CASE REPORT

EOSINOPHILIC GASTRITIS; AN UNUSUAL AND OVERLOOKED CAUSE OF CHRONIC ABDOMINAL PAIN

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Eosinophilic gastritis is an extremely rare disorder. The disease is associated with eosinophilic infiltration of various layers of gastrointestinal tract along with significant peripheral eosinophilia and increased Immunoglobulin E (IgE). We report a case of 37 year old Saudi male who presented with chronic non-specific upper abdominal pain. On initial workup, the diagnosis was missed. However the diagnosis was established after subsequent work up in Gastroenterology clinic. Our case demonstrates that patients with uncharacteristic abdominal pain who are unresponsive to conventional treatment, rare illnesses like eosinophilic gastritis should be considered. We also aim to review the clinicopathological features, differential diagnosis and various treatment options of this disorder. To the best of our knowledge, this disease has not been previously reported from Saudi Arabia.

Keywords: Eosinophilic Gastritis; Eosinophilia; Atopy; Food Allergy; Bronchial Asthma; Abdominal pain

INTRODUCTION

Eosinophilic Gastritis is an extremely uncommon disorder. The disease is characterized by eosinophilic infiltration of various layers of gastrointestinal tract in the absence of any known cause of eosinophilia. The infiltration may be mucosal, muscularis or serosal causing variability in presentation. Most patients have peripheral eosinophilia along with raised Immunoglobulin E (IgE). Endoscopy and histopthological examination of the biopsies are an essential part of the diagnostic work-up. Most patients are initially treated with high dose steroids. However the disease usually recurs after withdrawal of steroids. Other therapeutic options include immunosuppressive drugs, leuktriene inhibitors and immunomodulators like Alfa Interferons. These have variable success in induction and maintenance of remission. The prognosis is considered benign with a waxing and weaning course.

CASE HISTORY

Thirty seven year old Saudi gentleman presented in the medical clinic of this hospital in early 2004 with history of recurrent epigastric pain for the last few months before presentation. The pain was unrelated to food ingestion or bowel movement and was non-radiating. He denied any history of anorexia, weight loss, hematemesis, melena or ingestion of non-steroidal anti-inflammatory drugs. He was known to have bronchial asthma since childhood and has been on Salbutamol inhaler on as required basis. He was married, non-smoker and worked as a soldier. He denied any history of alcohol or substance abuse. There was no past or family history of eczema or atopy.

On examination, he was a young healthy looking gentleman with no evidence of pallor, jaundice, cyanosis or palpable lymphadenopathy. There were no stigmata of chronic liver disease. Abdominal examination did not reveal any organomegaly. Rest of the systemic examination was also within normal limits.

Initial investigations revealed haemoglobin of 15.2 g/dl, white blood cells of $7.3\times10^3/\mu L$ and platelets of $275\times10^3/\mu L$. The differential count was normal. ESR was 4 mm after 1st hour. Urea, Creatinine, electrolytes, glucose and liver function test were within normal limits. Serology for HBsAg, anti-HCV and HIV were negative. Prothrombin time (PT) and Partial Thromboplastin time (PTT) were normal. The abdominal ultrasound was reported as normal. An upper GI Endoscopy revealed small sliding hiatus hernia with features of marked antral gastritis. Gastric Antral mucosal biopsies revealed infiltration of lamina propria by lymphocytes and plasma cells. Helicobacter pylori (H. Pylori) were also observed in epithelial cells. Patient was treated with triple therapy of Amoxicillin, Clarithromysin and Omeprazole for H. Pylori eradication and was subsequently continued on once a day Omeprazole. He also received treatment with medications like anticholinergics, H_2 receptor blockers and antidepressants. However the patient remained symptomatic with abdominal pain. He was referred to Gastroenterology clinic in May 2005 for further evaluation and management. At this stage, his main symptoms were persistent abdominal pain and dyspepsia. It was decided to have a complete re-evaluation of patient with laboratory work-up and Endoscopy.

His CBC revealed a HB of 15.5 g/dl. WBC and platelets were normal. Differential white blood

count revealed neutrophils 22%, lymphocytes 34%, eosinophils 37% and monocytes 7%. Urea, electrolytes, LFT, calcium studies and glucose were normal. Upper GI Endoscopy revealed small sliding hiatus hernia with erythematous and hypertrophied gastric mucosal folds involving the antrum and body of stomach (Fig-1). Erosive changes were also seen in the duodenal mucosa. Histological examination of gastric mucosal biopsies showed dense infiltration of the lamina propria with eosinophils with mild cryptitis. No H. Pylori or metaplasia was observed (Fig-2 and 3). Duodenal mucosal biopsies also showed infiltration of lamina propria with eosinophils. Histology was highly suggestive of Eosinophilic Gastritis. Subsequent work-up with stool analysis and duodenal aspirate showed no evidence of ova and parasites. His antinuclear antibodies, anti-DNA, P-ANCA and C-ANCA were negative. Immuno-electrophoresis for IgE was 3888 mg/dl (Normal: <240.0 mg/dl). Colonoscopy and biopsies of colonic and terminal ileal mucosa were normal.

Patients was commenced on Prednisone 60 mg/day and kept o this dose for 4 weeks. Patient had subjective improvement in pain. Afterwards, steroids gradually reduced and patient was kept on small dose of maintenance steroids. After 3 months of treatment, his eosinophilic count dropped to 24% with an absolute eosinophilic count of 2230/μL but serum IgE did not show any significant change. However the abdominal pain recurred on reducing the dose of steroids. There was also no significant endoscopic and histological improvement. He was also given a trial of Montelukast, a leukotriene receptor antagonist without much clinical and haematological response. He was subsequently referred to a specialist hospital. Currently, he is being treated with Interferon Alpha 2a 3 MU three times/week with low dose steroids and is having significant clinical improvement.

DISCUSSION

Eosinophilic Gastrointestinal disorder (EGID) is an uncommon and rarely reported disorder affecting various parts of the gastrointestinal (GI) tract. The disease is defined as a disorder characterized by eosinophilic infiltration of one or more areas of GI tract in the absence of any known cause of eosinophilia and exclusion of eosinophilic infiltrations in organs other than gut.[1] Depending upon the area involved, the disease can present as eosinophilic oesophagitis, oeosinophilic gastritis (EG), eosinophilic gastroenteritis (EGE) or eosinophilic colitis.[2] The disease was probably first reported by Foit and Gross in 1950.[3] Since then, an increasing number of cases from different regions of the world involving different parts of the GI tract have been reported. More cases have been described in paediatric populations. The disease has not been previously reported from Saudi Arabia. This forms the first case report of patient with eosinophilic gastritis from Saudi Arabia.

The exact pathophysiology of the disease is unknown, but is associated with selective infiltration of eosinophils in parts of GI tract.[4] The disorder is classified into primary or secondary sub-types. The primary sub-types include atopic, non-atopic and familiar variants. This has also been called allergic idiopathic eosinophilic gastritis. Eosinophilic involvement of the gut may be mucosal, muscularis and serosal causing variability in the presentation.[5] Allergic mechanisms maybe responsible in some patients. Most patients have increased total Immunoglobulin E (IgE) and food specific IgE. In some patients, increased secretion of interleukin 4 (IL4) and interleukin 5 (IL5) from peripheral blood T cells home have been reported.[6]

The disease predominantly affects white Caucasian males in the third to fifth decade of life. A history of atopy and allergy is considered to be a risk factor. Clinical presentation depends on the site of GI tract and depth of bowel wall involved. The mucosal form usually presents with abdominal pain, vomiting, diarrhoea, GI blood loss, malabsorption and/or protein losing Enteropathy.[7] The muscularis form presents with various GI obstructing symptoms and the disease may resemble pyloric stenosis or malignancy.[8] The serosal form is extremely rare and usually present with eosinophilic ascites.[9] About 50% of patients have history of atopy (asthma, hay fever or food allergy). Younger children and adolescents may present with developmental delays and failure to thrive. The differential diagnosis of Eosinophilic gastrointestinal disease includes a variety of condition including Celiac Sprue, Chrug-Staruss Syndrome, Eosinophilic Granuloma, Lymphomas, Polyarteritis Nodusa, Dermatomycosis, Parasitic infections, and cow milk Enteropathy. A variety of drugs and hyper-oeoesinophilic syndrome can present with similar picture.[10]

The Diagnostic work-up of patients with EG and EGE are summarized in Table-I. Laboratory standard for the diagnosis of the disease are not well characterized but a few findings support the diagnosis.[2] Peripheral blood eosinophilia and elevated IgE level may suggest an atopic disorder but are not seen in all patients.[9] Lack of involvement of other organs and exclusion of other causes of eosinophilia support the diagnosis. Skin testing for food allergy may help in the management but has a minor role in diagnosis. Endoscopic features of EGE may include prominent mucosal folds, hyperemia, ulcerations or nodularity (Figure-1). Sometimes features may be subtle and

Endoscopist must, therefore, be aware of the disease and obtain biopsies in suspected cases. Histology is the 'gold standard' for diagnosis of EGE. Common histological features includes increase number of eosinophils (>50/HPF) in lamina propia (Figure-2 and 3). Large number of eosinophils may also be present in the muscularis and serosal layer which may produce crypt hyperplasia, epithelial cell necrosis and villous atrophy.[4,11] Our patient had full laboratory and endoscopic work up on initial presentation. He was diagnosed to have H. Pylori gastritis. Eosinophilic infiltration of the mucosa was not obvious at this stage. It is possible that that the disease may not have fully presented or the endoscopist may have failed to obtain the biopsies from involved areas. It is not clear whether H. Pylori has any causal relationship with eosinophilic gastritis or is it a chance coincidence.[12] However, our patient failed to improve symptomatically and endoscopically after successful H. Pylori eradication.

Table-1: Diagnostic work-up for EGE

Laboratory
• General History & Examination
• Complete blood count and differential
• Erythrocyte Sedimentation Rate
• Chemistry (serum bilirubin)
• Total IGE
• Fecal Protein
• Infection Workup (stool, colonic aspirate analysis)Skin Prick Test
Imaging studies
• Barium Studies
• Ultrasound
• CT Abdomen.
Others
• Endoscopy & biopsy of Upper & Lower GI tract
• Ascitic fluid analysis
• Echocardiogram

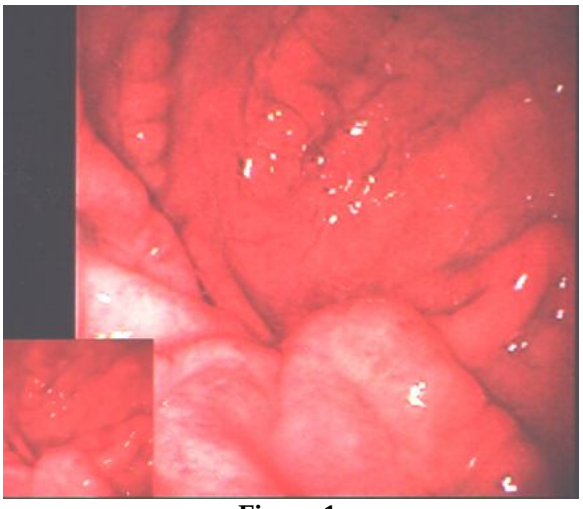

Figure-1.

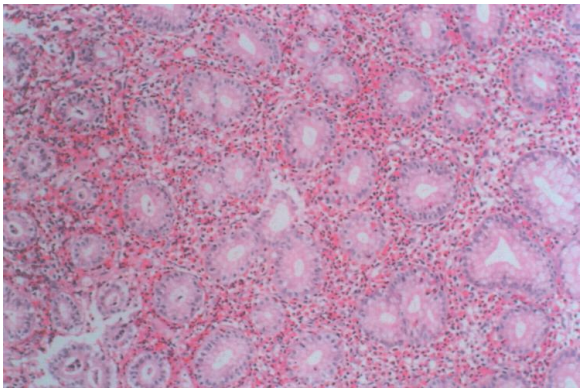

Figure-2.

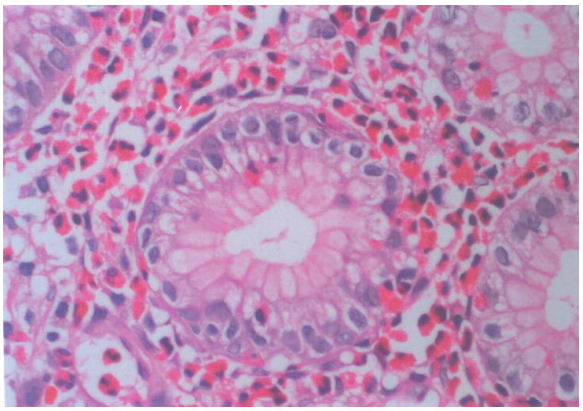

Figure-3.

A variety of treatment regimens have been used for management of patients with varying degree of success. The therapeutic regimens are not based in any randomised controlled trials or evidence based guidelines, as most of the published studies are based on case series. It is not clear whether goals of treatment should be aimed at symptomatic improvement, histological improvement or both. Avoiding the dietary intake of food implicated by skin prick and use of elemental diet has been reported to have a variable effect.[13] In adults, compliance may be a major problem. Moreover, food allergies are more common in children and more readily identified than children.

Systemic or topical steroids are the mainstay of therapy in cases where dietary restriction is not feasible or has failed to produce any improvement.[14] However, long term use of steroids is complicated by esophageal candidiasis and adrenal suppression. Most patients relapse symptomatically and histologically after cessation of therapy and may require repeated courses or maintenance steroids. Other treatment options that target eosinophils have been reported in case studies Leukotriene Inhibitor, montelukast has been reported to be beneficial in some case reports in producing symptomatic improvement.[15] Drugs like Cromoglycate, Ketotifen and Nycophenolate notefil have also been tried but are generally considered to be

unsuccessful.[16] In some refractory cases immunosuppressive drugs like Azathioprine or 4-mercaptopurine have been tried with variable success. Alpha Interferon has been reported to be successful in few patients with hypereosinophilic syndrome and chronic eosinophilic leukemia.[17] Whether Interferon Alpha can produce symptomatic and histological improvement in patients with EG remains to be seen.

The long-term prognosis of the disease has not been clearly documented. It tends to be a chronic waxing and waning disorder with no significant effect on morbidity and mortality. No increased risk of malignancy has been demonstrated.

CONCLUSION

Eosinophilic gastritis is rare disorder and can present with a variety of symptoms. The physicians should have a high index of suspicion in patients presenting with uncharacteristic symptoms or unresponsive to conventional therapy. Histological confirmation is essential for diagnosis. The disease needs to be differentiated from generalized eosinophilic disorder presenting with organ involvement other than GI tract. Currently the steroids appear to be the main stay of treatment, but most patient relapse after withdrawal of treatment.

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