



“HISTOPATHOLOGICAL ANALYSIS OF APPENDIX IN CLINICALLY DIAGNOSED AND OPERATED ACUTE APPENDICITIS CASES- A RETROSPECTIVE STUDY”

General Surgery

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ABSTRACT

Appendicitis is the inflammation of the appendix. Acute appendicitis is the most common surgical cause of acute abdomen. There is no doubt that early diagnosis with prompt surgical intervention is the goal. Delay in treatment can cause certain complications. On the other hand, prompt diagnosis and emergency operation can result in a number of negative appendectomies. The diagnosis of acute appendicitis is predominantly a clinical one, many patients present with a typical history and examination findings. The cause of acute appendicitis is unknown but is probably multifactorial. Despite technologic advances, the confirmation of diagnosis of appendicitis is still based on histopathological examination of resected specimens. In some cases the histopathology will not reveal any active inflammation of the appendix. Hence this study is conducted to audit the appendectomy specimens received with clinical diagnosis of acute appendicitis.

KEYWORDS

Acute appendicitis, Eosinophilic, Tubercular, Xanthogranulomatous, Carcinoid.

INTRODUCTION:

Appendicitis is the inflammation of the appendix. Appendicitis is a disease of the young, with 40% of cases occurring between the ages of 10 and 29 years.^[1] In 1886, Sir Heneage Ogilvie says “Acute appendicitis is one of the common condition which the surgeon is called upon to treat as an emergency”.^[2] It requires utmost skill and care of the attending doctor, besides good clinical judgement. Acute appendicitis is the most common surgical cause of acute abdomen. There is no doubt that early diagnosis with prompt surgical intervention is the goal. To obtain accurate preoperative diagnosis may be difficult in many cases. Delay in treatment can cause certain complications. On the other hand, prompt diagnosis and emergency operation can result in a number of negative appendectomies. The diagnostic accuracy of acute appendicitis and acceptable rate of negative appendectomy had been reported in several studies.^[3,4]

The diagnosis of acute appendicitis is predominantly a clinical one, many patients present with a typical history and examination findings. The cause of acute appendicitis is unknown but is probably multifactorial- luminal obstruction and dietary factors have all been suggested.^[4] Despite technologic advances, the confirmation of diagnosis of appendicitis is still based on histopathological examination of resected specimens. In some cases of appendectomy, the histopathology will not reveal any active inflammation of the appendix.^[3]

AIMS AND OBJECTIVES OF THE STUDY:

1. To study histopathological findings in appendectomy specimens diagnosed clinically as Acute Appendicitis
2. To study the various morphological types of appendicitis

Research Hypothesis: All clinically diagnosed acute appendicitis cases will not show acute inflammation of the appendix on histopathological examination.

METHODOLOGY: A retrospective study was conducted at Department of Pathology, Indira Gandhi Government Medical College & Research Institute, Pondicherry, over a period of three years from January 2015 to December 2017. The study design comprised of thoroughly scrutinized information gathered from histopathology documents.

INCLUSION CRITERIA:

- All clinically diagnosed cases of acute appendicitis who had undergone appendectomy were included in our study.

EXCLUSION CRITERIA:

- Cases who had been clinically diagnosed other than acute appendicitis were excluded.

- Cases where proper clinical details, histopathological and morphological findings are not available were also excluded.

DETAILS OF METHODOLOGY: The case details initially collected from histopathology section of Pathology department and their clinical details were collected from case sheets at medical record section. Details were entered in the proforma and investigation findings like total leucocyte count, Neutrophilia, radiological findings were collected from the case records. The other acute abdominal presentations like gynaecological or obstetric pathology, right ureteric colic, Meckel's diverticulum, mesenteric lymphadenitis, regional ileitis, obstructed carcinoma of caecum etc were excluded. Intra-operative findings were collected from case records. Gross findings like edema of appendix, luminal presence of fecolith, any worms, presence of serosal exudates, any perforations were noted. The appendix was bisected and one representative longitudinal section to include the tip and one or more cross sections of each appendix were processed into paraffin blocks. Haematoxylin and Eosin-stained sections were examined microscopically; in selected cases, special stains were done. Microscopy findings like mucosal ulceration, dense acute inflammation composed of neutrophils or eosinophils infiltrating muscle layer or beyond, periappendicitis, granulomatous inflammation, carcinoid tumors, presence of lymphoid hyperplasia, submucosal fibrosis etc were noted under histopathology findings in the proforma. Finally, correlation of clinical and histopathology findings was done.

RESULTS: Total of 591 appendectomy cases were received during the study period constituting average of 6.7% of surgical specimens received (Table 2). The age range was wide with slight male preponderance. The age ranged from 8 years to 78 years with mean age of presentation of 42 years. Maximum numbers of appendectomies were observed in 3rd decade of life. Acute appendicitis was more commonly seen in male patients (363 cases, 61.42 %) than females (228 cases, 38.57%). The chief complaint of the acute onset pain in the periumbilical region migrating to the right iliac fossa was seen in 98% of cases. Increased leucocyte count was seen in 78% cases with Neutrophilia. The mean length of appendix was 6.0 cm in our study. Intra-operative findings were given in Table 1 and histopathological reports issued were given in table 2.

TABLE1: Showing details of intra-operative findings noted in Appendectomy cases:

SL no	Intra-operative findings	No of cases and %
1	Acutely inflamed appendix	538 cases (91.03%)
2	Perforated appendix	20 cases (3.38%)
3	Appendicular mass	11 cases (1.86%)
4	Gangrene of Appendix	2 cases (0.33%)
5	Normal looking appendix	20 cases (3.38%)

TABLE 2: Showing details of histopathological diagnosis issued in Appendicectomy cases:

Sl No	Diagnosis offered	2015	2016	2017	Total cases and %
1	Acute Appendicitis	131	153	169	453 (76.64%)
2	Chronic Appendicitis/ Healed/ Resolved/ Recurrent	23	16	25	64 (10.82%)
3	Lymphoid hyperplasia	30	19	10	59 (10%)
4	Eosinophilic appendicitis	1	3	7	11 (1.8%)
5	Tuberculosis	1	0	0	1 (0.16%)
6	Xathogranulomatous	1	0	0	1 (0.16%)
7	Enterobius Vermicularis	1	0	0	1 (0.16%)
8	Carcinoid tumor	0	1	0	1 (0.16%)
9	Normal appendix	0	0	0	0
	Total	188	192	211	591 (100%)
	Total Surgical Specimens received during the year	2767	3049	2975	
	Appendicectomy %	6.8%	6.3%	7.0%	

DISCUSSION:

For many years most researchers were thought that there is no purpose of appendix and termed it as vestigial organ; but now, researchers discovered that it may be essential to maintain the flora of the gut and it acts as a "safe house" for commensal ("good") bacteria.^[4] The diagnosis of appendicitis can be difficult at times, occasionally taxing the skills of the most experienced clinician.^[1] Histopathological examination still remains the gold standard for the confirmation of appendicitis. Not only the pathologic diagnosis of acute inflammation, unusual findings such as incidental tumors noted in the appendix highlight the importance of pathologic analysis of every single resected appendix.^[11] The histopathological examination of the appendix serves two purposes. First it allows the diagnosis of acute appendicitis to be confirmed; second, it may disclose additional pathologies that may not be evident intraoperatively but may impact patient management.

1. "Acute appendicitis" was diagnosed based on the criteria of mucosal ulceration, transmural polymorph infiltrate, often with mural necrosis and a serosal inflammatory response.^[5] This constituted single largest category of diagnosis in the present study with 453 cases of 591 (76.64%). Grossly acute appendicitis cases revealed signs of acute inflammation like edema, congestion and serosal prominent blood vessels. On cut section, mucosa showed congestion with focal areas of ulceration and purulent exudates or sometimes fecolith in the lumen. Microscopically, the appendix showed focal mucosal ulceration with polymorphs infiltrating up to muscularis propria and presence of acute inflammatory exudate in the lumen (Fig No 1). Many cases also showed extension of acute inflammation to serosal layer and they are termed as "peri-appendicitis/ meso-appendicitis".^[3] Obstruction of the appendiceal lumen seems to be essential for development of appendiceal infection, most commonly caused by fecolith. Once obstruction occurs, continued mucus secretion and inflammatory exudation increase intraluminal pressure, which obstructs lymphatic drainage and oedema and mucosal ulceration develop, further distension of the appendix may cause venous obstruction and finally ischemic necrosis of the appendix wall produces acute appendicitis.^[16]

Unequivocal luminal obstruction usually in the form of a fecolith can be found in 35-40% patients with appendicitis.^[5] Other less common causes of obstruction include parasites, food residue in the form of vegetable debris or fruit seeds, barium from radiographic studies and neoplasms of the caecum and proximal appendix itself. Functional obstruction due to lymphoid hyperplasia has also been implicated.^[2,13]

Acute appendicitis with periappendicitis noticed in 51 cases (8.62%), perforation of acutely inflamed appendix was seen in 20 cases (3.38%) and acute gangrenous appendicitis was encountered in 2 cases (0.33%). Fink et al reported 33.75% incidence of perforation in acute appendicitis.^[13] Nampet et al reported the rate of gangrenous appendicitis as 8% in their studies.^[14] This discrepancy may be because of smaller sample size in our study or early intervention.

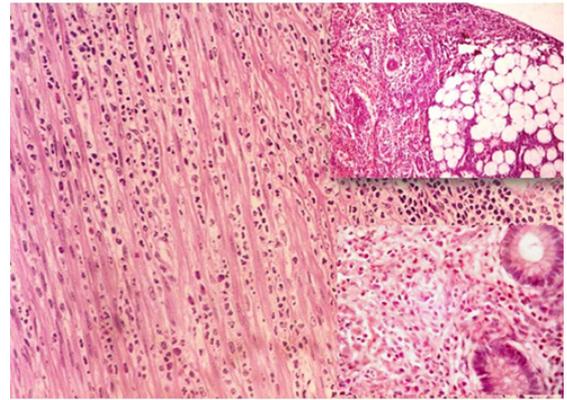


FIG.NO.1. Acute appendicitis: Section showing polymorphs infiltrating up to muscularis propria; right upper inset showing periappendicitis with inflammation extending to serosal fat; right lower inset showing acute eosinophilic appendicitis.

2. "Chronic appendicitis" is term of controversy used liberally by both clinicians and pathologists in different context. Histologically, criteria for diagnosis of chronic appendicitis were evidence of active chronic inflammation with infiltration of the muscle coat and serosa by lymphocytes and plasma cells.^[1] Some pathologists argue that, it is impossible to differentiate native lymphoid collections of appendix from chronic inflammatory component.^[11] Hence presence of submucosal fibrosis is considered as hallmark of chronic inflammation and it is named as "healed" or "resolved" appendicitis by different pathologists. The terms "sub-acute" and "resolving" are difficult to define and we observed use of these terms are subjective interpretations of minor degrees of inflammation seen histologically and can be confusing to both histologists and surgeons alike. As recommended by Herd et al^[3], this confusion can be avoided, and more uniformity and clarity achieved with five reporting categories: (i) established acute inflammation; (ii) no evidence of acute inflammation ("normal"); (iii) features suggestive of early inflammation, (iv) peri-appendicitis; (v) other features, such as granulomata, Enterobius vermicularis, tumours, etc. This group of chronic appendicitis constituted the second largest category of diagnosis 64 cases (10.82%) in the present study.

3. Lymphoid Hyperplasia: Fifty nine out of 591 cases (10%) of appendicitis showed hyperplastic lymphoid follicles with prominent germinal centres indicating stimulation of B cell mediated immune response.^[2] These cases were reported as "lymphoid hyperplasia" of appendix. Florid lymphoid hyperplasia is a rare condition with an unknown aetiology. This condition was first reported by Briquet in 1838 and later it was investigated radiologically by Marina and Carballo in 1941 and given a new name of "enteritis follicularis".^[2] Histologically, it reveals hyperplastic lymphoid follicles with large germinal centres in the lamina propria and superficial submucosa. Lymphoid follicular hyperplasia usually occurs in children and young adults and manifests clinically with signs and symptoms masquerading acute appendicitis.^[2]

4. Eosinophilic appendicitis: Eleven cases out of 591 (1.8%) were diagnosed as Eosinophilic appendicitis. Histopathological hallmark of this entity is eosinophilic infiltration of the muscularis propria with accompanying edema separating the muscle fibers, and absence of neutrophilic infiltration.^[6] Preoperative correct diagnosis of this entity is not possible and histopathological examination is the gold standard for the diagnosis. Primary eosinophilic appendicitis affects the appendix with eosinophil rich transmural inflammation in excess of 10 per cm (more than 25 eosinophils per high power field) in muscularis mucosa with absence of polymorphs or any other pathology in the wall as per Aravindhan, with no known cause for eosinophilia including drug reaction, parasitic infections and malignancy.^[6,8] Acute eosinophilic appendicitis was first proposed by Aravindan in 1997 and pathogenesis, etiology still remains unknown.^[6]

5. Tuberculosis of Appendix: Only one case of tuberculosis of appendix is diagnosed in the present study. Tuberculous appendix is surprisingly rare, even in countries where this infection is common. In a review of 2,921 appendectomies carried out in a tertiary centre in India, only 2.3% of cases were tubercular appendicitis.^[1] Singh et al

proposed a new etiopathological classification that categorised tuberculous appendix into primary or secondary involvement. Primary involvement occurs through contact with infected intestinal contents or through haematogenous spread from sources that are not clinically detectable. Secondary involvement occurs through local extension from ileocecal involvement, retrograde lymphatic spread from distant lesions in the ileum or ascending colon, or peri-appendicitis from peritoneal involvement.^[7] The initial management of acute presentations of tuberculous appendix is surgical. There is no specific guideline for the treatment of tuberculous appendix, and the treatment recommendation for gastrointestinal TB, which is similar to that for pulmonary TB, is followed.^[7]

6. Xanthogranulomatous appendicitis: It is a rare entity characterized by an infiltrate composed of lipid laden macrophages or foam cells, admixed with lymphocytes, plasma cells, neutrophils, and often multinucleated giant cells with or without cholesterol clefts.^[8] Proposed aetiologies include defective lipid transport, immunologic disturbances, infection by low-virulence organisms, and lymphatic obstruction. It has been most commonly reported in organs such as the kidney and gall bladder.^[9] In our study, we had one case of this entity. Involvement of the appendix by xanthogranulomatous inflammation is a rare phenomenon with only 10 cases reported in the literature.^[8]

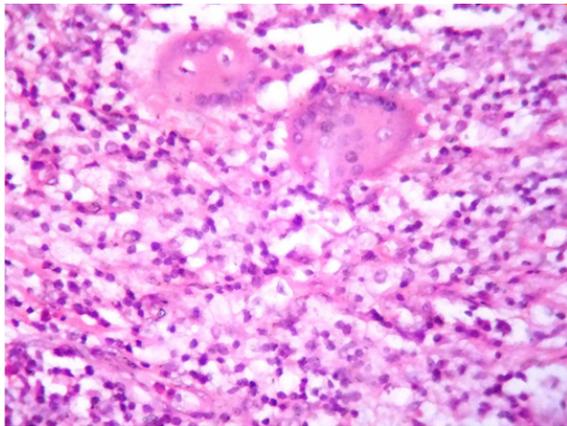


FIG.NO.2. Xanthogranulomatous appendicitis: Lipid laden macrophages with lymphocytes, plasma cells, neutrophils, and often multinucleated giant cells.

7. Enterobius Vermicularis infestation: Only one case of 11 year old child clinically diagnosed as acute appendicitis and underwent laparoscopic appendicectomy was diagnosed with *Enterobius vermicularis* infection. *E. Vermicularis* was identified in ranges from 0.18 to 4.1% of patients with clinical appendicitis and was most commonly seen in appendix with either chronic inflammation or where the appendix was normal on histology. *Enterobius vermicularis* was rarely associated with histological changes of acute appendicitis.^[12]

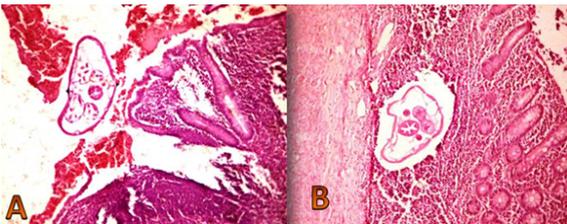


Fig.No.3. Enterobius Vermicularis infestation with acute appendicitis: Usually the larval form is seen in the lumen admixed with the inflammatory exudate (A); rarely in may be infiltrating the mucosa of appendix (B).

8. Carcinoid tumor/ Neuroendocrine tumor (NET): are the most common neoplasms of the appendix accounting for 85% of all tumors and occurring in 0.02-1.5% of all appendicectomy specimens.^[1] Appendiceal tumors are unusual, as quoted by Duzgun et al, the majority being neuroendocrine tumors, while the remaining includes adenoma, adenocarcinoma, lymphomas and Kaposi sarcoma.^[9] Criteria for diagnosis of appendiceal NETs are: a) Collection of cells demonstrating definite insular pattern of growth with extension of cells into or through the muscular wall. b) Gross nodule or an expansion of

the appendix.^[9] In our study, a single case of neuroendocrine tumor of the appendix was encountered in a 42 yr old male. Grossly the appendix cut section showed a tiny 1.2cm yellowish circumscribed nodule at the tip. Microscopically in addition to acute appendicitis there was a tumor composed of monotonous round to polygonal cells having centrally located nuclei with salt and pepper chromatin and scant to moderate amount of eosinophilic cytoplasm arranged in insular pattern (Fig.2).

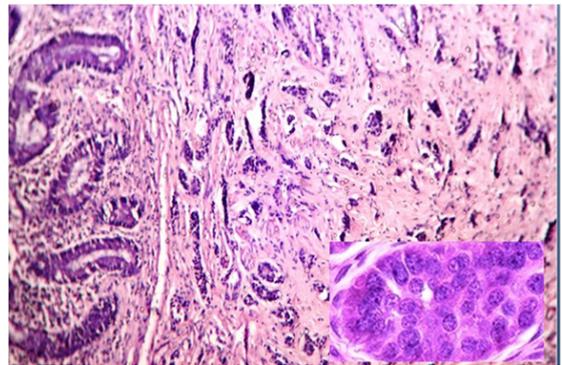


FIG.NO.4. Carcinoid tumor of Appendix: Collection of neuroendocrine cells arranged in nesting pattern of growth with extension into the muscular wall. Inset showing monotonous round cells having centrally located nuclei with salt and pepper chromatin.

9. Normal appendix: Those appendices which show no evidence of any acute inflammation or any significant histopathological findings fall into the "normal" category.^[10] There had been report that approximately 25 per cent of histologically normal appendices removed from patients with preoperative diagnosis of acute appendicitis showed presence of TNF- α and IL-2 in the mucosa similar to those of acute appendicitis.^[10] However, whether these inflammatory cytokines are responsible for the clinical symptoms remains unknown and is a subject of further study. Surprisingly in our study, we did not encounter any case of appendix reported as normal. Analysis of pathological diagnosis of appendicitis showed marked variation in terminology and classification especially in groups of normal appendix. Although it is more than 100 years since McBurney^[15] described his experience with early operative interference in cases acute appendicitis, it is perhaps surprising that only recently has attention been focused on the patient who not having inflamed appendix is nevertheless subjected to surgery and unnecessary appendectomy. Surgeons have believed it safer to remove a normal appendix than risk perforation if the organ is in fact inflamed.^[16]

CONCLUSION: Histopathological examination of every appendix is necessary for confirmation of clinical diagnosis of appendicitis. Obstruction of the lumen is the dominant factor for acute appendicitis. Some usual etiologic factors are fecoliths and lymphoid hyperplasia. Besides, parasitic infestations, neoplasms of appendix and unusual conditions like xanthogranulomatous appendicitis can be diagnosed only on histopathology. Hence histopathological auditing of the appendicectomy specimens is very crucial to confirm the diagnosis and it may reveal interesting findings.

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