



WONDERS IN APPENDIX – A CASE SERIES

Histopathology

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ABSTRACT

Introduction: Appendix is a true diverticulum arising from cecum; prone for inflammation. Acute appendicitis is the commonest surgical emergency operated world-wide, with fecolith induced luminal obstruction is the frequent cause; however unforeseen causes can amaze both surgeon and pathologist. **Material & Methods:** We report a case series on the rare etiologies for acute appendicitis. **Result:** Out of 383 cases of appendectomy specimens, we are reporting a case series on unconventional morphological findings (n=14) in alleged vestigial appendicectomy specimens accounting for 3.65%. These are: Acute appendicitis with worm infestation; *Enterobius vermicularis* (1.04%), Appendicular neuroma (1.04%), Carcinoid (0.26%), Schwannoma (0.26%), Primary Mucinous neoplasm of appendix (0.78%) and metastatic lesion (0.26%). **Discussion:** Luminal obstruction by fecolith (60-65%) is the most common cause for acute appendicitis. However, incidental association of parasites especially *E. vermicularis* (0.2-4.8%) and *E. histolytica* (0.5-2.3%) can be seen in the lumen along with predominantly eosinophilic infiltration in the wall. The appendiceal neuroma (<1%) causing proliferation of neural tissue, obliterating the appendiceal lumen thus mimicking as acute appendicitis. The association of neoplastic lesions like appendicular carcinoid (0.3-0.9%), mucinous neoplasms, appendiceal schwannoma (0.6-0.8%) and metastatic deposits into appendiceal wall (0.2-0.7%) are the other rare causes masquerading as appendicitis. **Conclusion:** Wonders in appendix are unconventional entities can be presented as surgical emergencies requiring immediate interventions and can be missed easily if morphology is studied offhandedly. Awareness and careful morphological assessment of appendicectomy specimens is essential for further management of the patients.

KEYWORDS

Acute appendicitis, *Enterobius vermicularis*, appendiceal neuroma, carcinoid, schwannoma, mucinous neoplasm

INTRODUCTION:

Acute appendicitis (AA), caused by a blockage of the hollow portion of the appendix represents one of the commonest causes for emergency gastrointestinal surgery worldwide with a cumulative lifetime incidence rate of 9.0%.¹ During the 20th century, the disease was mostly reported within the western countries; however, a rise in its incidence has been noted specially within newly industrialized countries in 21 centuries.^{1&2} This is the most common entity of surgical acute abdomen, frequently affect young individuals in second and third decades of life. The pathophysiology includes the obstruction of the appendicular lumen caused by various etiologies, including lymphoid hyperplasia, fecoliths, tumors, or foreign bodies, however it can rarely be caused by parasitosis.³ Infection caused by parasite *E. vermicularis*, usually called as pinworms is the commonest helminthic infection predominantly affecting people of developing countries with a global prevalence of 29.8%.⁴ If left untreated appendicitis can progress to deadly complications like perforation peritonitis or abscess formation thus increased immediate surgical attention and intervention.^{5,7} Similarly, another parasite which is most frequently associated with AA is *Entamoeba histolytica* with incidence around 0.5–2.3% in tropical area. It is associated with higher rate of surgical complications if left untreated.⁸

AA associated with various neoplasm are rare and reported finitely in the literature. The benign neoplasm like appendiceal neuroma and schwannoma; typically present as surgical emergency in older population mimicking acute abdomen.⁹ Appendiceal neuroma is also known as fibrous obliteration or neurogenic hyperplasia which is characterized by proliferation of spindle cells leading to luminal obstruction of appendix.⁹ Appendiceal schwannoma is also an unforeseen entity unexpectedly found in AA specimens as a base lesion and histologically shows characteristics monomorphic spindle cell proliferation with hypercellular and hypocellular areas with some palisading and ill-formed Verocay bodies.^{10&11}

Appendiceal carcinoid is the most common but rarely occurring

primary malignant neoplasm of appendix found in 0.3 to 0.9% of appendectomy specimen and has good prognosis (95-100% five-years survival rate) if reported early; with 1% recurrence rate.^{12&13} These tumors are frequently present at the tip and more than 80% of them have size less than 1 cm.¹⁴

Another very rare entity which can mimic clinically as AA is low-grade and high grade appendiceal mucinous neoplasm (L/H-AMN) which carries risk of serious complications consisting of rupture and also associated with seeding of mucin and malignant cells into the peritoneum leading to pseudomyxoma peritonei (PMP).¹⁵ Mucocoele of the appendix is rare tumour without having any specific clinical manifestations, with incidence of 0.2-0.7% and occurs over 50 years of age.¹⁶ Grossly the appendiceal lumen is obstructed and distended with mucus.¹⁷ If missed on examination, it may land into life threatening complications like PMP.²¹

METHODS AND MATERIAL

Retrospective, Observational study conducted for the period of two years from January 2023 to December 2024 at Department of Pathology, Tertiary health care center of central rural India. Total 383 cases (n=383) of appendicectomy specimens were received during the study period. Among these, we are reporting a case series of total 14 cases (n=14) showing unconventional incidental histopathological findings in appendix specimen that include; Acute appendicitis with worm infestation (n=04; 1.04%) having association of *Enterobius vermicularis* (n= 03) and *Entamoeba histolytica* (n=1) respectively, Appendiceal neuroma (n=04; 1.04%), Appendiceal Schwannoma (n=01, 0.26%), Carcinoid appendix (n=01, 0.26%), Primary Mucinous neoplasm of appendix (n=03; 0.78%) and metastatic appendicular lesion (n=01; 0.26%). [Table no. 1, Diagram 1]

Table 1: Table Shows All The Unusual Findings Reported Of Histopathology N = 14

Serial No	Case	Clinical Diagnosis	“WONDERS” in Appendix
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1	03	0.78%	Acute Appendicitis	Enterobius vermicularis
2	01	0.26%	Acute Appendicitis	Entamoeba histolytica
3	04	1.04%	Acute Appendicitis	Appendiceal neuroma
4	01	0.26%	Acute Appendicitis	Appendiceal schwannoma
5	01	0.26%	Acute Appendicitis	Carcinoid appendix
6	03	0.78%	Acute Appendicitis	Primary mucinous neoplasm of appendix
7	01	0.26%	Acute Appendicitis	Metastatic Appendicular lesion

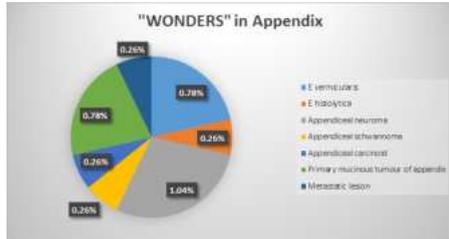


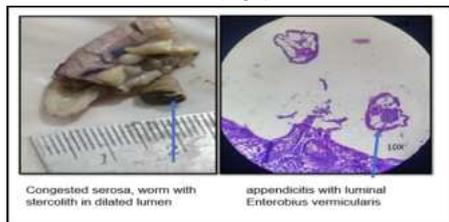
Diagram 1: Diagram shows pictorial representation of unusual entities associated with specimens of acute appendicitis

Case Series

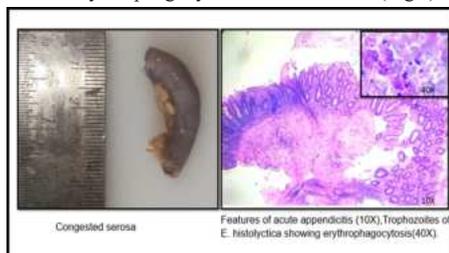
1. Acute appendicitis with parasitic infestations (n=4, 1.04%)

In this retrospective observational study, we have identified four cases where association of worm infestation is seen with AA. These are as follows:

1A: There are three cases (n=3, 0.78%) of 10 years old male, 21 years old female and 17 years old male respectively came with chief complaints of pain in abdomen along with fever and episodes of vomiting for which emergency laparotomy was performed and sample of appendectomy was sent for histopathology. On histopathological examination, grossly appendicular lumen was studded with grey white thread like parasites entangled in fecal matter which on microscopic examination of hematoxylin and eosin (H&E) stained section showed luminal Enterobius vermicularis. (Fig 1)



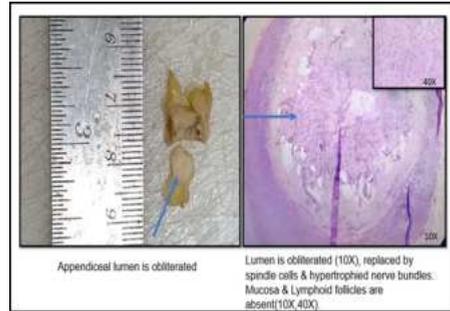
1B: A 32-years-old male patient presented to the casualty complaining of acute abdominal pain that had started in the umbilical region and later radiated to the right iliac fossa (RIF). With a clinical suspicion of acute appendicitis, laparoscopic appendectomy was performed and sample was sent for histopathological examination. Grossly, the appendix measured 5 cm in length with attached unremarkable mesoappendix. On the cut section, the lumen was seen filled with necrotic debris. H&E stained sections from the base and body of the appendix showed the presence of granular necrotic debris with ulceration of the mucosa along with trophozoites of Entamoeba histolytica (n=1, 0.26%) invading through the mucosa and going into the submucosa. Erythrophagocytosis was also noted. (Fig 2)



2. Appendiceal Neuroma (n=04, 1.04%)

The cases were 38 years and 54 years old male respectively and 40 years and 62 years female respectively admitted to surgical emergency

unit with complaints of acute abdominal pain radiating to RIF. With a clinical suspicion of acute appendicitis, laparoscopic appendectomy was performed and sample was sent for histopathological examination. Grossly, cut section of appendix showed the obliterated lumen. H&E stained sections showed lumen obliterated by spindle cells and hypertrophied nerve bundles with absence of mucosa and lymphoid follicles. (Fig 3)



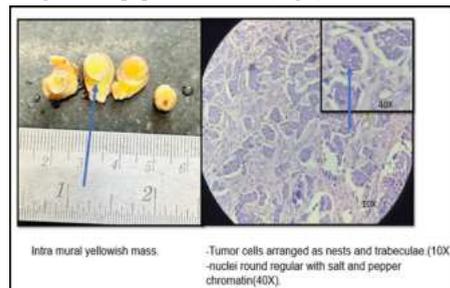
3. Appendiceal Schwannoma (n=01, 0.26%)

A 17 Years old boy admitted in surgical emergency unit with chief complaints of pain in abdomen which was radiating to RIF since 2-3 days accompanied with fever since 1 day and 3-4 episodes of vomiting. On clinic-radiological examination, diagnosis of acute appendicitis was made and emergency laparoscopic appendectomy was performed. Histoapthological examination of appendix revealed that appendicular lumen was completely obstructed due to fibrous growth grossly. However microscopy revealed H&E stained section showing unremarkable mucosa and underlying well circumscribed tumour composed of monomorphic spindle cells with wavy to elongated spindle nuclei having tapering ends, at places showing palisadation. Also noted are myxoid material in the background. (Fig 4)



4. Carcinoid appendix (N=01, 0.26%)

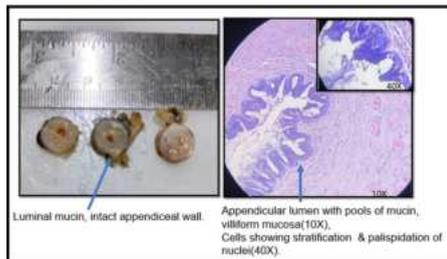
A 27 years old male patient came with complaints of epigastric pain which then radiating into right lower quadrant. Emergency appendectomy was done and sample of appendix sent for histopathological examination. On Gross examination, cut section showed mural yellowish mass. On microscopic examination, H&E stained section showed tumour cells arranged as nests, islands and trabeculae infiltrating into mucosa, submucosa and extending up to muscularis propria and serosa with individual cells are showing round nuclei having salt and paper chromatin. (Fig 5)



4. Primary Mucinous neoplasm of appendix (n=03, 0.78%)

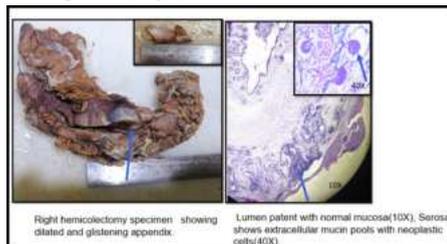
The cases were 67 years female, 43 years and 58 years old males respectively admitted to surgery department with complaints of acute abdominal pain radiating to RIF. With a clinical suspicion of acute appendicitis, laparoscopic appendectomy was performed and sample was sent for histopathological examination. Grossly, cut section of appendix showed the luminal mucin with intact appendiceal wall. H&E stained sections show villous and flat proliferation of mucinous epithelial cells originating from appendiceal lumen. Individual cell showing Individual cells showing stratification and palisadation of

nuclei with low grade nuclear atypia, lumen filled with abundant mucin reaches up to serosa. Also shows atrophy of underlying lymphoid follicles, effacement of muscularis mucosa, and serosa shows presence of congested blood vessels and abundant areas of mucin deposition. (Fig 6)



5. Metastatic Appendicular Lesion (n=01, 0.26%)

A 70 years old female patient presented with signs of perforation peritonitis. Emergency exploratory laparotomy was done with left hemicolectomy with omentectomy with appendectomy and sample sent for histopathological examination. Grossly, cut section of appendix showed luminal mucin. On microscopic examination, H&E stained section showed tumor cells arranged as simple to complex glandular pattern, micro-papillary pattern, and groups and scattered singly. Individual tumor cells were columnar with pleomorphic vesicular nuclei and prominent nucleoli. Cells showed stratification and loss of polarity. Cytoplasm was variable mucinous, pushing the nuclei to periphery with intracellular mucin giving signet ring appearance. Large pools of extra cellular mucin >50% cells floating with and dissecting muscularis propria. Foci of necrosis, mitosis and admixed inflammatory infiltrates also noted. Plenty of lymphovascular tumor emboli noted. Histomorphological features of Metastatic mucinous adenocarcinoma of appendix with tumor cells extending up to serosa was reported. (Fig 7)



DISCUSSION:

AA is the commonest surgical emergency operated world wide¹, with appendicolith induced luminal obstruction is the dominating cause among other causes of luminal obstructions comprising of appendiceal tumours, intestinal parasites or hypertrophied lymphoid tissues which account for about 60-65% of the cases presenting as AA.²² *E. vermicularis* is known by many names such as seatworm, pinworm, oxyuriasis or threadworm and first description of human infestation nearly dates back 10,000 years. However, Fabrius in 1634 first described the involvement of the worm in appendicitis.³ *E. vermicularis* remains one of the commonest parasitic infestation worldwide affecting almost 209 million of population.⁴ *E. vermicularis* in the appendix lumen can cause symptoms of acute appendicitis as ova, cyst and adult forms of this parasite can occlude the appendiceal lumen and later on present as a coincidental findings in specimen of appendicitis.^{6,7} Tropical appendicitis is clinically asymptomatic and can mimic acute abdomen causing immediate surgical attention. It can be seen secondary to enterobiasis, amoebiasis, ascariasis, trichuriasis, and taeniasis as an extension of cecal infestation. Amoebic appendicitis if left untreated can be associated with increased postoperative morbidity and mortality. It can lead to complications like sepsis, liver abscess, postoperative colonic fistula, necrotic surgical site infection, necrotizing fasciitis, fulminant colitis, and even brain abscess. The co-incidence of amoebic appendicitis has been seen with HIV, alcoholism, and other immunosuppressed states along with recent travel history to endemic areas. Poor hygienic conditions is the main cause for disease spreading and propagation. However, thorough histopathological examination is mandatory to rule out this rare cause of AA to avoid further complications and complete recovery of the patient.⁸ Similarly, in present case series we have entitled four cases of rare association of parasites in the appendectomy specimen which will help for further management of the patients. One of the unusual

conditions known as appendiceal neuroma, the term was coined by Masson; around 50 years ago affecting mostly older people. The pathogenesis showed proliferation of neuroendocrine cells due to frequent inflammatory attacks which typically begins at the distal part. It is usually an incidental and asymptomatic finding, mimicking appendicitis, similar to our case.⁹ Histopathological examination helps for accurate diagnosis of this benign entity and differentiating it from the other stromal tumors of the vermiform appendix such as leiomyoma, gastrointestinal stromal tumors, and neurogenic lesions.⁹ In the present case series we have mentioned four cases of this unusual entity which was diagnosed with thorough histopathological examination. Gastrointestinal schwannomas are rare type of slow growing and mostly asymptomatic benign mesenchymal neoplasm of schwann cells. Appendiceal schwannomas are very unusual diagnosis and mostly reported as an incidental finding thus limitedly found in literature till date and therefore possess little evidence to guide management and follow-up.¹⁰ Usually, the affected population are adults of sixth decades with female preponderance¹¹, however here we are presenting rarest case of teenage boy having appendiceal schwannoma. Carcinoids are well-differentiated neuroendocrine neoplasms associated with 55% of gastrointestinal malignancies followed by respiratory tract (30%) and other organs (15%).¹² However, carcinoid of appendix is a rare malignant neoplasm affecting population between third to fourth decades of life with female preponderance.¹³ Grossly, appendiceal carcinoid tumors appear as yellow or white, firm nodules, most composed of entero-chromaffin cells and on microscopy, carcinoids are well-circumscribed and unencapsulated, and consist of tightly packed nests and acini-containing neoplastic cells that fill the mucosa and variably extend into the appendiceal wall. The tumor cells contain abundant amphiphilic or eosinophilic granular cytoplasm with round, smooth nuclei and coarse "salt and pepper" chromatin and rare mitoses.¹² Approximately 70-95% of carcinoid tumors are present at the tip of appendix and measures less than 1 cm in size. Most of the appendix carcinoids behaves like benign or have low malignant potential, and shows metastasis very rarely. For the malignant tumors having diameter less than 1 cm have zero metastases rates thus simple appendectomy is considered as an adequate treatment. The risk of metastasis increases up to 85% in tumors with a diameter of 2 cm or more thus in such cases, right hemicolectomy should be performed.¹⁴ Consistent with the literatures, in our current study, appendix carcinoid tumor was an incidental finding in histopathological examination in which patient presented with signs and symptoms of acute appendicitis but didn't show findings of carcinoid syndrome and managed by appendectomy.

Another rare entity which we have reported in present case series are Primary mucinous neoplasm of appendix which is classified by World Health Organization (WHO) into neoplastic (mucinous adenoma, low-grade appendiceal mucinous neoplasm (LAMN) and appendiceal adenocarcinoma) and non-neoplastic (mucosal hyperplasia, simple cyst).²⁰ LAMN is mostly asymptomatic and stable, but carries high risk of rupture and dissemination of mucin and neoplastic cells into the peritoneal cavity resulting to pseudomyxoma peritonei (PMP) characterized by intraperitoneal accumulation of mucinous tumors and mucinous ascites that is associated with poor outcomes and high mortality risk. To prevent such complications, it is important to keep such rare entity in mind so that timely workup and management can prevent the progression into PMP and metastasis thus improving overall outcome and recovery.¹⁵ Olive W et al¹⁶ in their case study reported the similar findings as present case that LAMN are rare tumours having asymptomatic progression mimicking AA and incidentally diagnosed on appendectomy specimens.¹⁶ Kidogawa H et al¹⁷ and Guo Z et al¹⁸ also mentioned the importance of meticulous histopathological examination of appendectomy specimen showing presence of acellular mucin in appendiceal wall to rule out rare entity of LAMN as it lacks specific clinical presentation by carrying high risk of complications.^{17,18} The given case series also enlisted metastatic appendiceal tumour which is rarely reported in literature as mucocele of appendix which is classified into four histological types, based on the nature of the differentiation of the appendiceal epithelial lining: the retention cyst, mucosal hyperplasia, mucinous cystadenoma and mucinous cystadenocarcinoma.¹⁹ It has nonspecific clinical presentation which sometimes mimic AA, thus carries diagnostic difficulty and requires accurate diagnosis to avoid the dreaded complication of PMP. Careful histopathological examination will show mucinous neoplastic cell deposits at the serosal side with normal

appendiceal mucosa accompanied with primary malignancy elsewhere; most commonly in caecum /colon, stomach, breast.³¹ Radiological modality plays important role in establishing a diagnosis thus predicting prognosis and helping further management.

CONCLUSION:

“Wonders in Appendix” are unconventional entities can be presented as surgical emergencies requiring immediate interventions They can be missed easily if morphology is studied offhandedly and throwing it into waste basket. Awareness and careful morphological assessment of appendectomy specimens is essential as it can reveal morphological wonders inside and help in further management of the patients.

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