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Article Review

**Incidental histopathological finding in appendectomy
biopsies**

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بِسْمِ اللّٰهِ الرَّحْمٰنِ الرَّحِیْمِ

(إِنَّمَا يَخْشَى اللَّهَ مِنْ عِبَادِهِ الْعُلَمَاءُ إِنَّ اللَّهَ عَزِيزٌ غَفُورٌ)

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أبي المحترم

إلى نبع المحبة والإيثار والكرم

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إلى جميع الشهداء رحمهم الله

إلى جميع من تلقّيت منهم النصح والدعم من الأقارب والأصدقاء

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الحمد لله الذي هدانا وأعدنا وأمدنا والهمنا الصبر على المشاق ووفقتنا لما نحن عليه

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وفقها الله فقد كانت سندا لنا على طول الطريق

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Abstract

Introduction: Acute appendicitis is the most common indication for appendectomy; it is an inflammatory condition that is caused by the spread of an inflammatory process in the mucosal layer of the appendix vermiformis toward the serosa. Diseases and tumors of the appendix vermiformis are very rare, except for acute appendicitis. Other rare unusual finding that have been histopathologically may detect in appendectomy specimens are as follows; fibrous obliteration , parasitic infestations, endometriosis, Lymphoid hyperplasia, benign tumors (mucinous cystadenoma), and malignant tumors (neuroendocrine tumor, adenocarcinoid tumor, mucinous neoplasm).

Review: Most common incidental finding that associated with acute appendicitis were (carcinoid tumor , mucinous cystadenoma, fibrous obliteration, endometriosis).The aim of the current article review to find how important histopathology study and determine the incidental finding, specific the most common incidental pathology of appendix.

Aim: The aim of this review article is to determine the most common incidental finding in histopathological examination of appendix and their relationship to disease processe or the outcome of disease.

Conclusion: Histopathological examination of appendix is essential regardless the gross feature or the absence of symptoms. The most common incidental finding in routine histopathological examination of appendix is: most tumor { Carcinoid tumor,Neuroendocrine tumor,mucinous neoplasm ,mucinous cystadenoma,Adenocarcinoma}, Fibrous obliteration, Lymphoid hyperplasia, Endometriosis,Enterobius vermicularis, Acute appendicitis, Chronic appendicitis,Catarrhal appendicitis. Incidental finding range from benign lesions to frankly malignant lesion, in which another line of therapy must take place.

Introduction

The appendix is a blind muscular tube, at birth, the appendix is short and broad at its junction with the caecum, but differential growth of the caecum produces the typical tubular structure by about the age of 2 years (1). The histologically composed of four layers (Mucosa: Mucosal membrane, lining the inside of the tube), (Submucosa: Connective tissue layer), (Muscularis externa: Tubular wall of a bilayer of smooth muscle, interspersed with loose connective tissue and blood vessels), (Serosa: Outer serosal coat, lined with mesothelial cells) (2).

Appendectomy terminologically divided into four groups according to the timing of appearance and indication of surgery: emergency (stander) appendectomy, elective (interval) appendectomy, prophylactic appendectomy, incidental appedndectomy. Incidental appendectomy is defined as the resection of the appendix vermiformis due to various reasons that might occur during abdominopelvic surgery (3).

The most common reason for appendectomy is acute appendicitis, which is an inflammatory disease exacerbated by an inflammatory mechanism spreading from the mucosal layer of the appendix vermiformis to the serosa. The major initiator of this inflammatory mechanism is luminal obstruction, which may occur for a variety of causes. The most common etiopathogenic cause for luminal obstruction in children is lymphoid hyperplasia, and in adults it is fecalith(4). Surgeons and pathologists first recognised lymphoid hyperplasia of the appendix as a pathological entity in the early twentieth century. It was believed to play a part in the pathogenesis of acute appendicitis by obstructing the appendix. As a result, lymphoid hyperplasia tends to be a physiologic reaction to inflammation rather than the primary cause of appendicitis. The most frequent cases of lymphoid hyperplasia of the appendix are in children, and it's usually linked to inflammatory disorders like viral gastroenteritis and mesenteric adenitis(5).

Chronic appendicitis does not display the classic signs of acute appendicitis, and therefore, its diagnosis should be established with histopathological examination. Chronic appendicitis should also be considered in the differential diagnosis of patients with recurrent or chronic right lower quadrant pain. CT is the best test for its diagnosis, and appendectomy can be an effective treatment for these patients. In our

current study, of the three patients reported as having chronic appendicitis, two had a history of recurrent abdominal pain and one had chronic abdominal pain(6).

In addition to these, there are a number of rare findings that can be detected histopathologically in appendectomy specimens: Endometriosis, fibrous obliteration, parasitic infestations, lymphoid hyperplasia, endometriosis, benign tumors (mucinous cystadenoma), and malignant tumors (neuroendocrine tumor, adenocarcinoid tumor, mucinous neoplasm) (2).

Carcinoid tumor is the most common type of malignant tumor of the appendix. the preoperative diagnosis of carcinoids is quite rare, as they are usually detected incidentally after an appendectomy. The most carcinoid tumors are benign and <1 cm localized at the tip of the appendix, metastasis is rare (7,8).

The incidence of primary appendix lymphoma is estimated to be between 0.015 and 0.022 % of all appendix specimens. Appendix lymphoma is usually seen in those in their twenties and thirties. It clinically behaves like acute appendicitis and is often diagnosed via histopathological examination following surgery. The most common histopathological type is B cell lymphoma (7).

Neuroendocrine tumors account for 50–77 % of all appendiceal neoplasms and for 19 % of all gastrointestinal neuroendocrine tumors. The mean age at presentation of appendiceal NET is 32–43 years. Appendiceal NET are firm, grayish-white, and fairly well circumscribed. The majority of NET are located at the tip of the appendix. The tumors are smaller than 1 cm in the most cases. The calculated risk of metastasis from tumors 1 cm or smaller is nearly zero and therefore may be managed with a simple appendectomy. An increase in metastasis risk of up to 85 % occurs with a tumor of 2 cm or larger (9).

Endometriosis commonly involves the pelvic organs such as the ovaries, the uterosacral ligament, and the rectovaginal septum although endometriosis can also occur in the gastrointestinal tract, the ureter, the pleura, and the lungs (10). Endometriosis of the gastrointestinal tract occurs in about 5% of women with endometriosis, and appendiceal

involvement is seen in approximately 1% of women (11). Women with appendiceal endometriosis may present with acute or chronic symptoms such as lower abdominal pain, chronic pelvic pain, acute appendicitis, hemorrhage and intestinal perforation (10).

Enterobius vermicularis is a parasitic infection that affects nearly 200 million people worldwide. At the end of the nineteenth century, it was first shown that the localization of *E. vermicularis* on the appendiceal lumen causes appendicitis. Previous studies have shown that the incidence of *Enterobius vermicularis* is between 0.6 and 3.8 % in surgical specimens of patients suspected to have appendicitis (12).

Distribution of the 59 cases identified as having unusual findings according to etiological causes show in the article incidental findings in routine histopathological examination of appendectomy specimens (Table 1) (13).

Table 1

Total patient	n= 59
Carcinoid tumor	8
Mucinous cystadenoma	9
Lymphoma	1
Hyperplastic polyps	2
Granulomatous appendicitis	2
Chronic appendicitis	3
Appendiceal neuroma	3
Fibrous obliteration	16
Schistosomiasis	2
<i>Enterobius vermicularis</i>	11
Endometriosis	1
Crohn's disease	1

The aim of this review article is to identify the most common incidental findings in appendix histopathology and their contribution to disease process or outcome.

Review

1- Tumor of appendix

Carcinoid tumor: The carcinoid was 8 (13.5 %) for 1970 patients who underwent Histopathological Examination of Appendectomy Specimens, according to a review article by Ouzhan Dincel & Mustafa Göksu...etal. (13).

Another article by He Jong WIE, Jung Hun LEE, Min Sun KYUNG..etal, Carcinoid tumor 3 (2.8 %) was found in 106 women who underwent laparoscopic surgical treatment for ovarian endometrioma without a history of appendectomy, according to et al. (14).

In the article by Ouzhan Dincel..etal, there were (8=n) of carcinoid tumors since there were a significant number of patients with histopathology examinations, while in the article by He Jong WIE..etal, only 106 patients were examined, so the result was (n=3) of carcinoid tumors.

Neuroendocrine tumor: The neuroendocrine tumor was n=1 (0.6 percent) from 170 under incidental appendectomy for living liver donor, according to an article by Sami Akbulut, Cemalettin Koç, et al. (15).

In the report by Dario Tartaglia, Andrea Bertolucci, Christian Galatioto, Matteo Palmeri....et al., the outcome was neuroendocrine tumor 3(2%) in 1388 patients who had laparoscopic appendectomy for acute RLQA pain. (16).

Since these tumors are rarely associated with clinical symptoms and are often recognized during pathological evaluation of appendices resected mostly for acute RLQA pain, so it is reported further in the article Dario Tartaglia, Andrea Bertolucci...etal for accidental appendectomy patients presenting acute RLQA pain compared to first article.

Another article of Faten Limaiem & Nafaa Arfa& ... etal, the record of neuroendocrine tumor was neuroendocrine tumors (n = 8) from 1627 patient underwent Histopathological findings in appendectomy specimens {figure1} (17). The majority of patients in this sample have acute appendicitis, and all patients with malignant tumors were clinically

diagnosed with acute appendicitis, resulting in this percent of tumor relative to the previous paper.

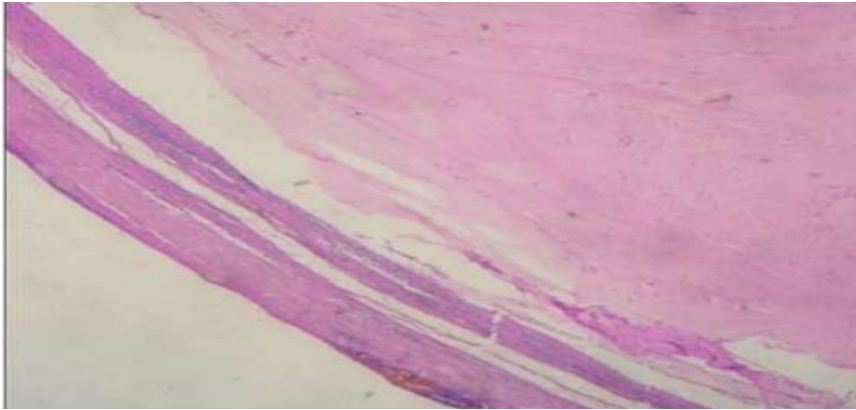


Figure 1 Neuroendocrine tumor of the appendix grade(hematoxylin and eosin, magnification ×200)

mucinous neoplasm (low-grade) : In review of article of Sami Akbulut, Cemalettin Koç, ...etal, the mucinous neoplasm was n=2(1.2%) from 170 under incidental appendectomy for living liver donor **{figure2} (15)**.

The mucinous neoplasms was (n = 12) from 1627 patients in Faten Limaiem & Nafaa Arfa&...research. etal **(17)**.

In the article by Faten Limaiem & Nafaa Arfa...etal, almost every patient with histological examination of the surgical specimen showed acute appendix inflammation as a retaliation to appendix tumor, so this report shows an increase in the incidence of mucinous neoplasm compared to the first paper.

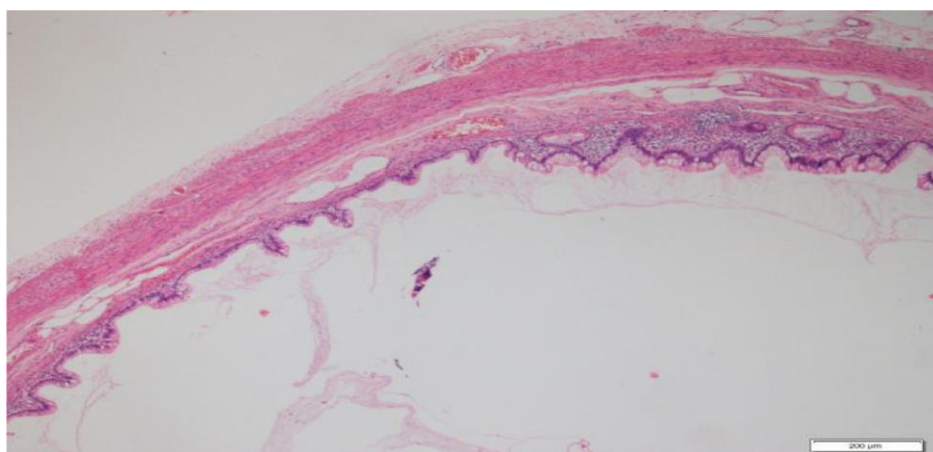


Figure 2 Low-grade mucinous neoplasia in the appendix vermiformis (H&E 40×).

mucinous cystadenoma: the mucinous cystadenoma n=1(0.6%) from 170 under incidental appendectomy for living liver donor in article of Sami Akbulut, Cemalettin Koç, ...etal, (15).

Second record in the article of Oğuzhan Dincel & Mustafa Göksu ...etal, the mucinous cystadeboma was 9(15.2%)for 1970 patient underwent Histopathological Examination of Appendectomy Specimens (13).

In the article by Ouzhan Dincel & Mustafa Göksu...etal, there were 1970 patients who underwent histopathology examination, while in the article by Sami Akbulut, there were only 170 patients, that explained high incidence by Ouzhan Dincel compared to article of Sami Akbulut

Adenocarcinoma: Adenocarcinoma was found (n = 2) in 1627 patients in a report by Faten Limaiem & Nafaa Arfa&...etal {figure 3} (17).

In this study, there is a greater connection between acute appendicitis and adenocarcinoma, and more people participated in the histopathology study, demonstrating that this finding is compared to that of other studies.

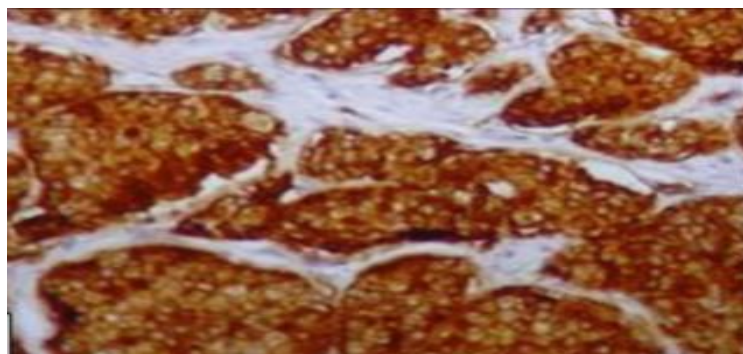


Figure 1 Primary appendiceal adenocarcinoma (hematoxylin and eosin, magnification ×100)

2-Fibrous obliteration: the fibrous obliteration was n=13 (7.6%) from 170 under incidental appendectomy for living liver donor {figure4}. (15).

The fibrous obliteration rate was 1 (0.9 percent) in 106 women who received laparoscopic surgical care for ovarian endometrioma with no history of appendectomy, according to the second article by He Jong WIE, Jung Hun LEE, etal. (14).

Almost the patient with appendicitis in study of Sami Akbulut..etal, that related to developed fibrous obliteration, to explain high incidental record compared to study of He Jong WIE..etal.

Another study by Ouzhan Dincel & Mustafa Göksu,...etal found that the fibrous obliteration rate was 16 (27%) for 1970 patients who had their appendectomy specimens histopathologically examined (13).

This percent of fibrous obliteration was generated by having a larger number of patients in the sample than in the previous article.

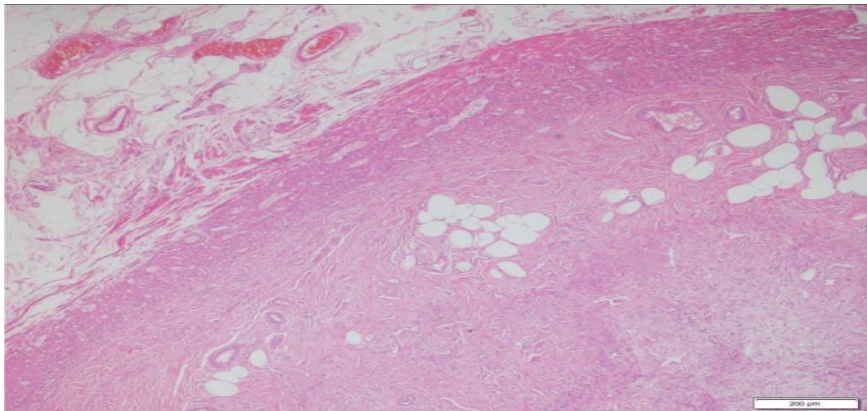


Figure 2 Fibrous obliteration of appendix vermiformis (H&E 40×).

3-Lymphoid hyperplasia: Lymphoid hyperplasia was observed in 4 (2.4 percent) of 170 individuals who had an accidental appendectomy with a living liver donor, according to Sami Akbulut, etal (15).

According to a report by He Jong WIE, Jung Hun LEE, Min Sun KYUNG, et al., lymphoid hyperplasia was found in 12(11.3 %) of 106 women who underwent laparoscopic surgery for ovarian endometrioma with no prior appendectomy (14).

In the report by He Jong WIE, Jung Hun LEE...etal, a woman with ovarian endometrioma was shown to have acquired lymphoid hyperplasia with a percent 12 (11.3%) higher than in the previous research.

4-Endometriosis: Endometriosis was 1(1.7 %) for 1970 patients who underwent histopathological analysis of appendectomy specimens, according to an article by Ouzhan Dincel & Mustafa Göksu..etal {figure5} (13).

In another study by He Jong WIE, Jung Hun LEE, Min Sun KYUNG, et al., 14 (13.2 %) of 106 women with ovarian endometrioma underwent laparoscopic surgical procedure for ovarian endometrioma with no history of appendectomy had endometriosis. (14).

Endometriosis is the most prevalent form of endometriosis in women of reproductive age. A high prevalence of histopathologically confirmed appendiceal endometriosis in women with endometriosis and CPP has been identified in several study of Berker... etal(18) and Harper and Soules(19), so high frequency incidence of appendiceal endometriosis in study of He Jong WIE, Jung Hun LEE..etal compared to study of Oğuzhan Dincel & Mustafa Göksu..etal.

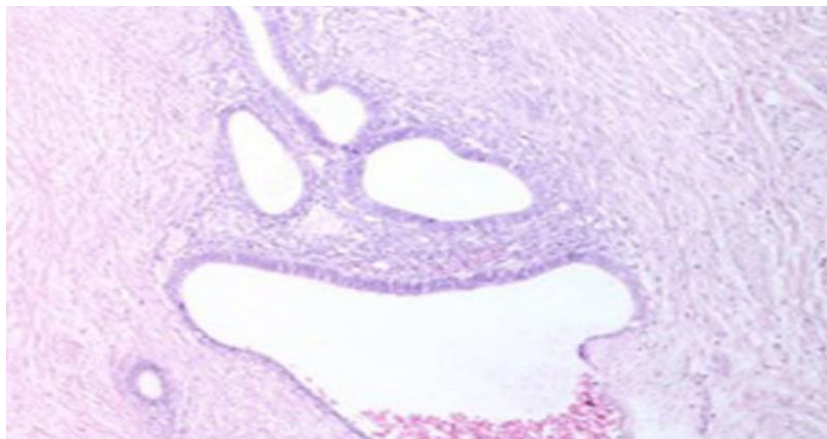


Figure 3 Endometriosis, endometrial stroma in the appendix wall, glandular structures with blood components (HE×100)

In a research by Faten Limaiem, Nafaa Arfa, and Lobna Marsaoui, et al., the outcome was endometriosis (n=1) in 1627 patients who had their appendectomy specimens histopathologically examined.s (17).

And in the study of Francesco Coratti, Silvia Vannuccini...etal, the incidence of endometriosis was 5 (14.7%) from (n=34) histology findings in group A of fertile age women (18–45 years) undergoing emergency surgery for acute RIF pain (20).

The study of endometriosis patients with right lower quadrant pain by Berker etal, reported higher incidence in appendiceal endometriosis (18). So, in the analysis by Francesco Coratti et al., A survey of all women of reproductive age (18–45 years) who underwent emergency surgery for

acute RIF pain found a high prevalence of 5 (14.7 percent) compared to Faten Limaiem..etal.

5-Enterobius vermicularis: In an article by Ouzhan Dincel & Mustafa Göksu...etal, the prevalence of enterobius vermicularis was found to be 11(18%) in 1970 patients who had their appendectomy specimens histopathologically examined (13).

In the second article by Sami Akbulut, corresponding author Cemalettin Koc...etal, enterobius vermicularis was found in n=4 (2.4%) of 170 people who had an accidental appendectomy for a living liver donor {figure 6} (15).

In the Ouzhan Dincel study, there were more patients than in the Cemalettin Koc study, so was incidence of enterobius vermicularis was higher.

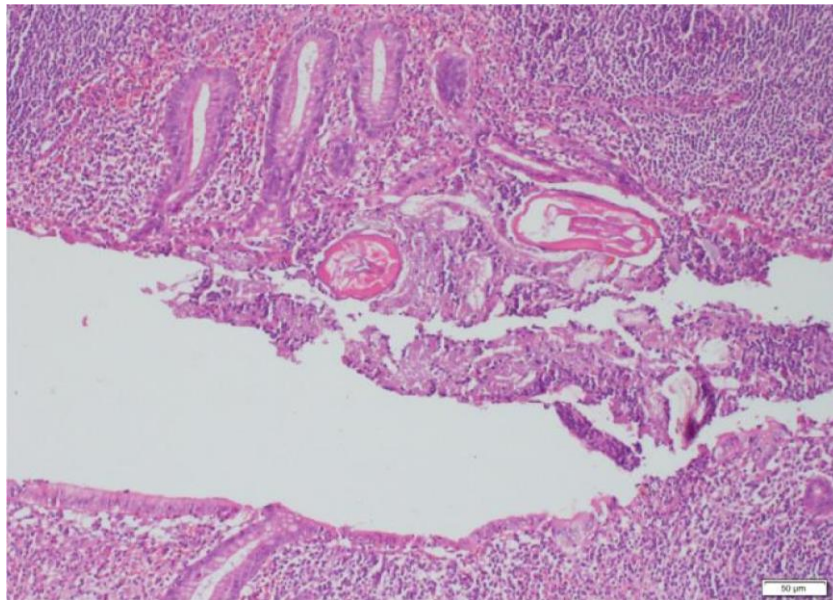


Figure 4 Enterobius vermicularis in the appendix vermiformis (H&E 100x).

Enterobius vermicularis (n=23) from 1627 patients experienced histopathological observations in appendectomy specimens in Faten Limaiem & Nafaa Arfa..research. etal (17).

Appendectomy was performed on all of the patients in this study (either open or laparoscopic). Laparoscopic appendectomy carries the danger of worm contamination of the peritoneal cavity, and surgeons should be aware of this possibility, especially when extracting a macroscopically non-inflamed appendix, and take the appropriate measures to avoid

peritoneal contamination (21). This may be due to the high prevalence of *Enterobius vermicularis* in this article.

6-Acute appendicitis: Acute appendicitis was seen in 1 (0.9 percent) of 106 women who received laparoscopic surgical care for ovarian endometrioma without a history of appendectomy, according to an article by He Jong WIE, Jung Hun LEE...etal (14).

In a second study by Sami Akbulut, Cemalettin Koc...etal, n=5 (2.9%) of 170 people who had an accidental appendectomy for a living liver donor developed acute appendicitis. {figure 7} (15).

In contrast to He Jong WIE.etal, the patient in Sami Akbulut... etal may be linked to Geographical spread with a high probability of acute appendicitis, and this may explain the higher incidence of acute appendicitis reported in Sami Akbulut..study. etal.

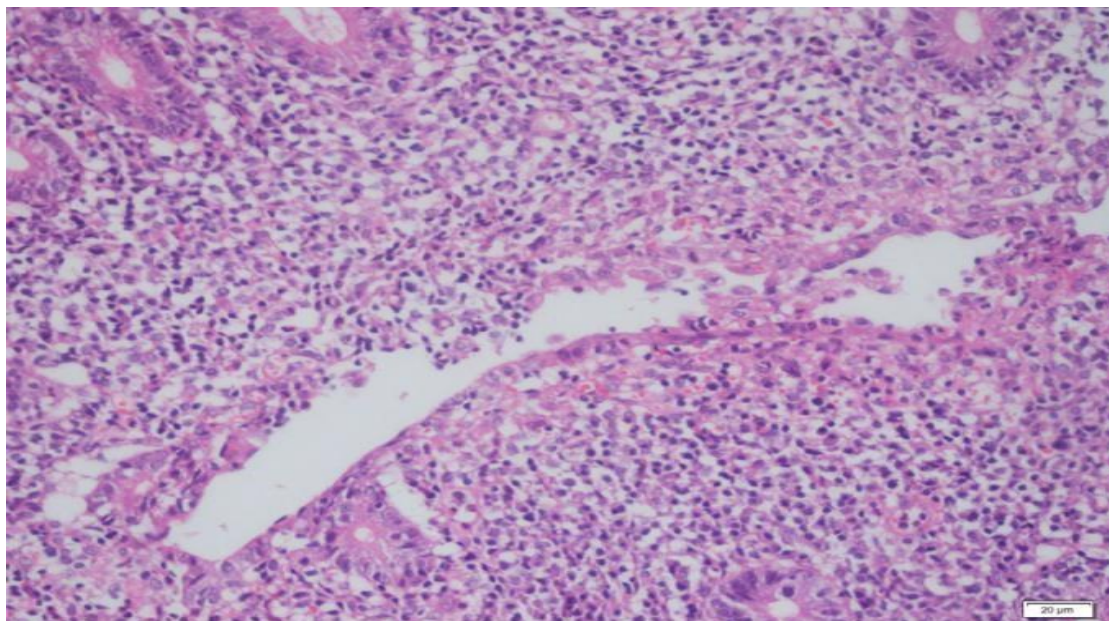


Figure 5 Early acute appendicitis findings (H&E 200×)

7-Chronic appendicitis: In the research of Ouzhan Dincel, Mustafa Göksu, and Bilge Aydın Türk..etal, in percentage 3(5%) chronic appendicitis for 1970 patients, appendectomy specimens were histopathologically examined (13).

Another piece of writing Jung Hun LEE, He Jong WIE, Min Sun KYUNG.. etal, chronic appendicitis occurred in 1 (0.9 percent) of 106 women who

underwent laparoscopic surgical treatment for ovarian endometrioma and had no prior appendectomy. (14).

Patients with frequent or persistent right lower quadrant pain should also include chronic appendicitis in their differential diagnosis. Three patients in Ouzhan Dincel... etal, had chronic appendicitis, two had a history of persistent abdominal pain, and one had chronic abdominal pain, which, along with the large number of specimens collected during the study, may explain the higher frequency of chronic appendicitis in this study relative to He Jong WIE... etal

8-Catarrhal appendicitis: record in the research Catarrhal appendicitis was found in 109 (66%) of 1388 patients who underwent laparoscopic appendectomy for acute RLQA pain, according to Dario Tartaglia, Andrea Bertolucci, Christian Galatioto, etal (16).

Catarrhal appendix was 8 (23.5%) in group A (n = 34) of fertile age women (18–45 years) undergoing emergency surgery for acute RIF pain, and Catarrhal appendix was 21 (18.3%) in group B (n=115) of controls in the study by Francesco Coratti, Silvia Vannuccini...etal (20).

All of the patients in Dario Tartaglia's study had RLQA pain, which may be linked to a high incidence of catarrhal appendicitis compared to study Francesco Coratti..etal.

Conclusion

1- Histopathological examination of appendix is essential regardless the gross feature or the absence of symptoms.

2 - The most common incidental finding in routine histopathological examination of appendix is: most tumor { Carcinoid tumor, Neuroendocrine tumor, mucinous neoplasm, mucinous cystadenoma, Adenocarcinoma}, Fibrous obliteration, Lymphoid hyperplasia, Endometriosis, Enterobius vermicularis, Acute appendicitis, Chronic appendicitis, Catarrhal appendicitis.

3- Incidental finding range from benign lesions to frankly malignant lesion, in which another line of therapy must take place.

4- The most common malignant finding in appendectomy specimen is (neuroendocrine tumor, adenocarcinoid tumor, mucinous neoplasm).

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