MAST CELLS IN APPENDICITIS: A STUDY
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ABSTRACT: AIM AND OBJECTIVE: To investigate the extent of mast cell involvement in surgically resected appendices of both the normal and inflamed appendices. INTRODUCTION: Mast cells are known to be effector cells in various inflammatory and immune reactions. The number of mast cells in appendicitis and its association is unclear. MATERIALS AND METHODS: One hundred and eight cases were studied with routine haematoxylin and eosin staining and a special stain toluidine blue. The number of mast cells was counted randomly in ten consecutive high power fields in all the sections with one percent toluidine blue and graded the mast cells count. RESULTS: Among one hundred and eight cases, the acute appendicitis were 60 cases (55.5%), with higher mast cell count and chronic appendicitis were 46 cases (42.6%), with highest mast cell count and normal appendices were 2 cases (1.9%), did not show any significant variation in mast cell count. CONCLUSION: We concluded that mast cell count was higher in acute appendicitis indicating immunological and non-immunological injury causing acute appendicitis. The mast cell count was highest in chronic appendicitis, indicating growth interaction between mast cells, nerves and fibroblasts.
KEYWORDS: Appendicitis, Mast cells.

INTRODUCTION: The appendix is a normal true diverticulum of the cecum that is prone to acute and chronic inflammation. The appendix was first described by Erengario Da Capri the physician, anatomist in 1521. The “Vermiform Appendix” was coined by Verneys in 1710. Reginald Fitz coined the term ‘appendicitis’ in 1886. The lifetime risk for appendicitis is 7%; males are affected slightly more often than females.[1]

Despite the prevalence of acute appendicitis, the diagnosis can be difficult to confirm preoperatively and may be confused with mesenteric lymphadenitis, acute salpingitis, ectopic pregnancy, mittelschmerz and Meckel diverticulitis.

Acute appendicitis is thought to be initiated by progressive increases in intraluminal pressure that compromise venous outflow. In 50% to 80% of cases, acute appendicitis is associated with overt luminal obstruction, usually caused by fecolith, or mass of worms. Ischemic injury and stasis of luminal contents, which favour bacterial proliferation, trigger inflammatory responses including tissue edema and neutrophilic infiltration of the lumen, muscular wall, and periappendiceal soft tissues.[2]

Von Recklinghausen et al., in 1863 described the mast cell for the first time.[1] Mast cells are bone marrow-derived cells found resident in tissues throughout the body particularly in association with structures such as blood vessels and nerves.[3] Mast cells have cytoplasmic membrane-bound granules that contain a variety of biologically active mediators like platelet activating factor and the leukotrienes. Therefore, the mast cells are regarded as “Disseminated unicellular endocrine glands”.[1] The granules also contain acidic proteoglycans that bind basic
dyes such as toluidine blue. Mast cells are activated by the cross-linking of high-affinity IgE Fc receptors.\[4\]

For some unknown reason mast cell counts were found to be significantly higher in acute appendicitis, highest in chronic appendicitis and absent in normal appendix. The mediators released from activated mast cells could be one of the important factors which are responsible for the nerve proliferation, hypertrophy and fibrosis in appendicitis. The present study was undertaken to investigate the extent of mast cell involvement in appendicitis and their role in its pathogenesis.

MATERIALS AND METHODS: The present study was done in the Department of Pathology, The Oxford Medical College, Atibele, and Bangalore rural. One hundred and eight appendicitis cases were studied; all the sections were stained with routine hematoxylin and eosin stain and a special stain Toluidine blue.

Mast Cell Counting John D Bancroft, Marilyn Gamble (2008)[1 & 5]: 1% Toluidine blue stained sections were examined under the high power magnification. The number of mast cells which were present in 10 consecutive high power fields was counted in all the sections. The total 108 cases were divided into three groups, based on the histopathological criteria.

Group – A: Acute appendicitis presenting with a neutrophilic and eosinophilic infiltration.
Group – B: The appendix removed incidentally during other abdominal surgeries and showing a normal picture.
Group – C: Chronic appendicitis presenting with a lympho mono nuclear infiltrate and fibrosis.

Grading:
Grade – 0: No cells.
Grade – 1 +: Few cells seen in few high power fields.
Grade – 2 +: Clusters of more than 10 cells seen in some fields.
Grade – 3 +: Such clusters seen in most fields.

RESULTS: The total number of appendices which were examined in the present study was 108 [Table 1]. The commonest lesion which was noticed was acute appendicitis in 60(55.5%) cases. The next common lesion which was noticed was chronic appendicitis in 46 cases (42.6%) and normal appendices were noticed in 2 cases (1.9%). In group a lesions, 38 cases showed grade I and 22 cases showed grade II. In group B lesions, 33 cases showed grade III and 13 cases showed grade II. In the group C lesions that is in both the cases we could not find any mast cells. The mucosal mast cell count was marginally more than that which was found in the sub mucosa. [Table 2 & 3]
Table 1

|                | Group A | Group B | Group C |
|----------------|---------|---------|---------|
| Dr. Nayak      | 29      | 43      | 45      |
| Dr. Sulochana  | 30      | 44      | 47      |
| Present Study  | 11      | 19      | 00      |

Table 2: Mast cell count in mucosa

|                | Group A | Group B | Group C |
|----------------|---------|---------|---------|
| Dr. Nayak      | 34      | 41      | 38      |
| Dr. Sulochana  | 36      | 38      | 40      |
| Present Study  | 13      | 22      | 00      |

Table 3: Mast cell count in sub mucosa

Fig. 1: Acute appendicitis

Fig. 2: Chronic appendicitis

Fig. 3: Acute appendicitis H & E 400x

Fig. 4: Acute appendicitis H&E 1000x
DISCUSSION: The present study showed a significant mast cell variation in both the normal and inflamed appendices. There was little variation in the average mucosal and the submucosal mast cells along the length of the appendix.

Out of the 108 cases, 60 cases (55.5%) of acute appendicitis showed neutrophilic and eosinophilic infiltration. Among that 49 cases showed luminal obstruction with a faecolith and mucosal ulceration was also noted in few of these cases. Chronic appendicitis was noted in 46 cases (42.6%), showing mononuclear cell infiltration and fibrosis of the wall. Normal histology of appendix was also noted in two cases, which was removed during hysterectomy. In toluidine blue stained sections mast cells was found to be present in both mucosa and submucosa of inflamed appendix. In group A lesions mast cells were present both in mucosa and submucosa mainly around the blood vessels, the mast cell count was in the range of 3-18 (mean value 11) in mucosa and 4-22 (mean value 13) in submucosa. In group B lesions mast cells were also found in both mucosa and submucosa. Clusters of mast cells grade III category of mast cells were noted in many of these chronic appendicitis cases, predominantly mast cell clusters were noted in lamina propria and near the fibrotic areas. The total mast cell count was in the range of 4-32 (mean value 19) in mucosa and 4-40 (mean value 22) in submucosa. In group C lesions there were no mast cells in both mucosa and submucosa.
This correlated with a study done by Nayak et al.\textsuperscript{6} Who concluded that the mast cell count was more in chronic appendicitis when compared to acute appendicitis. Similarly in 2012 Sulochana also noted mast cells were more in chronic appendicitis, moderate in acute appendicitis and mild to absent in histologically normal appendices. These studies correlated with the present study.

Therefore mast cells play an important role in the pathogenesis of appendicitis. Both immunological and non-immunological stimuli cause degranulation of the mast cells and granules released from activated mast cells trigger the various inflammatory cells and growth factors which further activates fibroblasts and causes fibrosis. Nerve growth factor released by granules of mast cells causes hyperplasia of both the mucosal and the sub mucosal mast cells.\textsuperscript{7} Even the fibroblasts have an ability to make the nerve growth factor; hence, there is an abundant potential for growth interactions between the mast cells, nerves and the fibroblasts.\textsuperscript{8}

We concluded that the mast cell count was higher in chronic appendicitis, thus indicating that an immunological or a non-immunological injury caused appendicitis. Indicating that there is an association between the mast cells, nerves and the fibroblasts.

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