

The Utility of Routine Histopathological Examination of the Appendectomy Specimens

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ABSTRACT

Background: Appendectomy is the most commonly performed surgical procedure worldwide to manage appendicitis. The practice of sending all the resected appendices for routine histopathology examination depends on the concerned clinician. This study was performed to reveal the importance of routine histopathology examination of the appendectomy specimens with recording of the occurrence and distribution of unusual pathologic findings

Methods: This was a retrospective record based comparative study performed in a single Hospital in Saudi Arabia, where the medical files of 766 patients were recruited. The appendectomy specimens were obtained either from our hospital or referred from any other hospital for histopathology examination. All the unusual diagnoses were reviewed by the histopathology author and blindly re-evaluated by other pathology consultant. Statistic analysis was performed manually.

Result: Seven hundred cases were seen within the usual histopathology scope. Unusual histopathological findings were observed in 66 cases (8.6%): four cases of mucinous neoplasms, 20 cases of fibrous obliteration or appendiceal neuroma, 18 cases showed parasitic infestation, and 24 cases were periappendicitis without appendicular acute inflammation.

Conclusion: Routine histopathology examination of the appendix not only confirms the clinical diagnosis of acute appendicitis, but also leads to the incidental diagnosis of much unusual pathologies which could have been missed by the surgeon, and these pathologies include parasitic infestation, peri-appendicitis, neuromas and appendiceal mucinous neoplasms.

Keywords: Appendicitis, Appendectomy, Histopathology.

Introduction

Appendicitis is the inflammation of the vermiform appendix, a small anatomical entity in the large intestine of amniotes. This inflammatory condition is usually bacterial. Increased total leukocyte count characterized by neutrophilia has been reported to be associated with the diagnosis of acute appendicitis¹. Intestinal parasitic diseases and neoplasms are the most common unusual histopathological findings observed in specimens after appendectomies due to any cause². Parasitic cause differs from country to country³.

Enterobius vermicularis (pinworms, oxyuris) is the parasitic infection that affects about 200 million people all over the world. At the end of the 19th century, it was first reported that the localization of *Enterobius vermicularis* on the appendicular lumen causes appendicitis⁴.

Schistosomiasis, also known also as Bilharziasis, is a rare cause of appendicitis that is usually seen only in endemic areas where the presence of fecal contamination and the snails in source of drinking water⁵. Those patients with parasitic infection should also take anthelmintic treatment,

as appendectomy treats only consequences but not the cause of the disease⁴.

Primary appendiceal neoplasms include lymphomas, mesenchymal tumors and epithelial tumors⁶. Primary epithelial tumors of appendix are classified as neuroendocrine tumors, mucinous tumors, and mixed endocrine and glandular tumors⁷.

Treatment of the mucinous tumors is based on histology and stage. Low-grade neoplasms are treated surgically in early stage disease with resection of the primary site, or peritoneal debulking and hyperthermic intraperitoneal chemotherapy (HIPEC) in patients with advanced disease stage⁸.

Appendectomy is the most commonly performed surgical procedure worldwide to manage appendicitis⁴. The practice of sending all appendices specimens for routine histopathology examination depends on the concerned clinician and is variable⁹. Some authors are against this policy and suggest that appendices should be sent for examination only if there is an obvious macroscopic

abnormality at surgery ^{10, 11}. They justify their opinion by the rarity of aberrant findings, together with the significant costs of specimen processing. Others said that histopathology examination of the appendix is necessary to confirm the diagnosis of acute appendicitis and to reveal additional findings that might not be evident clinically and intra-operatively but may change the course of further management of the patient ^{12, 13}. So this stratifies the benefit of histological examination of the appendix and is likely to help in the treatment of the underlying pathology. This study is performed to reveal the importance of routine histopathology examination of the appendectomy specimens with recording of the occurrence and distribution of unusual pathologic findings with spot lighting on the clinical benefits of detecting such lesion.

Materials and Methods

This was a retrospective record based comparative study performed in Prince Mishari bin Saud Hospital in Saudi Arabia, in patients whom were diagnosed clinically with acute appendicitis and underwent appendectomy between Jun 2018 and Jan 2020. The medical files of 766 patients were recruited in this study.

The patients’ gender, age, White Blood Cells (WBCs) count, and histopathology diagnosis were recorded. The appendectomy specimens were obtained either from our hospital or referred from any other hospital for histopathology examination, in either occasion cases were reported in our histopathology department. Appendectomy specimens that showed any clinical suspicion other than acute appendicitis were excluded. All the unusual diagnoses were reviewed by the histopathology author and blindly re-evaluated by other pathology consultant. The reporting and classification of the neoplastic lesions was based on the classification and staging of the modified Delphi consensus

process, Peritoneal Surface Oncology Group International (PSOGI) and the AJCC 8th edition.

The ethical approval was agreed by the local ethics committee. Statistical analysis of data was performed manually.

Result

In total, 766 appendectomy specimens were received in our histopathology department during 18 months with a clinical diagnosis written on the request form as acute appendicitis. Of these, there were 444 (58%) males and 322 (42%) were females with male: female ratio of 1.38: 1. The youngest patient was 4 years old and the oldest was 59 years old with mean age 17.9. Most commonly affected age group is the age between 11 years and 20 years (47.8%). Approximately half of the cases showed WBCs count less than 11,000/ul and half of them showed more than 11,000/ul.

Different histopathology diagnoses are presented in percents in a pie chart in (figure1).

Unusual histopathological findings were observed in 66 cases (8.6%) as follows; 4 cases of mucinous neoplasms (all of them are Low-grade appendiceal mucinous neoplasm (LAMN), 3 out of 4 are stage Tis and 1 out of 4 is T3 as the tumor reaches the mesoappendix) (figure2) , 20 cases showed fibrous obliteration or appendiceal neuroma (figure3), 18 cases showed parasitic infestation (17 patients of Enterobius vermicularis and one patient of Bilharziasis disease showing Bilharzial ova and granulomatous reaction within the wall and the surrounding fat) (figure4 a&b) and lastly 24 cases of periappendicitis (all of them are females) without appendicular acute inflammation (figure5).

All the studied clinicopathologic characteristics are shown in Table (1).

Table 1: Clinicopathologic characteristics of the patients in the study.

Patient characteristics	Result
All patients	766 (100%)
Age in years	
Overall (ranged 4-59 years old with mean age = 17.9)	766
0-10	108 (14.1%)
11-20	366 (47.8%)
21-30	181 (23.6%)
31-40	78 (10.2%)
41-50	12 (1.6%)
50-59	21 (2.7%)
Sex	
Male	444 (58%)
Female	322(42%)
WBCs count	
Overall (ranged 3.65-18.8 with mean WBCs count= 10.42)	766

Patient characteristics	Result
<11,000/ul	375 (49%)
>11,000/ul	391 (51%)
Usual Histopathology findings	
Overall	700 (91.4%)
Normal or catarrhal inflammation	82 (10.7%)
Acute appendicitis without complications	570 (74.4%)
Acute appendicitis with complications (gangrene, perforation, abscess formation)	48 (6.3)
Unusual Histopathology findings	
Overall	66 (8.6%)
Periappendicitis	24 (3.13%)
Parasitic appendicitis	18 (2.34%)
Neuroma or Fibrous obliteration	20 (2.61%)
Mucinous neoplasm	4 (0.52%)

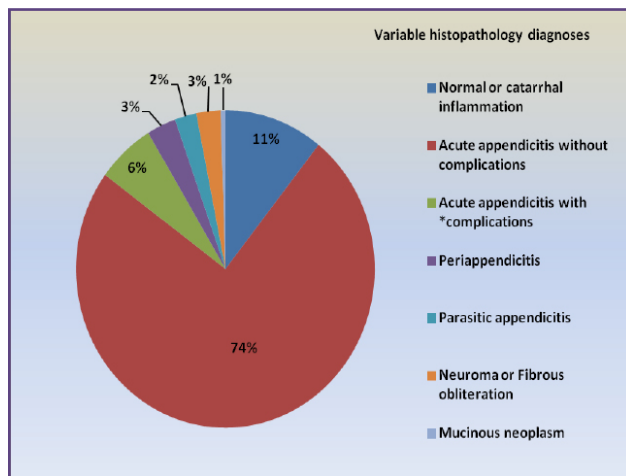


Fig. 1: A pie chart of the histopathology findings in percents. * (Complication) here is designated for gangrene, perforation, or abscess formation.

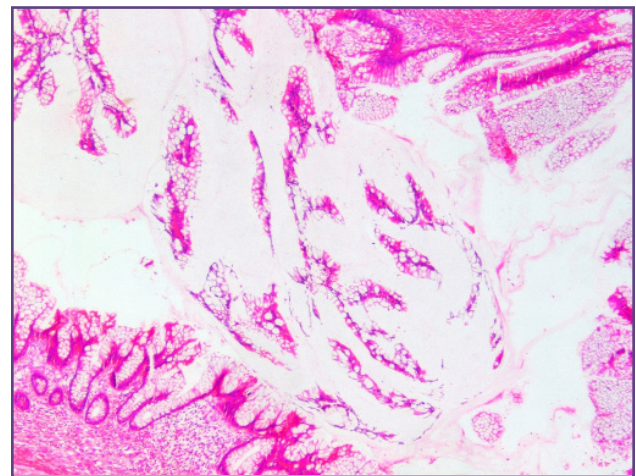


Fig. 2: Low Grade Appendiceal Mucinous Neoplasm showing mucin extravasation (H and E, ×4).

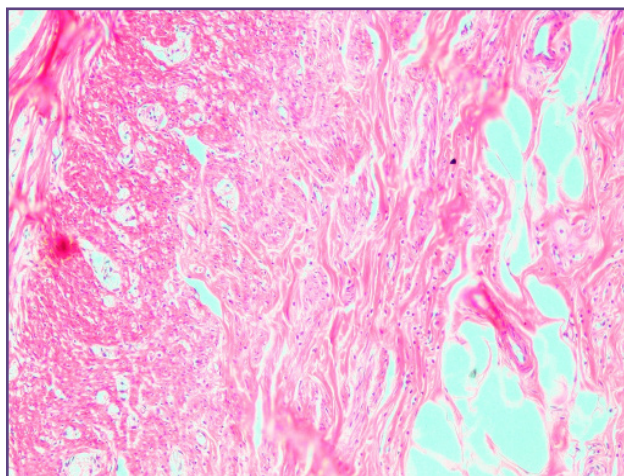


Fig. 3: Replacement of the lumen by spindle cells in fibromyxoid background with adipose tissue (H and E, ×10).

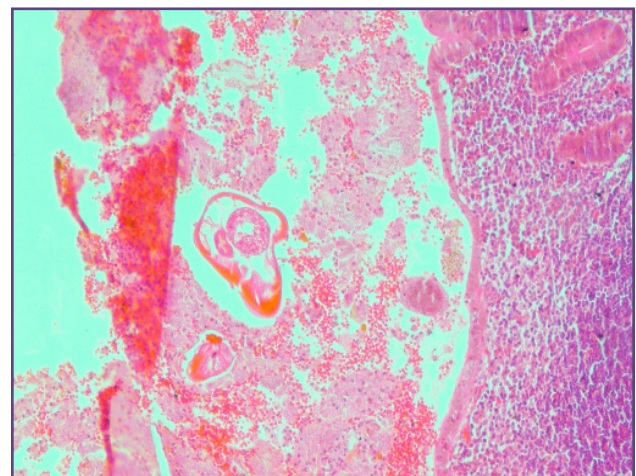


Fig. 4a: Parasitic infection; Enterobius vermicularis in the lumen of appendix (H and E, ×10).

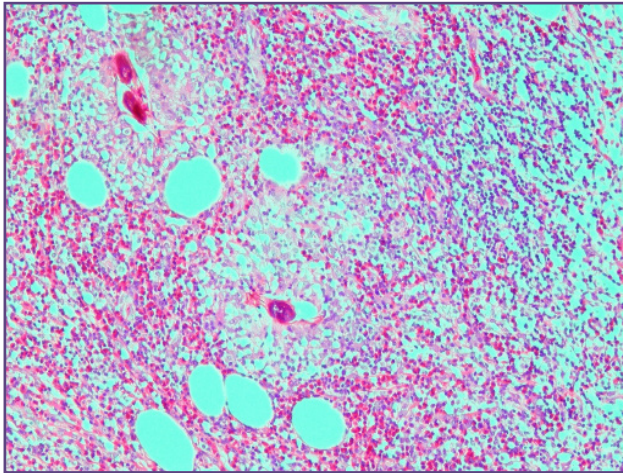


Fig. 4b: Parasitic infection; Bilharzial ova with surrounding granuloma and eosinophilic Infiltration within the appendiceal wall ((H and E, ×10).

Discussion

We found that the age incidence of appendectomies was higher in 10-20 years age group (47.8%). This result is different from a study done on 325 cases in India in 2016 showed higher incidence in 20-30 years age¹⁰. A higher incidence in 20-30 years age group was also seen in a study done in Turkey by Yilmaz *et al* in 2013¹⁴, however another study done also in Turkey in 2013 by Emre *et al* revealed 24.5% of all appendectomies are between 17-20 years old¹⁵. Matariswa study (2019) showed higher incidence of appendicitis between 31 to 40 years¹⁶.

In our study, the male patients undergoing appendectomy are more than females (58% males and 42% females). Similar findings were shown in studies done by Dincel *et al* of 2018⁴, Rabindranath *et al* of (2016)¹⁰, Rehman *et al* of 2017¹², Sharma *et al* of (2014)¹³, Yilmaz *et al* of (2013)¹⁴, and Chawda, Misikin, and Dombale of (2015)¹⁷. In contrast, there are two studies showed slightly female predominance, those are Shreshtha *et al* in 2012¹⁸ and Elfaedy *et al* in 2019 that recorded female to male ratio of 1.1:1¹⁹.

This current study declared that 51% of all cases count were more than 11,000/ul WBCs. Rehman *et al* in 2017 showed 86.7% of the appendectomies are more than 11,000/ul¹².

All the examined appendectomy specimens in our study were clinically diagnosed as acute appendicitis and sent to our lab for routine histopathological examination. Out of the 766 cases, 66 cases (8.6%) showed unusual findings. This is in concordance with the results of Yilmaaz *et al* study in 2013 that showed 134 out of 1621 cases (8.3%) had unusual histopathological features and slightly more than the percentages revealed by the 2013 Emre *et al*

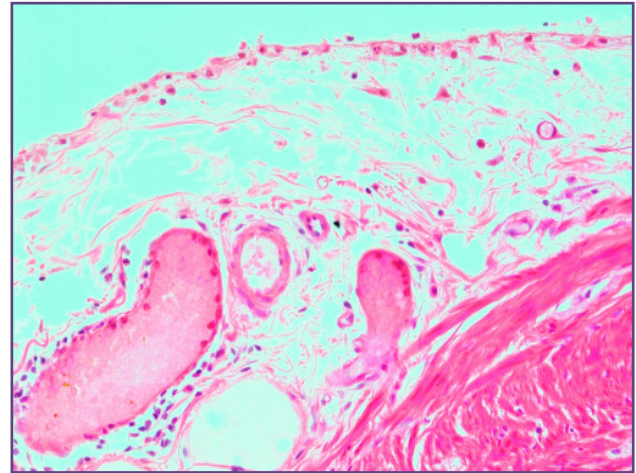


Fig. 5: Periappendicular neutrophilic infiltration ((H and E, ×20).

study (7%), and Chawda, Misikin, and Dombale study (6.7%)¹⁷. Some studies showed lesser percentages of unexpected findings (0.1–4.2%), other than normal or inflammatory appendix²⁰. Patel and Shah in 2017 recorded 5% unusual findings⁹ and Dincel *et al* in 2018 reported 3% unusual findings in the routinely examined appendectomy specimens⁴. Elfaedy *et al* (in 2019)¹⁹ recorded 256 out of 4012 (6.2%) unusual findings but they counted the chronic appendicitis finding as an unusual, in our study we did not find any case of chronic appendicitis.

We found that 24 out of 766 cases (3.13%) were diagnosed as periappendicitis, all of them are females, and this is to be compared with Rehman *et al* 2017 study that showed 56/316 cases (17.7%) were cases of periappendicitis¹². Peri-appendicitis is defined as a serosal inflammation of appendix without mural or mucosal involvement²¹. Peri-appendicitis is a condition that could clinically mimics the typical presentation of appendicitis with lower right quadrant pain, fever and leukocytosis. It is primarily caused by intra-abdominal pathology; the most common etiology is acute salpingitis²². We detected two cases out of the 24 cases showing pictures of infected ovarian cysts and underwent surgical cystectomy, other two cases showed salpingitis and received medical treatment, and the rest of cases could not be reached to know the follow-up results

In our study, we found that parasitic infection represents 2.3% of all appendectomies (2.15% are *E. vermicularis* and 0.15% Bilharzial infestation which highly mimics the results concluded in USA by Arca *et al*²³ and in Iran by Ramezani and Dehghani²⁴, who had reported *E. vermicularis* in 2.9% of surgically removed appendices. In Turkey, two studies recorded presence of *E. vermicularis*

in 3.8% of appendectomy specimens from a Turkish population^{25, 26}. A study from Denmark reported 4% incidence of appendiceal Entrobiasis²⁷. A study in Cairo of Egypt done by Helmy *et al*²⁸ reported that parasites were seen in 14.8% of surgically removed appendices; with approximately similar results from studies done by Jada *et al* in India that showed a (12%) prevalence of parasites in appendectomy specimens²⁹; this high incidence of parasitic infestation may be attributed to the high prevalence of these parasites in the community. Lower incidence was recorded in Nepal, where *E. vermicularis* was identified in only 1.62% of surgically removed appendices of Nepalese patients³⁰.

Fibrous obliteration also known as appendiceal neuroma or neurogenous hyperplasia whereas neurogenic proliferation is identified in most of the specimens¹⁷. Therefore, various definitions including neurogenic appendicopathy and appendiceal neuroma have recently been used⁴. 20 out of 766 cases (2.61%) in this study were diagnosed as Neuroma or Fibrous obliteration, however in 2013 Emre *et al* reported that ~30% of all resected appendix specimens showed fibrous obliteration. But in 2018 Dincel *et al*⁴ reported that ~1% of the resected appendix specimens showed fibrous obliteration and neuroma. Neuroma of the appendix is a rare disease of neural origin that usually mimics the symptoms of the acute appendicitis³¹, patient's physical examination and laboratory findings can help in the differential diagnosis, but most of these cases only become evident when the histopathology examination is available³².

Histopathology examination is the key as most patients are usually detected as an incidental finding³³. Regardless, the molecular mechanism underlying this pathologic process remains unknown. It is believed to occur secondary to hyperplasia of the neuroendocrine cells, because appendicular lumen replacement by and chronic inflammatory cells and fibrous tissue is generally accompanied by increased proliferation of neuroendocrine cells and nerve cells¹⁷. The importance of detecting appendiceal neuromas is that it can be a potential precursor to malignant neoplasms since the enteroendocrine cells within the nerve bundles may be hypertrophied and can be the origin of carcinoid. Complete excision of the appendix (appendectomy) is the treatment of choice³³.

Appendiceal neoplasms are identified in 0.9 to 1.4% of appendiceal specimens, and the incidence is increasing, the neuroendocrine tumors (carcinoids) have long been professed as the most common neoplastic lesion of the appendix; recent data, however, has suggested a shift in epidemiology³⁴.

In 2016 Carr *et al* announced that a new classification of appendiceal mucinous neoplasia is developed, and it is agreed that "mucinous adenocarcinoma" term should be reserved only for lesions with infiltrative invasion. The term "low-grade appendiceal mucinous neoplasm" is supported (It is agreed that "cystadenoma" term should no longer be recommended). The term "high-grade appendiceal mucinous neoplasm" is proposed for lesions with high-grade cytological atypia but without infiltrative invasion³⁵.

Although a dilated, mucus-filled appendix is often called mucocele, this term is ambiguous and better to describe the imaging appearance rather than the pathologic feature³⁶.

In our study we considered the cases with "mucocele" in clinical data as a non-routine pathology examination so we excluded those cases from our study. All the studied four cases came with clinical suspicion of acute appendicitis, two male patients and two females one of them was a pregnant woman, all of them are between 30-39 years old. After histological examination; all of them revealed features of acute inflammation along with Low-grade appendiceal mucinous neoplasm (LAMN).

As our four cases showed histological features of acute inflammation, the clinical symptoms of all those neoplastic cases were right lower abdominal pain, tenderness and vomiting and three of them showed high WBCs count (>11,000/ul). In 2018, Gündoğar *et al* studied 19 cases of appendiceal mucinous neoplasms revealing that the most common clinical symptoms were right lower abdominal pain (27%), abdominal mass (16%), weight loss (10%), and bowel habits change in (5%), and (61%) of their cases presented with lower abdominal pain, whereas the rest were detected incidentally. The mean age of these 19 cases was 60±15 (30–84) years³⁷.

A major limitation of this study is the unavailability of patient's follow-up information especially patients with unexpected findings. Unusual findings were discovered in more than 8% of the appendectomy specimens at Histopathology examination which were not suspected in clinical assessment before surgery, intra-operatively or even on macroscopic examination but had an impact on the patient outcome. This study supports the strategy of sending all appendectomy specimens for routine histopathological examination and meticulous microscopic examination of all of those.

Conclusion

This was a retrospective record based comparative study performed in prince Mishari bin Saud Hospital in Saud Arabia, in patients whom were diagnosed clinically with acute appendicitis and underwent appendectomy between

Jun 2018 and Jan 2020. The study concluded that routine histopathology examination of the appendix not only confirms the clinical diagnosis of acute appendicitis, but also leads to the incidental diagnosis of much unusual pathologies which could have been missed by the surgeon, and these pathologies include parasitic infestation, peri-appendicitis, neuromas and low grade appendiceal mucinous neoplasms. The diagnosis of the above mentioned pathologies is imperative for further patient management.

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Competing Interests

Authors have no competing interests to declare.

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