis of acute appendicitis, especially when there has been no evidence of inflammation intra-operatively. Also it may show some other pathologies which may have not been visible intra-operatively, but may affect clinical management and follow up of the patient. The histopathologic diagnosis of “negative for acute appendicitis” allows elimination of acute appendicitis and then further investigations should be performed to explain the cause of the patient’s symptoms. Some of these patients would later be found to have non-surgical pathologies such as urinary tract infection, mesenteric lymphadenitis, and etc. Patients’ symptoms may disappear post-operatively in these negative appendicitis cases. Some authors suggest that these cases may have an early sub-clinical appendicitis.^{2,3,8,9}

Negative appendectomy is defined as absence of intramural neutrophils on histopathology¹. In a study which examined the outcomes of appendectomies from 30 pediatric hospitals, the negative appendectomy rates ranged from 0 to 17%.¹⁰ The incidence of negative appendectomies are consistently higher in females. The age range of a negative appendectomy was 15 to 27 years in females.¹ The high incidence of gynecologic disorders such as pelvic infections, ruptured ovarian cysts and ectopic pregnancies, may be the main reason of this, especially in the second and third decades of life.

In a study of Singhal et al, the number of negative appendectomies was much larger in female patients.¹¹ they reported that in 27 of 49 normal appearing appendices in females, the

histopathological findings consisted of serositis, luminal inflammation, and lymphoid hyperplasia. They suggested that another abdominal pathology may have been missed or the appendix may still have been the cause for symptoms. Oyetunji et al also mentioned that negative appendicitis rate was increased in children under 5 years and in females.¹²

The gold-standard for the definite diagnosis of appendicitis is a histopathological examination. The inflamed parts of the appendix may be histopathologically normal with molecular evidence of inflammatory changes. One study found this fact in up to 50% of histopathologically normal appendices in patients with clinical diagnosis of appendicitis³. This subgroup also contributed to the high rate of negative appendectomy.

Wang et al. provided new perspectives to the immunopathological events in histologically classified normal appendices in clinically diagnosed acute appendicitis patients. In these patients, they demonstrated tumor necrosis factor- α and interleukin 2 messenger RNA expression in germinal centers, submucosa, and lamina propria of the appendectomy specimen.¹³ Performing of early appendectomy as a successful treatment has resulted in a relatively high incidence of histologically classified normal appendices in patients who present with signs and symptoms of acute appendicitis. In these patients the incidence of histologically classified normal appendices reported between 11% to 54%. In most of these patients appendectomy relieves symptoms, so it is likely that an unidentified causative pathologic condition exists in the appendiceal tissue of these

patients.

In the present study, we had demonstrated that the rate of histologically negative appendectomies decrease by sampling the organ totally on macroscopical examination. The small neutrophilic focus in the mucosa layer may easily be missed when a partial macroscopical sampling is performed. Negative appendectomy rate of 17.2% in conventional macroscopical sampling decreased to 8% after total macroscopical sampling; and these cases had a diagnosis of acute focal appendicitis. In the further management of these patients there was no need for clinical work-up to exclude other etiologies such as diverticular disease, Meckel's diverticulitis, regional enteritis, and tubo-ovarian lesions in females.¹⁴

The treatment of complicated appendicitis is commonly performed by a prolonged antibiotic course, although there is no consensus on the exact duration of the treatment. For complicated appendicitis, antibiotic treatment is advised to reduce postoperative infections.¹⁵ In the present study, after total macroscopical sampling, in 4 (4.5%) cases of acute suppurative appendicitis the diagnosis was changed to acute suppurative and perforated appendicitis; and the clinicians had been warned of the complicated nature of the disease to do better management the patient.

Conclusion

In the present study, we compared the histopathological diagnosis of conventional macroscopically sampled and total macroscopically sampled appendectomy specimens. Our study has some limitations that need to be considered when

interpreting the findings. One of these limitations is the small number of the patients. Although the number of the patients in the present study is not quite sufficient, this is the first study which evaluates the correlation of histopathological diagnosis of the different macroscopical sampling methods. Total macroscopical evaluation of the appendectomy specimen in negative appendectomies would improve the histopathological diagnosis and can document early appendicitis cases. This will allow to avoid the expensive clinical and radiological searches to exclude other causes of abdominal surgical emergencies.

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Conflict of interest

There was no conflict of interest

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