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Vedolizumab treatment may reduce steroid burden and improve histology in patients with eosinophilic gastroenteritis

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Keywords

vedolizumab; corticosteroids; symptom response; histologic response; eosinophils

Introduction

Eosinophilic gastritis (EG) and eosinophilic gastroenteritis (EGE) are rare diseases characterized by marked eosinophilic infiltration of the gastrointestinal (GI) tract and symptoms which typically reflect the location(s) of GI involvement.[1,2] Knowledge of these conditions is limited, and treatments, which are largely based on case series, most frequently involve corticosteroids. As long-term steroid treatment is fraught with complications, novel treatment options are needed.

Vedolizumab is a humanized monoclonal antibody to the α4β7 integrin that blocks leukocyte migration into GI mucosa.[3] Vedolizumab is approved for treatment of moderate to severe inflammatory bowel disease (IBD), and provides benefit via inhibition of gastrointestinal-homing of T lymphocytes.[4] However, there is evidence that increased levels of eosinophils can be associated with IBD and may play a role in IBD pathogenesis, that the α4β7 integrin may play an important role in eosinophil localization in IBD, and that blocking α4β7 may inhibit eosinophil recruitment to intestinal mucosa.[5,6] Based on this eosinophil effect, there is a strong rationale that vedolizumab may benefit patients with EG/

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Kim: Manuscript drafting; data analysis/interpretation; critical revision
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Dellon: Project conception; supervision; data analysis/interpretation; manuscript drafting; critical revision.

EGE, but it has not yet been assessed in these conditions. Therefore, this study aimed to assess whether vedolizumab therapy is associated with improved clinical symptoms, endoscopic features, and histologic findings in patients with EG/EGE who failed to respond to prior therapies.

Methods

We conducted a retrospective cohort study of patients with confirmed EG or EGE treated with off-label use of vedolizumab at University of North Carolina (UNC) Hospitals from 2015 through 2017. Cases were defined by a peak eosinophil count of ≥30 eosinophils per high-power field (eos/hpf) on either gastric or duodenal biopsy, which is consistent with prior reports given there are no diagnostic guidelines for these conditions.[1,7] Data regarding symptoms, endoscopic features, tissue eosinophil counts, peripheral blood absolute eosinophil counts, and treatments prior to and after vedolizumab were extracted from the electronic medical record. Outcomes included clinical response (global assessment by the patient), ability to wean systemic steroids and other medications, improvement in endoscopic findings (global assessment by the endoscopist), and decrease in tissue eosinophil counts. This study was approved by the UNC IRB (IRB 15-2882).

Results

We identified 5 adults with EG/EGE who were treated with vedolizumab (Table 1). Ages ranged from 23–54 years, 40% were female, and all were white. Three patients had gastric involvement, all had small bowel involvement, one had colonic involvement, and three had overlapping esophageal involvement; two had protein losing enteropathy. At diagnosis, counts ranged from 80 to 400 eos/hpf in the most highly involved location. Prior to vedolizumab, all patients had been treated with systemic steroids and topical/enteral release steroids, four with elimination diets, four with cromolyn, all with immunomodulators, one with infliximab, and one with omalizumab. Patients had a disease course of 6.5–17.2 years prior to treatment with vedolizumab, and received vedolizumab for 0.2–1.3 years (median: 0.6 years).

After vedolizumab, patients 4 and 5 were able to wean and/or discontinue corticosteroids, reported symptom improvement, and had normal gastric and small intestinal biopsies (Table 1). Patient 1 reported symptom improvement, but declined repeat endoscopic evaluation. Patients 2 and 3 reported no change in symptoms and eosinophil counts did not consistently improve. No patients had documented improvement in endoscopic findings. Esophageal eosinophils increased in patient 3 and peripheral blood eosinophils increased in patient 4. Median time to initial histologic follow-up was 2.2 months.

Discussion

Corticosteroids remain the mainstay of treatment for EG/EGE. However, patients often require long-term steroid treatment due to a relapsing course that necessitates maintenance therapy. Due to undesired adverse effects associated with prolonged systemic steroid use, alternatives have been proposed including topical/enteral release steroids, elimination diets,

leukotriene inhibitors, mast-cell stabilizers, anti-histamines, immunomodulators, and immunosuppressants. However, the efficacy of such therapies has been controversial, side effects of immunomodulators and immunosuppressants are a concern, and data are limited to case reports or small case series.[1,7,8]

In our severely ill group of treatment refractory or steroid dependent patients with EG/EGE, 2 of 5 (40%) had overall clinical and histologic improvement with vedolizumab, and were able to decrease or wean systemic steroids. An additional patient had clinical improvement but did not undergo repeat endoscopic evaluation. Our study was limited by a small sample size with no uniform follow-up. However, these results suggest that more formal assessment of vedolizumab is warranted in EG/EGE, though perhaps in a less refractory population where its effect as a steroid-sparing agent could be studied. In addition, a mechanistic understanding of the effect of vedolizumab on GI infiltration of eosinophils is needed, as we observed some increase in esophageal and peripheral blood eosinophilia.

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Abbreviations

EG	eosinophilic gastritis
EGE	eosinophilic gastroenteritis
IG	gastrointestinal
IBD	inflammatory bowel diseases
UNC	University of North Carolina

References

1. Prussin C. Eosinophilic gastroenteritis and related eosinophilic disorders. Gastroenterol Clin North Am. 2014; 43(2):317–327. DOI: 10.1016/j.gtc.2014.02.013 [PubMed: 24813518]
2. 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(1):36–42. DOI: 10.1097/MPG.0000000000000865 [PubMed: 25988554]
3. Wyant T, Fedyk E, Abhyankar B. An Overview of the Mechanism of Action of the Monoclonal Antibody Vedolizumab. J Crohn's Colitis. 2016; 10(12):1437–1444. DOI: 10.1093/ecco-jcc/jjw092 [PubMed: 27252400]
4. Gomollón F, Dignass A, Annese V, et al. 3rd European Evidence-based Consensus on the Diagnosis and Management of Crohn's Disease 2016: Part 1: Diagnosis and Medical Management on behalf of ECCO. J Crohn's Colitis. 2016; :1–23. DOI: 10.1093/ecco-jcc/jjw168

5. Woodruff SA, Masterson JC, Fillon S, Robinson ZD, Furuta GT. Role of eosinophils in inflammatory bowel and gastrointestinal diseases. J Pediatr Gastroenterol Nutr. 2011; 52(6):650–661. DOI: 10.1097/MPG.0b013e3182128512 [PubMed: 21593640]
6. Brandt EB, Zimmermann N, Muntel EE, et al. The α4β7-integrin is dynamically expressed on murine eosinophils and involved in eosinophil trafficking to the intestine. Clin Exp Allergy. 2006; 36(4):543–553. DOI: 10.1111/j.1365-2222.2006.02456.x [PubMed: 16630161]
7. Reed C, Woosley JT, Dellon ES. Clinical characteristics, treatment outcomes, and resource utilization in children and adults with eosinophilic gastroenteritis. Dig Liver Dis. 2015; 47(3):197–201. DOI: 10.1016/j.dld.2014.11.009 [PubMed: 25547198]
8. Ko HM, Morotti RA, Yershov O, Chehade M. Eosinophilic gastritis in children: Clinicopathological correlation, disease course, and response to therapy. Am J Gastroenterol. 2014; 109(8):1277–1285. DOI: 10.1038/ajg.2014.166 [PubMed: 24957155]

Table 1

Patient demographics, treatments prior to vedolizumab, treatments following vedolizumab induction, and clinical, endoscopic, and histologic improvement

Patient number	**1**	**2**	**3**	**4**	**5**
Current age (years)	39.7	22.7	28.2	35.3	53.7
Sex	Male	Male	Female	Male	Female
Race	White	White	White	White	White
Location of GI involvement [1]	S, SB, C	E, S, SB	E, S, SB	E, S, SB	S, SB
Duration of disease at vedo start (years)	8.1	17.2	11.3	13.1	6.5
Vedolizumab continued at end of follow-up	No	No	No	Yes	Yes
Last known treatment	Ustekinumab	Study drug	Study drug	--	--
Treatments					
Prior to vedolizumab start					
Swallowed fluticasone		Yes		Yes	
Swallowed budesonide		Yes		Yes	
Entocort	Yes	Yes	Yes		Yes
Systemic steroids	Yes	Yes	Yes	Yes	Yes
Omalizumab			Yes		
Food elimination diet	Yes	Yes	Yes	Yes	
Cromolyn	Yes	Yes	Yes	Yes	
6MP/azathioprine [2]	Yes		Yes	Yes	Yes
Methotrexate	Yes	Yes	Yes		
Infliximab	Yes				
After vedolizumab start					
Swallowed fluticasone		Yes			
Swallowed budesonide					
Entocort	Yes	Yes			Yes

Patient number	1	2	3	4	5
Systemic steroids	Yes			Yes	Yes
Omalizumab					
Food elimination diet		Yes	Yes		
Cromolyn					
6MP/azathioprine					Yes
Methotrexate					
Infliximab					
Stopped systemic steroids post induction	No	N/a	N/a	Yes	Yes
Length of vedolizumab course (years)	0.3	0.2	0.6	1.0	1.3
Number of infusions	4	3	5	10	16
Overall clinical improvement[3]	Yes	No	No	+/−	Yes
Endoscopic improvement	N/A[4]	No	No	No	No
Eosinophil counts (per hpf)					
Esophagus					
Diagnosis[5]	0	90	42	45	0
Baseline[6]	0	100	3	0	N/A
Post-vedolizumab[7]	N/A	100	24	3	N/A
Stomach					
Diagnosis	210	80	23	400	230
Baseline	180	0	0	1	25
Post-vedolizumab	N/A	0	30	0	0
Duodenum					
Diagnosis	0	N/A	80	0	170
Baseline	0	N/A	76	8	150
Post-vedolizumab	N/A	N/A	0	0	0

Patient number	1	2	3	4	5
Jejunum					
Diagnosis	N/A	40	N/A	40	140
Baseline	130	82	N/A	6	N/A
Post-vedolizumab	N/A	58	N/A	0	N/A

[1] E: esophageal involvement, S: stomach involvement, SB: small bowel involvement, C: colonic involvement;

[2] 6MP: 6-mercaptopurine;

[3] Patient 1 stopped due to adverse events of migraine and recurrent nasopharyngeal infections, and Patients 2 & 3 stopped due to lack of clinical, endoscopic, or histologic resposne;

[4] N/A: not assessed;

[5] Eosinophil counts at diagnosis or off treatments;

[6] Eosinophil counts at baseline prior to vedolizumab treatment, including patients on the treatments listed above;

[7] Eosinophil counts after vedolizumab treatment

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