

Unexpected Histopathological Findings in Appendectomy Specimens: a Retrospective Study of 1627 Cases

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Abstract Pathologic evaluation of the appendix after appendectomy is routine and can occasionally identify unexpected findings. The aim of the present study was to determine the incidence and type of pathologic diagnoses found in appendectomy specimens at our institution. The clinicopathological data of 1627 patients who underwent appendectomies for presumed acute appendicitis from January 2008 to October 2014 were reviewed retrospectively. There were 986 men and 641 women (sex ratio M/F=1.5) aged between 16 months and 90 years (mean=30 years). All patients underwent appendectomy (either open or laparoscopic). Histological examination of the surgical specimen showed acute inflammation of the appendix in 1455 cases (89.42 %), fibrosed appendix in 37 cases (2.27 %), and *Enterobius vermicularis* ($n=23$). In 101 cases (6.2 %), the appendix was histologically normal. Incidental unexpected pathological diagnoses were noted in 57 appendectomy specimens. They included pinworm ($n=23$), mucinous neoplasms ($n=12$), neuroendocrine tumors (NET) ($n=8$), adenocarcinoma ($n=2$), granulomatous inflammation ($n=5$), tuberculosis ($n=2$), hyperplastic polyp ($n=1$), tubular adenoma ($n=1$), diverticulitis ($n=1$), endometriosis ($n=1$), and actinomycosis ($n=1$). The routine histopathological examination of the appendix is of value for identifying unsuspected conditions requiring further postoperative management. Gross examination alone does not appear to be a good indicator of an unexpected finding on microscopic

exam. It is recommended that in order to avoid misdiagnoses, all appendices should be histopathologically examined.

Keywords Appendix · Appendectomy · Appendicitis · Mucinous neoplasms · Neuroendocrine tumors · Adenocarcinoma

Introduction

Appendicitis is one of the most common acute conditions of the abdomen requiring emergency surgery. The practice of sending appendectomy specimens for histopathological evaluation varies from institutes. Although lymphoid hyperplasia and fecalith are the most common etiologic factors of acute appendicitis, some unusual factors including pinworms and tumors have been identified [1, 2]. Histopathological examination of the appendectomy specimens may be relevant as it yields important clinical information in addition to operative findings [3, 4]. The aim of this study was to assess the value of routine histological examination of the resected appendix.

Patients and Methods

Between January 2008 and October 2014, 1627 patients with presumed acute appendicitis underwent surgical treatment at the Surgery Department of Mongi Slim Hospital, La Marsa. All emergency appendectomies performed on clinically suspected appendicitis and incidental appendectomies which were realized during other abdominal or pelvic surgeries were included in this study. In our department, appendectomy specimens are routinely sampled for microscopic examination, with representative sections including the tip and two cross sections from the base and body of the appendix (Fig. 1). Complementary sections were taken in cases of normal, granulomatous, or tumoral appendices. Negative appendectomy

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Fig. 1 Macroscopic findings of appendectomy specimens. **a** Low-grade appendiceal mucinous neoplasm. Cystic swelling of the appendix due to accumulation of mucus within the lumen. **b** Low-grade appendiceal mucinous neoplasm. On cut section, the cystically dilated lumen was filled with mucinous material. Note the thin appendiceal wall. **c** Gangrenous appendicitis. The specimen showed blackish discoloration of the appendix with perforation of its wall. **d** Phlegmonous appendicitis with fibrinopurulent coating on the serosal surface



was defined as a specimen that was microscopically normal with no evidence of acute or chronic inflammation, tumors, parasitic infestation, and other pathological abnormalities.

The data of 57 patients who were pathologically reported to have unusual appendix findings were retrospectively collected. The records analysis was composed of the patient's age, gender, clinical presentation, operative reports, radiological tools, pathological report, and follow-up. All surgical specimens were fixed in 10 % phosphate-buffered formaldehyde, embedded in paraffin, and sections were prepared for routine light microscopy after staining with hematoxylin and eosin. Immunohistochemical analysis was performed in cases of neuroendocrine tumors using the avidin-biotin complex technique with antibodies against chromogranin A and synaptophysin. Patient confidentiality was maintained.

Results

Study Population

Among 1627 patients, 986 (60.6 %) were males and 641 (39.4 %) were females with a sex ratio M/F=1.5. The mean age was 30 years with a range from 16 months years to 90 years. All patients were diagnosed clinically with acute appendicitis on the basis of physical and laboratory examinations. All patients underwent appendectomy (either open or laparoscopic). All patients with malignant tumors were diagnosed clinically

with acute appendicitis, and none of them had symptoms of carcinoid syndrome or were preoperatively diagnosed with an appendicular tumor.

Histopathological Findings

Histological examination of the surgical specimen showed changes consistent with acute inflammation (acute appendicitis, acute suppurative appendicitis, gangrenous appendicitis, and periappendicular abscess) in 1455 cases (89.42 %) and fibrosed appendix in 37 cases (2.27 %). Incidental unexpected pathological diagnoses were noted in 57 cases (3.5 %) of appendectomy specimens. They included pinworm ($n=23$), mucinous neoplasms ($n=12$), neuroendocrine tumors (NET) ($n=8$), adenocarcinoma ($n=2$), granulomatous inflammation ($n=5$), tuberculosis ($n=2$), hyperplastic polyp ($n=1$), tubular adenoma ($n=1$), diverticulitis ($n=1$), endometriosis ($n=1$), and actinomycosis ($n=1$) (Figs. 2 & 3). Among the 23 appendices with *Enterobius vermicularis*, 10 cases were associated with acute inflammation and 13 cases were within normal limits. In 101 cases (including 61 females (60.4 %) and 40 males (39.6 %)), the appendix was histologically normal.

The histopathological findings of appendectomy specimens and the characteristics of patients with appendicular malignancy in our series are summarized respectively in Tables 1 and 2.

Fig. 2 Microscopic findings of benign lesions of the appendix. **a** Pinworms (oxyuriasis) were an incidental finding in this patient. The lateral spines are the identifying features of this parasite (hematoxylin and eosin, magnification $\times 100$). **b** Hyperplastic appendiceal polyp characterized by elongated and serrated crypts with no cytological dysplasia (hematoxylin and eosin, magnification $\times 40$). **c** Two ectopic endometrial glands surrounded by endometrial stroma located in the outer layer of the muscularis propria (hematoxylin and eosin, magnification $\times 40$). **d** The endometrial glands were lined by a ciliated epithelium with no cytological atypia (hematoxylin and eosin, magnification $\times 200$)

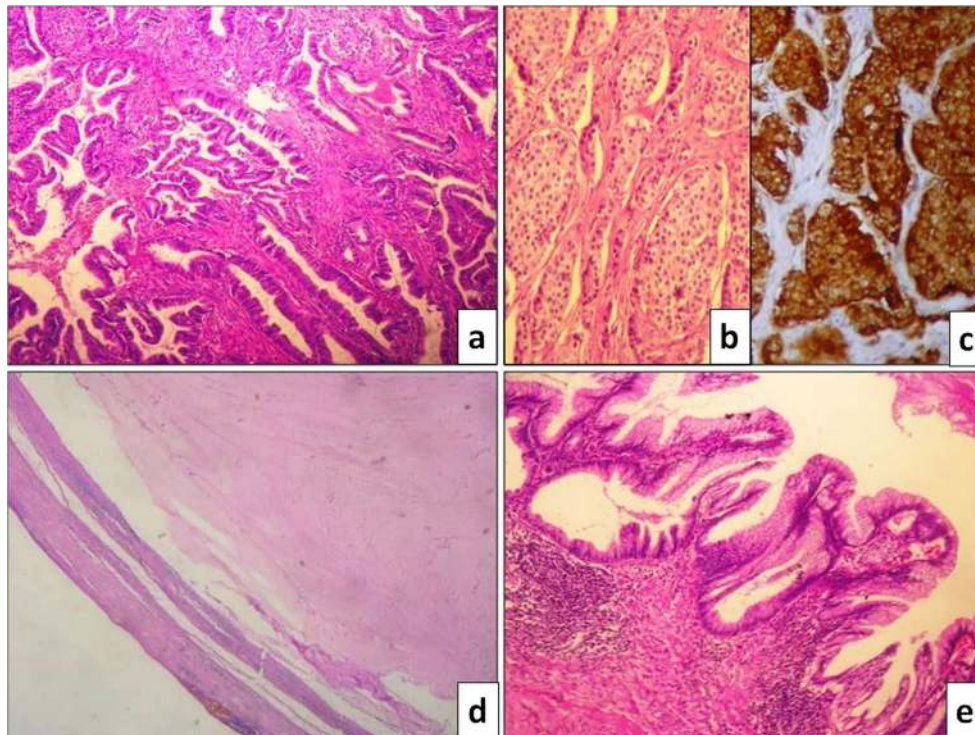
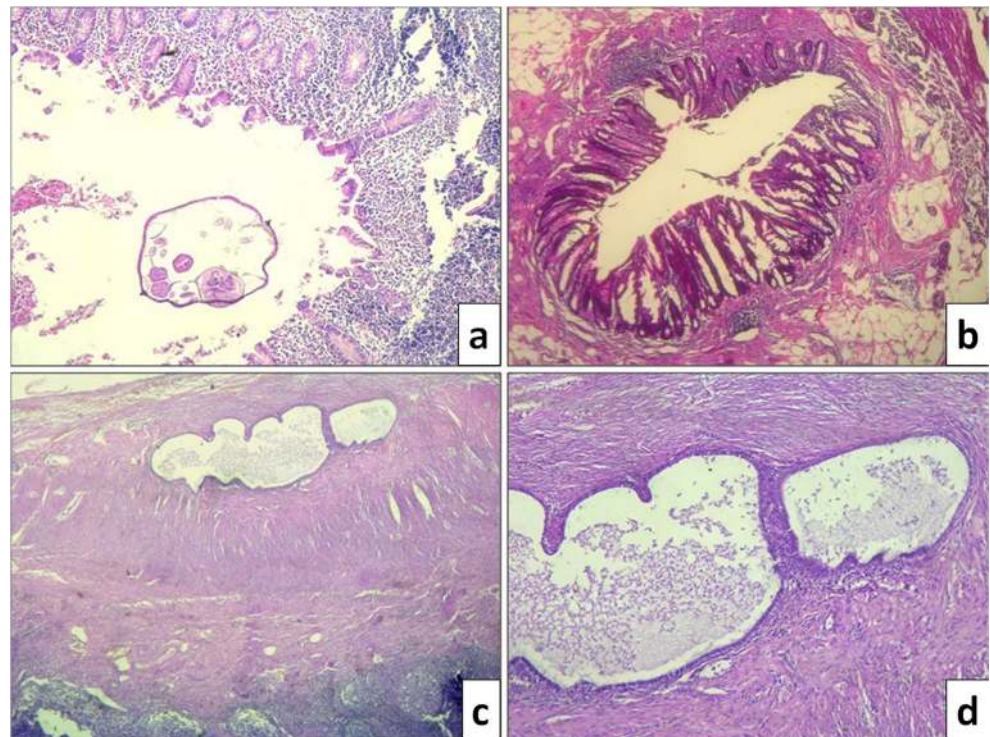


Fig. 3 Microscopic findings of neoplastic lesions of the appendix. **a** Low-grade appendiceal mucinous neoplasm. Cystic swelling of the appendix due to accumulation of mucus within the lumen. **b** Low-grade appendiceal mucinous neoplasm. Typical epithelium with pseudostratified, columnar cells containing elongated, crowded, hyperchromatic nuclei, and scattered goblet cells. **c** Primary appendiceal adenocarcinoma. Tumor cells were

arranged in glandular structures within a fibrous stroma (hematoxylin and eosin, magnification $\times 100$). **d** Neuroendocrine tumor of the appendix grade 1. Homogeneous population of small polygonal cells arranged in nested and trabecular patterns (hematoxylin and eosin, magnification $\times 200$). **e** Tumor cells were strongly immunoreactive for chromogranin A (immunohistochemistry, magnification $\times 200$)

Table 1 Histopathological findings in appendectomy specimens

Findings	Number of cases	%	Treatment
Acute inflammation	1455	89.42	Appendectomy
Normal	101	6.2	Appendectomy
Oxyuriasis	23	1.41	Appendectomy
Fibrosed appendix	37	2.27	Appendectomy
Neuroendocrine tumors	8	0.49	Appendectomy
Mucinous neoplasms	12	0.73	Appendectomy
Granulomatous inflammation	5	0.30	Appendectomy
Tuberculosis	2	0.12	Appendectomy
Endometriosis	1	0.06	Appendectomy
Hyperplastic polyp	1	0.06	Appendectomy
Tubular adenoma	1	0.06	Appendectomy
Diverticulitis	1	0.06	Appendectomy
Actinomycosis	1	0.06	Appendectomy
Adenocarcinoma	2	0.12	Appendectomy and right hemicolectomy

Treatment and Follow-Up

The two patients with primary appendiceal adenocarcinoma underwent right hemicolectomy. All patients with NET and mucinous tumors were alive and disease-free during a mean follow-up of 26 months. The rest of the patients with granulomatous inflammation, tuberculosis, actinomycosis, oxyuriasis, diverticulitis, adenoma, hyperplastic, and endometriosis were lost to follow-up.

Discussion

Histopathological examination of the appendix serves two purposes: First, it allows the diagnosis of acute appendicitis

Table 2 Characteristics of the patients with appendicular malignancy

Case n	Age	Sex	Histological type	Tumor size	Parietal spread
1	47	M	NET G1	15 mm	Subserosa
2	18	F	NET G1	10 mm	Muscularis propria
3	18	M	NET G1	23 mm	Muscularis propria
4	25	F	NET G1	12 mm	Subserosa
5	30	M	NET G1	15 mm	Subserosa
6	17	F	NET G1	15 mm	Subserosa
7	60	M	NET G1	1 mm	Submucosa
8	21	M	NET G1	20 mm	Subserosa
9	74	F	Adenocarcinoma	50 mm	Subserosa
10	50	M	Adenocarcinoma	NP	Subserosa

NP not precised in the histopathological report

G1 grade 1

to be confirmed. Second, histopathological examination may disclose additional pathologies that are not evident intraoperatively but may affect subsequent clinical management of the patient [4]. Specimens reported as negative for acute appendicitis are useful in eliminating acute appendicitis as a cause of symptoms and allowing further investigations to be performed should symptoms persist [5]. The study of Khairy showed that 70 % of negative appendectomies were females [6]. In our study, negative appendectomies were more prevalent in females (60.4 %). This likely reflects the difficulties in diagnosing acute appendicitis in female patients because of the gynecological disorders that mimic acute appendicitis [7].

Some institutions, including ours, send all resected appendices for histopathological analysis. Other centers send specimens only if they appear macroscopically abnormal at the time of surgery [8]. This latter practice has the potential to miss important diagnoses which may subsequently affect patient management and is illustrated in our study, where evaluation of the histopathology reports of 1627 specimens revealed 57 unexpected findings. 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 [4, 9, 10].

Neuroendocrine tumors account for 50–77 % of all appendiceal neoplasms and for 19 % of all gastrointestinal neuroendocrine tumors [11]. They are found in 0.3–0.9 % of patients undergoing appendectomy. In our study, the incidence of appendiceal carcinoid was 0.49 %, which was similar to other studies. The mean age at presentation of appendiceal NET is 32–43 years [12]. Appendiceal NET are firm, grayish-white, and fairly well-circumscribed. The majority of NET are located at the tip of the appendix (75 %). The tumors are smaller than 1 cm in 70–95 % of cases [13]. 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. An appendiceal carcinoid tumor larger than 2 cm should be managed with a formal right hemicolectomy [13]. Adenocarcinoma of the appendix occurs in 0.1–0.2 % of appendectomies, corresponding to an estimated incidence of 0.2 per 100,000 per year [14]. The median age is in the sixth or seventh decade of life. Adenocarcinomas behave aggressively and in a fashion similar to that of colonic adenocarcinomas, so in the case of an appendicular adenocarcinoma, oncologic resection with right hemicolectomy is the treatment of choice [14]. By analogy with the rest of the large intestine, an adenoma-carcinoma sequence is assumed to occur in the appendix. The classification of appendiceal adenomas is the same as that in the colon. The prevalence of mucinous neoplasms is 0.2–0.4 % of appendectomies [15]. Mucinous tumors of the appendix are classified according to WHO 2010 as low grade or as high grade. Low-grade

appendiceal neoplasms generally grow slowly and tend to produce clinical picture of low-grade pseudomyxoma peritonei in which spread beyond the peritoneum or nodal metastasis is unusual. High-grade mucinous adenocarcinomas can also produce pseudomyxoma peritonei but are more likely to invade the underlying organs and exhibit hematogenous and lymphatic metastasis (Fig. 3). The incidence of granulomatous appendicitis, a rare condition that may be discovered incidentally in a patient with a clinical presentation of acute appendicitis, ranges from 0.31 to 0.95 %. Various infectious and noninfectious factors cause granulomatous appendicitis. Systemic conditions, such as Crohn's disease and sarcoidosis, may also be associated with granulomatous inflammation of the appendix [16]. Distinguishing idiopathic granulomatous appendicitis from early Crohn's disease, which affects only the appendix, is difficult. A definitive diagnosis can only be made after long-term follow-up, and sometimes, further investigations are required [16]. The reported incidence of appendicular tuberculosis varies from 0.1 to 3 % among all appendectomies performed [17]. An accurate diagnosis is usually established after histopathological examination of a specimen. Classic histopathological analysis of an appendectomy specimen usually reveals the presence of caseating granulomas and Langhans giant cells, suggesting tuberculosis of the appendix. Although some studies have reported that treatment is not necessary for the primary disease and that appendectomy alone is sufficient, no consensus has been reached [17]. Actinomycosis is an uncommon chronic infectious disease. In abdominal actinomycosis, the ileocecal region including the appendix is the most commonly involved site. A correct diagnosis can be made by culture or histopathological examination, although a definitive diagnosis of actinomycosis requires microscopic proof of either the pathogen itself or the presence of specific sulfur granules. After the diagnosis has been confirmed, the general therapeutic recommendation is to initiate treatment with intravenous antibiotic therapy for 2–12 months [18]. *E. vermicularis*, also known as pinworm or oxyuriasis, is a widespread parasitic infection estimated to affect up to 200 million people worldwide. While the reported incidence of pinworm in appendectomy specimens of patients with presumed appendicitis ranged from 0.2 to 41.8 %, the reported rates of inflammation in specimens from appendices infested with pinworm ranged from 13 to 37 % [19]. Patients must receive antihelminthic treatment because the appendectomy treats only the consequence and not the cause of the disease [19]. Both congenital and acquired types of appendiceal diverticula are rare with reported incidence rates of 0.014 % and 0.20 to 1.7 %, respectively [20, 21]. Acquired diverticula are false diverticula with herniation of the mucosa through the muscularis propria and typically arise at the vascular hiatus points of low resistance along both the mesenteric and antimesenteric surfaces [21, 22]. Increased intraluminal pressure (fecalith, proximal tumors, excessive luminal

mucous) is central to the formation of acquired appendiceal diverticula [22]. Appendiceal diverticula and their complications are sporadically discussed in the medical literature. They are often asymptomatic but may present clinically when diverticulitis develops and mimics the acute abdomen of acute suppurative appendicitis.

In summary, appendectomy specimens removed from patients with suspected acute appendicitis often appear macroscopically normal, but histopathological analysis of these cases may reveal an underlying pathology. We emphasize and strongly recommend that all appendectomy specimens be examined histopathologically regardless of whether the specimens are macroscopically normal.

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