

Original Research Article**Eosinophilic Enterocolitis in Intestinal Biopsies: A Unicentre Study****Bhat Shwetha K.¹, Mysorekar Vijaya V.²**¹Post Graduate ²Senior Professor, Department of Pathology, M.S. Ramaiah Medical College, Bengaluru, Karnataka 560054, India.**Abstract**

Context: Eosinophilic enterocolitis is a rare inflammatory disease of unknown origin, characterised by diffuse eosinophilic infiltration of gastrointestinal tract, accompanied by varying abdominal symptoms. The condition is increasing in frequency in recent years and is associated with major complications if untreated. Hence, it is very necessary to diagnose the condition. Hence, the present study was done to evaluate for eosinophilic enterocolitis in intestinal biopsies, and to correlate with peripheral eosinophilia.

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Aims: 1. To evaluate intestinal biopsies for eosinophilic enterocolitis. 2. To correlate with peripheral eosinophilia.

Settings and Design: All the intestinal biopsies received in the department of Pathology of M.S. Ramaiah Medical College, Bangalore, from November 2015 to November 2016 were evaluated. Specific criteria for diagnosis of eosinophilic enterocolitis was used, criteria being eosinophils ranging from 10-50/HPF in the biopsies. Correlation with peripheral eosinophilia was also done.

Methods and Material: All the intestinal biopsies received in the department of Pathology of M.S. Ramaiah Medical College, Bangalore, from November 2015 to November 2016 were evaluated. Specific criteria for diagnosis of eosinophilic enterocolitis was used, criteria being eosinophils ranging from 10-50/HPF in the biopsies. Correlation with peripheral eosinophilia was also done.

Statistical Analysis used: Statistical analysis is not required as it is a analytical study.

Results: A total of 52 cases of intestinal biopsies were obtained during the one year study period. Out of the 52 cases, 5 cases (9.6%) were diagnosed as eosinophilic enterocolitis. Out of the 52 cases, 3 cases (60%) were associated with peripheral eosinophilia. Out of the 5 patients with eosinophilic enterocolitis, 4 were men and only 1 was a woman, suggesting male preponderance (80%).

Conclusions: The incidence of eosinophilic enterocolitis is increasing in recent years. Hence this condition should be considered in the differential diagnosis whenever a patient presents with chronic diarrhea. Timely treatment can prevent major complications in these patients.

Keywords: Eosinophilic Enterocolitis; Peripheral Eosinophilia.

Introduction

Eosinophilic enterocolitis is a rare inflammatory disease of unknown origin, characterised by diffuse eosinophilic

infiltration of gastrointestinal tract, accompanied by varying abdominal symptoms [1,2]. Any part of gastrointestinal tract may be involved, although stomach and small bowel are the most common sites. A large

proportion of these patients demonstrate peripheral eosinophilia. Though, it is a rare condition, reports of eosinophilic enterocolitis has markedly increased over the last fifteen years [1]. Certain conditions like drug related gastroenteritis, parasitic diseases, Crohn's disease, milk protein enteropathy, Churg-Strauss syndrome, scleroderma, polyarteritis nodosa should be ruled out. The clinical importance of the condition is that it can result in certain complications such as malnutrition, intestinal obstruction and perforation [3,4].

Eosinophils are predominantly tissue-dwelling cells; at any time comparatively few are circulating in the blood. Most are found in the bone marrow, where they are formed, and in the lamina propria of the gastrointestinal tract, of which they are a normal component. They act as a protective agent against parasites. Eosinophils respond to stimuli like trauma, infection and allergens, by degranulating to release inflammatory mediators: leukotrienes, vasoactive intestinal polypeptide, tumour necrosis factor, and interleukins [3].

The clinical features of eosinophilic enterocolitis usually are non-specific like abdominal pain, diarrhea, rectal bleeding [3]. Due to lack of distinctive clinical findings, and its relapsing-remitting course, it is necessary to establish the diagnosis of eosinophilic enterocolitis by examination of colonic biopsy. As the condition is increasing in frequency in recent years and is associated with major complications if untreated, it is very necessary to diagnose the condition. In cases of certain non-specific signs and symptoms like nausea, vomiting, diarrhea, this entity has to be considered. Hence, the present study was done to evaluate for eosinophilic enterocolitis in intestinal biopsies, and to correlate with peripheral eosinophilia.

Materials and Methods

All the intestinal biopsies received in the department of Pathology of M.S. Ramaiah Medical College, Bangalore, from November 2015 to November 2016 were evaluated. Patients who had clinical symptoms like abdominal pain, nausea, vomiting, diarrhea, gastrointestinal bleeding, were subjected to endoscopic evaluation. Depending on the clinical features and areas that showed lesions on

endoscopy, biopsies were obtained from different sites like, duodenum, jejunum, ileum, colon and rectum. Thus a total of 52 cases of intestinal biopsies were obtained during the one year study period. Specific criteria for diagnosis of eosinophilic enterocolitis was used, criteria being eosinophils ranging from 10-50/HPF in the biopsies [5]. A minimum of 10 high power fields were checked for the presence of eosinophils and counting was done. The average of the counts obtained in all the high power fields evaluated, was taken as the final count.

Other conditions that can cause secondary eosinophilic infiltration in the bowel were looked for such as parasitic colitis, drug induced colitis, inflammatory bowel disease, and those were excluded before making a diagnosis of eosinophilic enterocolitis. Correlation with peripheral eosinophilia was also done. In a single case, bone marrow biopsy was also done and correlation with the bone marrow biopsy finding was done. Correlation with other clinical features was also done. The age and sex distribution as well as range of peripheral eosinophilia in all cases were tabulated.

Results

A total of 52 cases of intestinal biopsies were obtained during the one year study period. Out of the 52 cases, 5 cases (9.6%) were diagnosed as eosinophilic enterocolitis. The range of eosinophil counts seen in the biopsies was 10-40/HPF. The ages of the patients having eosinophilic enterocolitis ranged from 14 years to 67 years, mean age being 38.4 years. Out of the 5 patients with eosinophilic enterocolitis, 4 were men and only 1 was a woman, suggesting male preponderance (80%). The age of the woman affected was 39 years.

Out of the 52 cases, 3 cases (60%) were associated with peripheral eosinophilia. One of the patients was a boy aged 14 years who had peripheral eosinophilia of 62% with absolute eosinophil count 5135/ μ l. Another case had 22% of eosinophils in the peripheral blood while the third case had 15% eosinophils in the peripheral blood. Majority of the cases (80%) were associated with a history of diarrhea, vomiting. Other symptoms like gastrointestinal bleeding and abdominal pain were also seen in a single case.

Table 1: shows the age, sex, clinical features, number of eosinophils/HPF in the colonic biopsies and percentage of eosinophils in the peripheral blood in the 5 cases that were diagnosed as eosinophilic enterocolitis.

Sl. No.	Age	Sex	Clinical features	No. of eosinophils/HPF in colonic biopsies	% of eosinophils in peripheral blood
1	39 yrs	Female	Vomiting, diarrhea	15/HPF	No eosinophilia
2	37 yrs	Male	Vomiting, diarrhea	15/HPF	No eosinophilia
3	67 yrs	Male	Gastrointestinal bleeding, vomiting, abdominal pain	25/HPF	22%
4	35 yrs	Male	Vomiting, diarrhea	18/HPF	15%
5	14 yrs	Male	Vomiting, diarrhea	42/HPF	62%

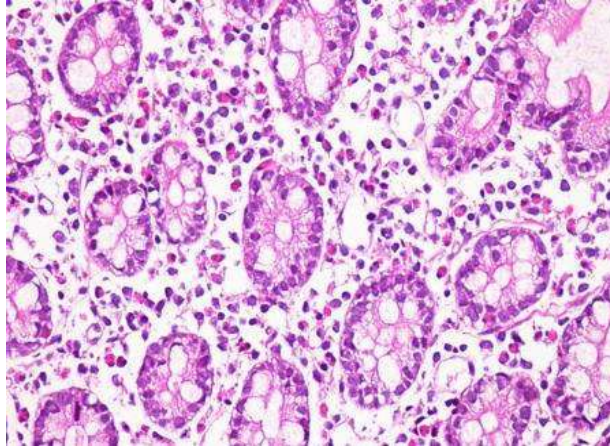


Fig. 1: Colonic biopsy showing increased eosinophils in the lamina propria (Hematoxylin and Eosin, x200)

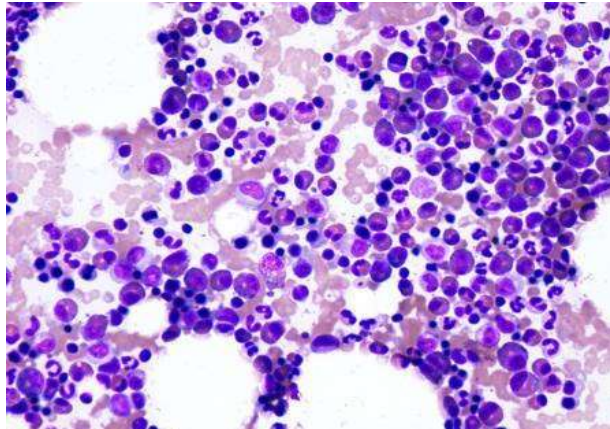


Fig. 2: Bone marrow aspirate in one case showing increased eosinophils (Leishman's stain, x400)

In the 14 year old boy with history of vomiting and diarrhea with peripheral eosinophilia of 62%, biopsies studied from multiple sites: oesophagus, stomach, duodenum and colon showed eosinophils ranging from 30-42/HPF. The bone marrow aspirate which was also evaluated, showed eosinophilia. (Table 1 & Figure 1,2).

Discussion

Eosinophilic enterocolitis is a rare clinical entity characterized by inflammation rich in eosinophils, without evidence of known causes for eosinophilia, such as parasitic infection, drug reaction, or malignancy [5,6]. The disease can affect any segment or combination of segments of the gastrointestinal tract from the esophagus to the rectum, giving rise to various clinical presentations including eosinophilic esophagitis, eosinophilic gastritis, eosinophilic gastroenteritis, and eosinophilic colitis. Since secondary eosinophilic inflammation may occur in numerous gastrointestinal disorders such as IgE-mediated food allergy, gastroesophageal reflux disease, and

inflammatory bowel disease, the true incidence and prevalence of primary eosinophilic enterocolitis remains largely unknown [5,6].

Eosinophilic enterocolitis has three hallmarks including peripheral eosinophilia (typically in the range of 5% to 35%), segmental eosinophilic infiltration of the gastrointestinal tract, and functional abnormalities. Signs and symptoms of eosinophilic enterocolitis are very non specific and depend on the site that is affected, usual signs and symptoms being nausea, vomiting, diarrhea, gastrointestinal bleeding, abdominal pain, ascites [7,8].

The diagnosis of eosinophilic enterocolitis is made from the presence of gastrointestinal symptoms, peripheral eosinophilia, endoscopic and histological findings, and eosinophilic ascites, with no well-defined causes of eosinophilia on thorough evaluation. Various other causes for tissue eosinophilia include inflammatory bowel disease particularly Crohn's disease, parasitic infestations by pinworms, roundworms, whipworms, drugs like clozapine, carbamazepine, gold, tacrolimus, non steroidal anti-inflammatory drugs, and autoimmune conditions like scleroderma, polymyositis, dermatomyositis. All these are to be ruled out before diagnosing eosinophilic gastroenteritis [7,8].

The etiology of primary eosinophilic enterocolitis remains largely unknown. Several studies suggested association with certain food allergies like cow's milk and soy proteins. Some studies suggested that around 75% had history of allergy or atopy [7,8]. Eosinophilic enterocolitis, if not treated can result in major complications such as malnutrition, intestinal obstruction and perforation. Hence, diagnosis of eosinophilic enterocolitis is very important [9].

Our study highlights the incidence, age and sex predilection, association with peripheral eosinophilia and associated clinical features of the condition. The incidence of eosinophilic enterocolitis in our study was 9.6% (5 out of 52 intestinal biopsies). Majority of previous studies state that the incidence of eosinophilic enterocolitis is very low being less 1% with increase in the incidence in recent years. Our study supports the fact that the incidence is slightly increasing.

In a review study conducted by Ingle et al, it was stated that, eosinophilic gastroenteritis occurs over a wide age range from infancy through the seventh decade, but most commonly between third to fifth decades of life [5]. Another review article by Ishihara et al. stated that eosinophilic gastroenteritis is more common in the third and fourth decades [10]. In our study, the mean age of patients with eosinophilic enterocolitis was 38.4 years with 3 out of 5 being in the fourth decade, the ages being, 37, 35 and 39 years. This shows good correlation with other studies.

Ingle et al. stated that there is a slight male

preponderance in the patients with enterocolitis [5]. Ishihara et al also stated that men are more affected by eosinophilic enteritis [10]. Our study also shows male preponderance with 4 out of 5 patients being men, supporting their statement.

A study of 15 cases of eosinophilic gastroenteritis done by Chen et al stated that the most common clinical symptoms seen were diarrhea and abdominal pain. Our study showed majority (4 out of 5) patients showing similar clinical features, the main symptoms being diarrhea and vomiting [11].

Ishihara et al states that peripheral eosinophilia is seen in 40-60% of patients with eosinophilic enterocolitis which is supported by our study that shows 3 out of 5 cases (60%) showing peripheral eosinophilia [10].

Conclusion

The incidence of eosinophilic enterocolitis is increasing in recent years. Hence this condition should be considered in the differential diagnosis whenever a patient presents with chronic diarrhea. Timely treatment can prevent major complications in these patients.

Acknowledgement

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Conflict of Interest:

Nil

Key Messages

The incidence of eosinophilic enterocolitis is increasing in recent years and it is associated with complications. Hence, keeping it in mind while diagnosis is very important.

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