Original Research Article

Journal of Bharatpur Hospital (JoBH), Vol-1, No.1, Jan-Jun 2025

ISSN: 3059-9733

Incidental Lesions on Routine Histopathological Examination of Appendectomy Specimen

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ABSTRACT

Background

Acute appendicitis is one of the most common causes of acute abdomen and appendectomy is the most commonly performed surgical procedure. The lifetime frequency of acute appendicitis is 8.6 % in males and 6.7 % in females. Fecalith and lymphoid hyperplasia are the usual causative factors of acute appendicitis causing intraluminal obstruction. Intestinal parasitic diseases and malignant or benign lesions are the most prevalent unusual incidental pathological findings observed in appendectomy specimens. Almost all cases present with clinical features of acute appendicitis thus a routine histopathological study is required to identify the cause of appendicitis. Unusual incidental findings must be noted and reported as it may vary the patient management as well as outcome.

Methods

A cross-sectional study was performed in the Department of Pathology, College of medical sciences, Bharatpur, Nepal over a period of three years. Histopathologic data on all appendectomy specimens (total 921) with a clinical diagnosis of acute appendicitis were retrieved from the archives of department of pathology and analyzed. Mean and percentage were calculated and findings were tabulated.

Results

21 cases with incidental unusual pathology leading to acute appendicitis were identified and included in the study. Unusual lesions of the appendix comprised 2.28% (21/921) of the appendectomy specimens examined. Mean age of presentation with unusual lesion was 49 years. Male: Female ratio was 1:1.

Conclusions

There are many pathologies behind acute appendicitis apart from the usual one as fecalith and lymphoid hyperplasia. Hence routine histopathological examination of appendectomy specimens is of value to discover unusual incidental pathologies that might require additional postoperative management.

Keywords: appendix; incidental lesion; histopathology.

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INTRODUCTION

Acute appendicitis is one of the most common cause of acute abdomen and appendectomy is the most commonly performed surgical procedure. The lifetime frequency of acute appendicitis is 8.6 % in males and 6.7 % in females.[1] Fecalith and lymphoid hyperplasia are the usual etiology for acute appendicitis causing intraluminal obstruction.[2-4] Intestinal parasitic diseases and malignant or benign lesions are the prevalent unusual incidental pathological findings observed in appendectomy specimens. [5] Obstructions in the appendiceal lumen is the major enticing event causing continued mucous secretion that leads to pathophysiological events as : increased intraluminal pressure, compromised lymphatic drainage, edema resulting in distension of the appendix, venous obstruction and eventually ischemia and necrosis on the appendix wall.[3-4] Almost all cases present with features of acute appendicitis clinically, thus a routine histopathological study is required to identify the cause of appendicitis and unusual incidental findings must be noted as it may vary the patient outcome as well as management.

METHODS

A cross-sectional study was performed in the Department of Pathology, College of medical sciences, Bharatpur, Nepal. This study was conducted in appendectomy specimen received for histopathological evaluation over a period of three years. Ethical approval was taken from institutional review committee of College of Medical Sciences (Ref No.2024-111). Histopathologic data on appendectomy specimens (total 921) with a clinical diagnosis of acute appendicitis were retrieved from the archives of department of pathology and analyzed. 21 cases with incidental unusual pathology leading to acute appendicitis were identified and included in the study. Frequency, percentage, mean were calculated and findings were tabulated. The gross and microscopic findings were reviewed and diagnosis were revised if needed. Histologic categorization and staging for neoplastic lesions was done according to WWHO - tumors of GIT 5th edition, 2019 guideline.

Table 1. Summary of unusual lesions in the study.

Age (years)	Sex	Histopathological diagnosis
Mucinous Lesion		
63	F	Retention cyst
45	F	LAMN, Tis
67	M	LAMN, Tis
51	F	LAMN, Tis
65	F	LAMN, Tis
60	M	LAMN, Tis
48	F	LAMN, Tis
53	F	LAMN, Tis
72	F	LAMN, Tis
Malignant tumor		
58	M	Adenocarcinoma, well differentiated
80	F	Neuroendocrine tumor, G1
17	M	Neuroendocrine tumor, G1
Serrated lesion		
74	M	Sessile serrated lesion with low grade dysplasia
84	M	Sessile serrated lesion with low grade dysplasia
Granulomatous/xanthogranulomatous lesion		
32	M	Granulomatous appendicitis
18	F	Xanthogranulomatous appendicitis
38	M	Xanthogranulomatous appendicitis
35	M	Xanthogranulomatous appendicitis
Organism		
22	F	Oxyuriasis appendicitis
13	M	Oxyuriasis appendicitis
32	M	Oxyuriasis appendicitis

RESULTS

A total of 921 patients with the clinical diagnosis of acute appendicitis underwent appendectomy at a duration of three years. The diagnoses of all patients were confirmed via histopathological examination of the appendectomy specimen. Most of the cases were diagnosed as acute appendicitis, acute suppurative appendicitis and gangrenous appendicitis which are the usual pathologies encountered. Unusual lesions of the appendix comprised only 2.28% (21/921) of the appendicectomy specimens examined. Mean age of

presentation with unusual lesion was 49 years. Male: Female ratio was 1:1.

Mucinous lesion:

The mucinous lesion were identified in nine cases (0.97%). One case of mucinous lesion was non-neoplastic comprising of retention cyst and eight of them were neoplastic comprising of low grade appendiceal mucinous neoplasm (LAMN) (0.86%). Age group of mucinous neoplasm ranged from 45- 72 years with mean age of 57.6 years. 75% of the patient with mucinous neoplasm were female.

Malignant lesion:

One case of appendicular adenocarcinoma (0.10%) was identified in 58 year old male. Tumor invaded into muscular layer extending to subserosa and was staged pathologically as pT3.

Two cases of neuroendocrine tumor (0.22%) were found in 80 year old female and 17 year old male with mean age of 48.5 years. It was well differentiated grade 1 tumor as tumor cells were fairly uniform with scant cytoplasm, mitotic rate <2/2 mm^2. Necrosis was not identified.

Serrated lesion

Two cases (0.22%) were diagnosed as sessile serrated lesion with low grade dysplasia. Both patient were elderly male with age of 74 and 84 years with mean age of 79 years.

Granulomatous/xanthogranulomatous lesion

One case was of granulomatous appendicitis (0.10%) with focal presence of granuloma at serosa and numerous giant cells were identified in a 32 year old male patient.

Three cases were diagnosed as xanthogranulomatous appendicitis (0.33%) of age group 18-38 years with mean age of 30 years. Foamy macrophages were noted in the wall of appendix and mesoappendix.

Organism

Three cases of Oxyuriasis appendicitis (Enterobious vermicularis) (0.33%) were noted. Lumen of appendix reveal adult worm with presence of lateral alae and thick cuticle. Age group ranged from 13-32 years with mean age of 22 years.

DISCUSSION

Fitz coined the term appendicitis and also described the signs, symptoms of acute and perforated appendicitis. He was among the first to recommend early diagnosis and operative intervention.[6] There is marked variation in the etiopathogenesis of appendicitis. Luminal obstruction is emphasized as prime initiating event occurring as a cause of acute appendicitis, irrespective of the various etiologies.[6]

Mucinous lesion

Mucinous lesions are less frequently encountered on appendectomy specimens. It accounted for 0.97 % of total appendectomy cases in our study which is in accordance with other studies where they ranges from 0.6 to 1.2% of all appendectomy specimens.[7-9] Significant female predominance was noted in our study in mucinous lesions with male to female ratio of 1:3. Similar, findings were observed in other studies with male to female ratio of 2:3 and 1:2.[7,9] Mucinous lesions can comprises of simple mucocele or retention cysts, benign neoplastic adenomas to malignant lesions including invasive mucinous adenocarcinomas.[9] The most common non-neoplastic entity in our study was a simple retention cyst that showed flattened mucinous lining epithelium without atypia and areas of epithelial denudation with giant cell reaction. LAMNs comprised 0.86% (8/921) of the appendicectomy specimens which is similar to the incidence of~0.5% in other study.[7] Six out of the eight LAMN cases in our study (75%) were in females with similar findings in a study by Shrestha et al.[7] Intussusception, volvulus, and pseudomyxoma peritonei are known possible complications of LAMN with appendiceal pathology being the most common cause of pseudomyxoma peritonei.[10, 11]

Histopathology of LAMN showed circumferential involvement of the appendix by filifirm villous to flat mucinous epithelial cells with low-grade dysplasia. Pushing type of invasion into the muscularis propria was noted with absence of lymphoid tissue and normal crypts. All the LAMN cases showed the mucinous epithelium with mucin limited to the muscularis propria and were staged as Tis.[12] The

prognosis of stage Tis LAMN is excellent while those with peritoneal dissemination have a variable prognosis.[13,14]

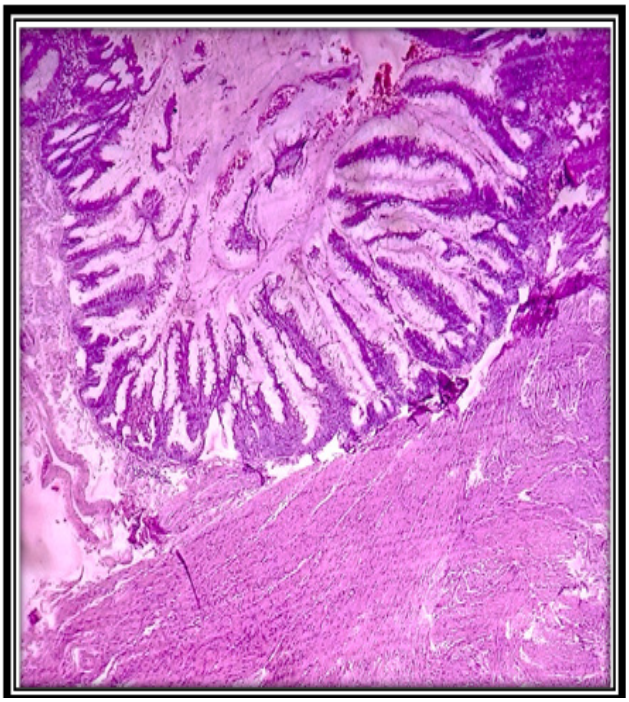

Figure 1. Slender villous mucosa in LAMN

Malignant lesion

Appendiceal adenocarcinoma accounts for <0.5 % of all gastrointestinal cancers.[15] Primary appendiceal adenocarcinomas are very rare malignant neoplasm accounting for 0.05–0.2% of all appendectomies and 6% of all malignant tumors of appendix.[16] In our study incidence of adenocarcinoma was 0.10% in 58 year old male. Though malignancy is a rare cause of appendicitis, many cases are arising each year and thus when elderly patient present for appendicitis, malignancy should always be on the differential diagnosis.[17] Non mucinous adenocarcinoma have irregular glands infiltrating the wall with desmoplastic response and has poorer prognosis than mucinous adenocarcinoma.[18] Neuroendocrine tumor (NET) is an incidental finding in most of the appendectomy cases with prevalence of 0.2%-0.7%[19] which is similar to our study with prevalence of 0.22%. Appendiceal NET is the fifth most common NET of gastrointestinal tract and neuroendocrine neoplasms of the appendix account for 50~70% of all appendix tumors.[20] The incidence rate of neuroendocrine tumors is low and the tumors are usually treated on basis of appendicitis symptoms due to the lack of specific clinical manifestations.[21] While simple appendectomy is sufficient in the treatment of NET, in some cases it requires a right hemicolectomy together with lymphadenectomy following chemotherapy.[22] The average age of the patients presentation with NET was 33 years in study by Pawa et al[22], while it differ in our study with wide age of presentation of 17 and 80 years and mean age of 48.5 being the age of diagnosis.

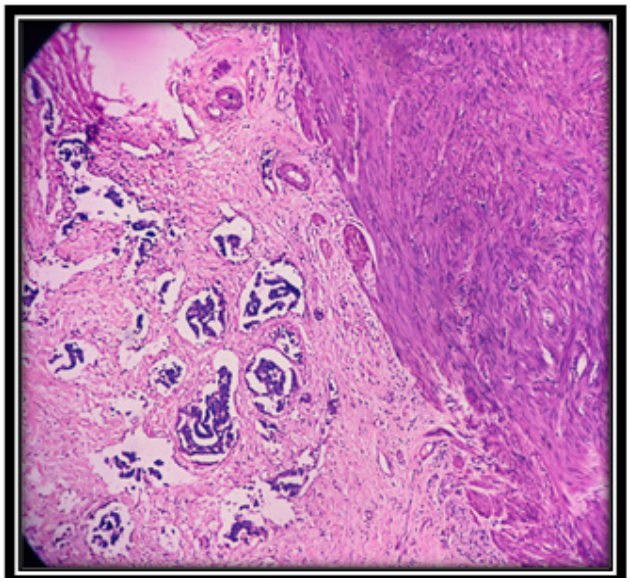

Figure 2. Neuroendocrine tumor

Serrated lesion

Sessile serrated lesion are a relatively recent described entity most commonly occurring in the right colon and rarely in the appendix.[23] The diagnosis of sessile serrated lesion is based on basic histological features such as serration, dilatation, horizontal orientation, goblet cell differentiation, proliferative region with an L-shaped or inverted T-form at the base of the crypts.[24, 25] These features also helps to differentiate it from hyperplastic polyps. In our study both cases were over 7th decade of life whereas patient's median age was 48 (29-72) years in study by Kaya et al. [26]

Granulomatous/xanthogranulomatous lesion

Granulomatous inflammation of the appendix is a rare entity with a frequency of less than 2% of appendectomies.[27-28] Its causes can be infectious or

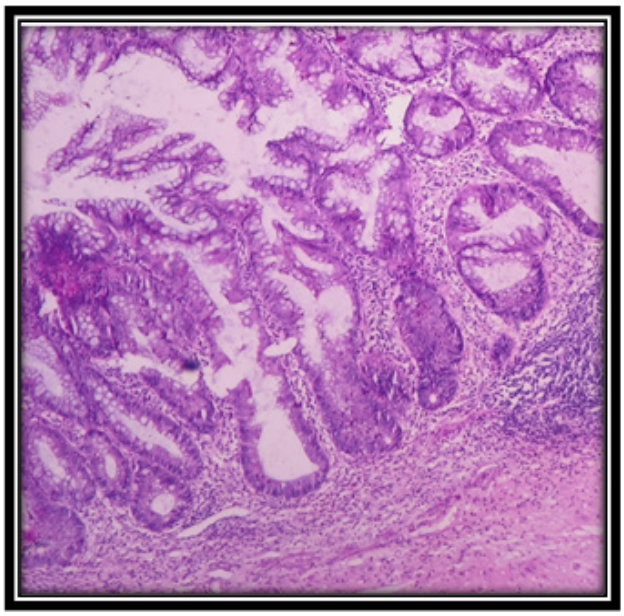

Figure 3. Sessile serrated lesion with low grade

non-infectious. The non-infectious causes comprises of diverticulitis, Crohn's disease, foreign-body reactions, tumors and sarcoidosis. While infectious causes may be due to Yersinia, Mycobacterium tuberculosis or other microorganisms.[29-30]

Xanthogranulomatous inflammation is a form of chronic inflammation characterized by lipid-laden macrophages with admixed lymphocytes, plasma cells, neutrophils, and multinucleated giant cells with or without cholesterol clefts.[31] It is a chronic inflammatory process involving various organs with rarity in appendix. Xanthogranulomatous appendicitis is usually identified on histopathological examination as it has no unique features on imaging studies or clinical presentation.[32] In a study by Guo et al. xanthogranulomatous inflammation occurred in 36.4% of interval appendectomies but did not occur in emergency appendectomies group.[33] While 0.3% of acute appendicitis were diagnosed as xanthogranulomatous in the indexed study.

Organism

Gastrointestinal infection due to Enterobious vermicularis /pinworm is most common helminthic infection worldwide. These are commonly noted in people of lower socioeconomic status with poor hygiene and unsafe drinking water.[34] Oxyuriasis / Enterobious appendix might be lesser encountered entity in the developed nations, as opposed to the developing nation like Nepal. There were three cases of oxyuriasis appendix (0.33%) discovered in the index study with mean age of 22 years. Single case of oxyuriasis was noted in studies by Mukharjee et al and Upadhyaya et al whereas 11 cases were reported by Dincel et al.[35-37] Presence of organism should be reported in appendectomy sections if noted, as the patient may require further antihelminthic therapy to prevent other complications.[35] In a study by Dincel et al., 1970 appendectomies cases were evaluated at a duration of four years and rare findings were found in 59 (3 %) patients. The unusual findings identified were fibrous obliteration, Enterobius vermicularis, schistosomiasis, appendiceal neuroma, granulomatous appendicitis, Crohn's disease, chronic appendicitis, endometriosis, hyperplastic polyps, mucinous cystadenoma, carcinoid tumors, and lymphoma.[37] Similarly in a study by Mukharjee et al. well-differentiated (G2) neuroendocrine tumor, neurogenic appendicopathy, granulomatous appendicitis of tubercular etiology, xanthogranulomatous appendicitis, pseudomyxoma peritonei with synchronous LAMN and borderline mucinous tumor of the ovary and LAMN were some unusual findings discovered.[36]

CONCLUSIONS

There are many pathologies behind acute appendicitis apart from the usual one as fecalith and lymphoid hyperplasia. Hence routine histopathological examination of appendectomy specimens is of value to discover unusual incidental pathologies that might require additional postoperative management.

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to all the faculties, residents, technical and non-technical staffs at Department of Pathology, College of Medical Sciences.

Conflict of interest: None

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Citation: Baral A, Goyal B, Pun CB. Incidental Lesions on Routine Histopathological Examination of Appendectomy Specimen. JoBH, Nepal. 2025; 1(1): 5-11.