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EOSINOPHILIC GASTROINTESTINAL DISORDERS: EXPERIENCE OF A TUNISIAN CENTER

***Elleuch Nour, Sonda Jardak, Dahmani Wafa, Jaziri Hanene, Aida Ben Slama, Aya Hammami, Salem Ajmi, Braham Ahlem, Ksiaa Mehdi and Jmaa Ali**

Department of Gastroenterology, Hospital Sahloul, Sousse, Tunisia.

***Corresponding Author: Elleuch Nour**

Department of Gastroenterology, Hospital Sahloul, Sousse, Tunisia

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ABSTRACT

Introduction: Eosinophilic gastrointestinal disorders (EGD) are rare chronic digestive pathologies characterized by an eosinophilic infiltration of the digestive tract in the absence of secondary causes for eosinophilia. Their diagnosis reprensents a real challenge to clinicians because of aspecific clinical features. **Objective:** to analyze the clinical, biological, radiological characteristics of EGD as well as the endoscopic, histological and therapeutic features of these disorders through to the experience of a Tunisian center. **Methods:** a retrospective study from 2006 to 2017 including patients diagnosed with EGD based on three criteria: Suspicious clinical symptoms, histologic evidence of eosinophilic infiltration in the bowel and exclusion of other pathologies with similar findings. Results: A total of 16 cases of EGD were collected, divided into eosinophilic esophagitis (9 patients), eosinophilic gastroenteritis (3 patients) and eosinophilic colitis (4 patients). Mean age was 36.8 (12-52 years). The sex ratio was 1.66 (M/F=10/6). More than half of patients had a personal history of atopic disease (n=9). Symptoms were non-specific and various: dysphagia (n=7), diarrhea (n=3), abdomianl pain (n=3), vomiting (n=2) and ascitis (n=1). The third of patients had increased numbers of circulating eosinophils. Total IgE levels were increased in 37.5% of patients (n=6). The definitive diagnosis was based on histological results : tissue obtained during upper gastro intestinal endoscopy (n=11), colonoscopy (n=4) and laparoscopy (n=1). The treatment was based on corticosteroids (n=9), proton pump inhibitor (n=4), salicylates (n=2) and dietary therapy (n=1). **Conclusion:** EGD are uncommon and heterogeneous diseases. Up to now, many problems still left to be answered. In the future, large and high-quality studies are needed to further investigate the pathophysiology of EGD and to make standard guidelines for the diagnosis and management.

KEYWORDS: Eosinophilic esophagitis, Eosinophilic gastroenteritis, Diagnosis, Therapy.

INTRODUCTION

Eosinophilic gastrointestinal disorders (EGD), first described in 1937 by Kaijser, are rare chronic pathologies of the digestive system, with an immuno-mediated pathogenesis.[1] They are characterized by selective infiltration of gastrointestinal tract by eosinophils, in absence of other causes of known eosinophilia.[2] These disorders can be divided into five principal groups: eosinophilic esophagitis (EoE), eosinophilic gastritis, eosinophilic gastroenteritis (EG), eosinophilic enteritis, and eosinophilic colitis (EC).[3] Their clinical manifestations are aspecific, depending on the involved intestinal segments and layers[4], which makes their diagnosis difficult. The diagnosis is centered on biological, radiologic and endoscopic findings and cofirmed by histological examination from biopsy samples. Treatment of EGD includes dietetic and pharmacological approach.[2] Corticosteroids represent the main therapy.[3] The EGD was studied only in the latest decades and, also due to the rarity of these disorders, the data about epidemiology, pathogenesis, therapy and outcomes thus far available are partial. This study was aimed to analyze the diagnostic and therapeutic features of these disorders through to the experience of a Tunisian center.

PATIENTS AND METHODS

Study design

This was a retrospective study including patients with EGD admitted in the hepato-gastroenterology department of Sousse between January 2006 and December 2017. The diagnosis was made based on three criteria: Suspicious clinical symptoms, histologic evidence of eosinophilic infiltration in one or more areas of the GI tract (>20–25 eosinophils per high-power field (HPF) for gastroenteritis, >15 eosinophils/HPF for oesophagitis) and exclusion of other potential causes of eosinophilia.[3]

Data collection

Data including patients' signs and symptoms, past personal and familial history especially allergic diseases were collected. Routine blood evaluation (including

white blood cell count, percentage of eosinophils, and absolute eosinophil count) was carried out. Immunologic status (quantitative immunoglobulins and IgE, antinuclear antibody, protein electrophoresis) was analyzed. In patients with ascites, abdominal paracentesis was preformed. All patients underwent upper gastrointestinal endoscopy (UGE) with esophageal, gastric and duodenal biopsies. According to the clinical symptoms, patients underwent colonoscopy, abdominal ultrasonography or laparoscopy. For the histological diagnosis, specimens were obtained both from abnormal appearing sites in the GI tract and/ or sites that appeared normal, and slides were reviewed by an experienced histopathologist.

RESULTS

Epidemiology and clinical features

We reported 16 cases of EGD: EoE (9 cases), EG (3 cases) and EC (4 cases). Mean age was 36.8 (12-52 years). The sex ratio was 1.66 (M/F=10/6). Fifty six percent of patients had personal history of atopic disease (n=9). Three patients (18.7%) had a history of allergy to food or pollen. The median duration of symptoms before diagnosis was 36 months (3- 60 months). Clinical signs were non-specific and various. The most common symptoms in our series are shown in Table 1.

Laboratory findings

One third of patients (n=5) had an elevated total peripheral eosinophil count (mean 0.52 ± 0.34 × $10^3/mm^3$) and an elevated percentage in total white blood lines (mean 5.2 ± 0.3%). Six patients (37.5%) had elevated total serum IgE. No patient had specific IgE antibodies. Skin prick tests perfomed in two patients, were positive in one case. In the patient with ascites, peritoneal fluid analysis revealed an exudative ascites with a leucocyte count of 1600/ mm^3 (70% eosinophils). The fluid was sterile on bacterial and tubercule culture and negative for malignant cells.

Radiological and endoscopic findings

Abdominal ultrasound (US) was performed in 3 patients complaining of abdominal pain and showed ascites in one case. Computer tomography (CT) (performed in 4 patients) demonstrated intestinal wall thickening (n=2) and ascites (n=1). UGE was normal in 62.5% of patients (n=10). Four patients had mucosal signs suggestive of EoE diagnosis (44.4% of patients with EoE). In particular, endoscopy revealed fixed esophageal rings (n=2), whitish exudates (n=1) and longitudinal furrows (n=1). One patient had antral mucosal erythema and 1 patient had antral mucosal nodules.

Ileocoloscopy with biopsies was performed in 10 patients (62.5%). Endoscopic aspect was normal in 80 % of cases (n=8) and showed abnormalities in 2 cases: colic mucosal erythema (n=1) and ulcerated mucosa (n=1). Laparoscopy was performed in one patient with ascites and showed hyperemia of parietal peritoneum and free ascites.

Histological data

Microscopic evaluation of endoscopic biopsy samples showed an eosinophilic infiltration of esophageal mucosa (n=9), stomach (n=2) and colic mucosa (n=4). Mean number of eosinophils/hpf in the biopsy was 63 (range: 20-260).

Treatment modalities

All patients underwent treatment. For one patient who refused medical treatment, we opted for dietary therapy. No patient underwent endoscopic or surgical treatment. Treatment modalities were summarized in Table II.

Outcomes

Symptoms were relieved in 87.5% of cases after a mean follow up of 10 months (2-105 months). Two patients had a relapse after discontinuing steroids.

Table I: Epidemiological and clinical characteristics of patients with eosinophilic gastrointestinal disorders according to the involved intestinal segment.

	EoE (n=9)	EG (n=3)	EC (n=4)
Age (years)	39 (28-52)	32 (12-47)	39.5 (28-47)
Sex ratio (M/F)	5/4	2/1	3/1
Atopic disease	3	1	0
-bronchial asthma	1	1	1
-allergic rhinitis	1	0	1
-atopic dermatitis			
Symptoms	7	0	0
- Dysphagia	3	0	0
- Chest pain	2	0	0
- Food impaction	0	2	2
-Abdominal pain	0	1	0
-Vomiting	0	1	0
-Ascites	0	0	2
-Diarrhea			

EoE: eosinophilic esophagitis, EG: eosinophilic gastroenteritis, EC: eosinophilic colitis.

Table II: Treatment modalities of eosinophilic gastrointestinal disorders.

	EoE (n=9)	EG (n=3)	EC (n=4)
Corticosteroids	4	3	2
Proton pump inhibitor	4		
Salicylates	0	0	2
Dietary therapy	1	0	0

DISCUSSION

In our study, we reported 16 cases of EGD: 9 cases of EoE, 3 cases of EG and 4 cases of EC. The Mean age was 36.8 with a male predominance. Our results are in agreement with these findings in literature. In fact, based on the hundreds of cases or small case series reported worldwide, EGD can affect any age group from infancy to the aged, however, most commonly between thirties to forties years of age, with a slightly male predominance.[5] Concomitant allergic disorders, including asthma, rhinitis, eczema and drug or food intolerances, are present in 45% to 63% of the reported EGD cases which is comparable to our results.[6] Symptoms are non-specific and various depending on the site of affected GI tract and the layer of the GI wall involved.[3] EG can

affect any GI segment, but with a predominance of the small intestine and stomach. The disease is divided into three subtypes according to klein's classification: mucosal which is the most frequent, muscular and serosal.[4] Abdominal pain is the predominant symptom. In our series, 2/3 of patients with EG were complaing of abdominal pain and had a mucosal and gastric localisation. One patient had an involvement of the serosal layer associated with an eosinophilic gastritis. Concerning EoE, the major symptoms are solid food dysphagia and esophageal food impaction. Less commonly, patients present with heartburn and chest pain mimicking gastroesophageal reflux disease.[7] Our results were concordant with the litterature. EC is the least frequent manifestation of EGD.[8] The clinical presentation includes abdominal pain, diarrhea (bloody or nonbloody), and/or weight loss[8], this is the case in our study. Following assessment of the patient's initial presentation, the next step toward diagnosis will require laboratory tests, endoscopy or imaging studies.[4] Peripheral eosinophilia in the context of gastrintestinal symptoms is a useful clue to EGD, but this test is not a reliable diagnostic criterion.[3] In fact, it can be absent in authentic GID, such as our series which 66% of patients had not an eosinophilia. Added to this, it is not correlated to the disease activity and is not reliable for following up patients after therapy.[9] Total IgE level and specific IgE antibodies can be elevated but are non-specific.[3] Imaging studies are another diagnostic modality that has proven useful. Abdominal US and CT can detect diffuse thickening of mucosal folds, intestinal wall thickening, ascites and obstruction.[4] But, in most of patients with EGD, radiological findings are normal. In our series, imaging studies performed in 7 patients were normal in 3 cases.

The endoscopic appearance in EG and EC is non specific, including erythematous, friable, nodular, and occasional ulcerative changes.[10] Several reports had shown endoscopic exams were normal in about half of patients.[3] For EoE, linear furrows, concentric rings, white exudates, decreased vasculature in the esophageal mucosa, esophageal strictures, and the esophagus of narrow caliber, have been reported to be the suggestive of the disease, although neither of these is specific.[11] The results were similar in our study: 4 patients had endoscopic findings suggestive of EoE, 2 patients had mucosal erythema, 1 patient had mucosal nodules and 1 patient had ulcerated mucosa (n=1).

Histologic examination remains the cornerstone of diagnosis. Eosinophilic infiltrates are usually patchy in distribution and may be present in otherwise normal, non-inflamed bowel wall. Therefore, multiple biopsies may be required to avoid missing the diagnosis.[10] In our study, the definitive diagnosis was established by endoscopic biopsy in all of patients. Recently, a peak of 15 eosinophils/HPF for EoE and 20-25 eosinophils/HPF for EG and EC had been defined as the diagnostic minimum threshold in the majority of clinical studies.[3]

Up to now, there is no consensus optimal treatment strategy of EG. Case series have demonstrated that corticosteroids are the optimum therapeutic drugs.[3] Because of a high proportion of association with food allergy, dietary therapy can be used as an initial therapy or when other modalities of treatments fail.[7] Intestinal obstruction can be reversible with medical treatment, contrary to perforation which indicates surgery to repair damage.

Our study has several limitations: especially her retrospective character, and the small number of patients. This is related to the rarety of the disease. Therefore, a prospective study will be more appropriate, but to our knowledge, any prospective study has yet been published in the literature. The strength of this is study is that it is the first one that interested to EGD in Tunisian patients.

CONCLUSION

EGD are uncommon and heterogeneous diseases. Their diagnosis requires a combination of clinical and pathologic criteria. Corticosteroids represent the main treatment but have serious side effects of long-term application that cannot be ignored. Up to now, many problems still left to be answered. In the future, large and high-quality studies are needed to further investigate the epidemiology and pathophysiology of EGD and to make standard guideline for the diagnosis and management.

REFERENCES

1. Liacouras CA, Furuta GT, Hirano I, et al. Eosinophilic esophagitis: updated consensus recommendations for children and adults. J Allergy Clin Immunol., 2011; 128: 3–20.
2. Erminia Ridolo, Valerie Melli, Gianluigi De' Angelis, and Irene Martignago. Eosinophilic disorders of the gastro-intestinal tract: an update. Clin Mol Allergy., 2016; 14: 17.
3. Zhang M, Li Y. Eosinophilic gastroenteritis: A state-of-the-art review. J Gastroenterol Hepatol. 2017 Jan; 32(1): 64-72.
4. Abou Rached A, El Hajj W. Eosinophilic gastroenteritis: Approach to diagnosis and Management. World J Gastrointest Pharmacol Ther 2016 November 6; 7(4): 513-523.
5. Chang JY, Choung RS, Lee RM, et al. A shift in the clinical spectrum of eosinophilic gastroenteritis toward the mucosal disease type. Clin. Gastroenterol. Hepatol., 2010; 8: 669–675.
6. Jensen ET, Martin CF, Kappelman MD, Dellon ES. Prevalence of Eosinophilic Gastritis, Gastroenteritis, and Colitis: Estimates From a National Administrative Database. J Pediatr Gastroenterol Nutr, 2016; 62: 36-42.
7. Monjur Ahmed. Eosinophilic esophagitis in adults: An update. World J Gastrointest Pharmacol Ther., 2016 May 6; 7(2): 207–213.
8. Abdulrahman A. Alfadda, MD and Martin A. Storr, MD Eosinophilic colitis: epidemiology, clinical

features, and current management. Therap Adv Gastroenterol., 2011 Sep; 4(5): 301–309.
9. Ko HM, Morotti RA, Yershov O, et al. Eosinophilic Gastritis in Children: Clinicopathological Correlation, Disease Course, and Response to Therapy. Am. J. Gastroenterol., 2014; 109:1277–1285.
10. Ming-Jen Chen, Cheng-Hsin Chu, Shee-Chan Lin, Shou-Chuan Shih, and Tsang-En Wang. Eosinophilic gastroenteritis: Clinical experience with 15 patients. World J Gastroenterol., 2003 Dec 15; 9(12): 2813–2816.
11. Kim HP, Vance RB, Shaheen NJ, Dellon ES. The prevalence and diagnostic utility of endoscopic features of eosinophilic esophagitis: a meta-analysis. Clin Gastroenterol Hepatol., 2012; 10(9): 988–96.