

Eosinophilic gastroenteritis in an adolescent male with history of chronic bullous disease

Carol Stephanie C Tan-Lim ¹, Juan Miguel L Murillo,² Marysia Stella T Recto,¹ Mary Anne R Castor ¹

¹Division of Allergy and Immunology - Department of Pediatrics, Philippine General Hospital, Manila, Philippines

²Division of Pediatric Gastroenterology, Hepatology and Nutrition - Department of Pediatrics, Philippine General Hospital, Manila, Philippines

Correspondence to

Dr Carol Stephanie C Tan-Lim; cctan7@up.edu.ph

Accepted 23 January 2021

SUMMARY

Eosinophilic gastroenteritis is a rare inflammatory disorder of the gastrointestinal tract. Although commonly associated with allergic diseases, it is also rarely associated with autoimmune disorders. This case report describes a 17-year-old Filipino male with eosinophilic gastroenteritis, manifesting as abdominal pain, vomiting and diarrhoea. He had no allergic diseases, but he was previously diagnosed with chronic bullous disease. His symptoms improved with the initiation of corticosteroids. To date, this is the first case report of a patient with eosinophilic gastroenteritis and chronic bullous disease.

BACKGROUND

Eosinophilic gastroenteritis is a rare inflammatory disorder characterised by abnormal infiltration of eosinophils in the gastrointestinal tract. The disease was first reported in 1937. Since then, there have been around 300 cases reported in literature, with increased incidence noted in the past 50 years.^{1 2} Although commonly associated with allergic diseases, it is also rarely associated with autoimmune disorders. This is a case report of an adolescent Filipino male with eosinophilic gastroenteritis who was also previously diagnosed with chronic bullous disease.

CASE PRESENTATION

A 17-year-old male was admitted in our institution due to a 3-week history of cramping abdominal pain and vomiting after every meal intake, occurring three times a day. He also had watery, non-bloody diarrhoea occurring two to three times a day. Symptoms were severe enough to affect his daily activities, and the patient was unable to go to school.

Eight months prior to admission, he had similar symptoms of abdominal pain, vomiting and diarrhoea that lasted for 3 weeks. He was admitted at a provincial hospital but the medical records were not made available to the authors. A holoabdominal ultrasound showed ascites; however, CT scan imaging was not ordered. Due to a consideration of partial gut obstruction from appendicitis, exploratory laparotomy was done. Intraoperatively, no obstruction was noted. Appendectomy was done. The histopathology report at this time showed appendix with congested serosal surface that was partly covered with exudates, and omentum that was yellow brown and firm. He was diagnosed to have acute suppurative periappendicitis and acute suppurative omentitis. He was discharged on oral

metronidazole for 1 week, with improvement of symptoms.

During the present admission, he was placed on nil per ore for 10 days with persistence of symptoms. The patient had no history of travel, no ingestion of raw food and no pets at home. He was previously diagnosed with chronic bullous disease at 3 years old, and was given dapsone until he was 12 years old with no recurrence of symptoms since then. He has no known food allergies, nor any other allergic diseases. Family history was unremarkable.

The patient weighed 47.5 kg and had a height of 164 cm, yielding a body mass index (BMI) of 17.66 kg/m². The Z-score of his BMI is below -1 based on the WHO growth chart. His abdomen was non-distended, soft and non-tender, with fluid wave. The rest of the physical examination was unremarkable.

He underwent exploratory laparotomy due to consideration of partial gut obstruction from post-operative adhesions. Intraoperatively, there was note of 1.1 L of serous ascites, with non-dilated thickened small bowels, enlarged mesenteric lymph nodes and minimal soft adhesions. Adhesiolysis, omental biopsy and mesenteric lymph node biopsy were done. Postoperatively, abdominal pain, vomiting and diarrhoea persisted. He was referred to the Allergy and Immunology service due to hypereosinophilia.

INVESTIGATIONS

The patient's laboratory examinations showed an absolute eosinophil count (AEC) of 12 067 on admission. Subsequent examinations showed persistent hypereosinophilia ranging from 11 752 to 14 823. His AEC during the previous admission 8 months prior was also elevated at 775. His preoperative abdominal radiograph showed few, non-distended and faeces-filled bowels with no signs of obstruction.

Biopsy of the omentum revealed fibroadipose tissue, acute on chronic inflammation, with increased eosinophils and foreign body-type giant cell reaction. Biopsy of the mesenteric lymph node revealed lymphadenitis with increased eosinophils. Cytology of peritoneal fluid collected intraoperatively showed acute inflammatory pattern with multiple eosinophils admixed with neutrophils, with 10–15 eosinophils per high power field (hpf), as shown in figure 1.

Upper gastrointestinal endoscopy revealed erythematous gastropathy. Biopsy of the obtained specimens showed chronic non-specific oesophagitis with 5–10 eosinophils/hpf, chronic non-specific



© BMJ Publishing Group Limited 2021. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Tan-Lim CSC, Murillo JML, Recto MST, et al. *BMJ Case Rep* 2021;**14**:e238532. doi:10.1136/bcr-2020-238532

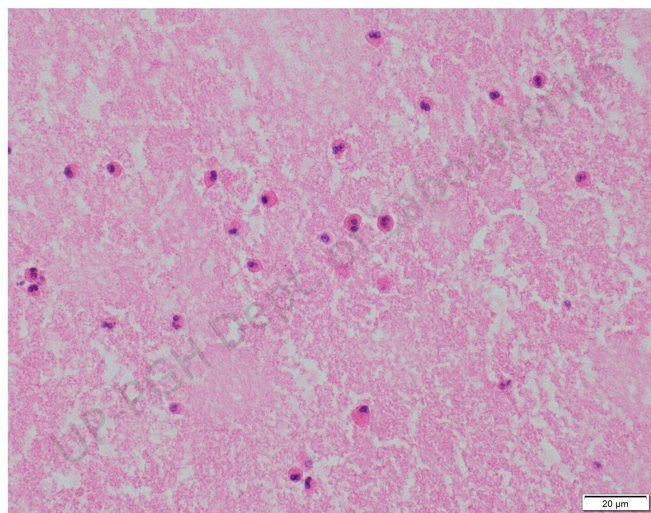


Figure 1 Ascitic fluid showing multiple eosinophils.

gastritis with 5–10 eosinophils/hpf in the antrum and 3–5 eosinophils/hpf in the body, and chronic non-specific duodenitis with 25–28 eosinophils/hpf (figure 2). These results are below the cut-off values for eosinophilic infiltration of the mucosa, which are >15 eosinophils/hpf in the oesophagus, >30 eosinophils/hpf in the stomach and >28 eosinophils/hpf in the duodenum.^{3 4}

His antinuclear antibody (ANA) test at 1:160 dilution was positive at +4, with speckling. However, his clinical manifestations were not consistent with an autoimmune disorder such as systemic lupus erythematosus. Bone marrow aspiration showed no malignant cells, but with multiple eosinophilic precursors (at least 20% of the cells per field), as shown in figure 3. His haemoglobin was 176 g/L, while his serum albumin was 41 g/L. Other laboratory examinations yielded unremarkable results. Examination of the stool revealed no parasites and negative rotavirus, *Cryptosporidium* and *Giardia* antigen tests. Electrolytes, liver function tests, renal function tests, amylase, lipase, chest radiograph, ECG, 2D echocardiogram, troponin I, procalcitonin

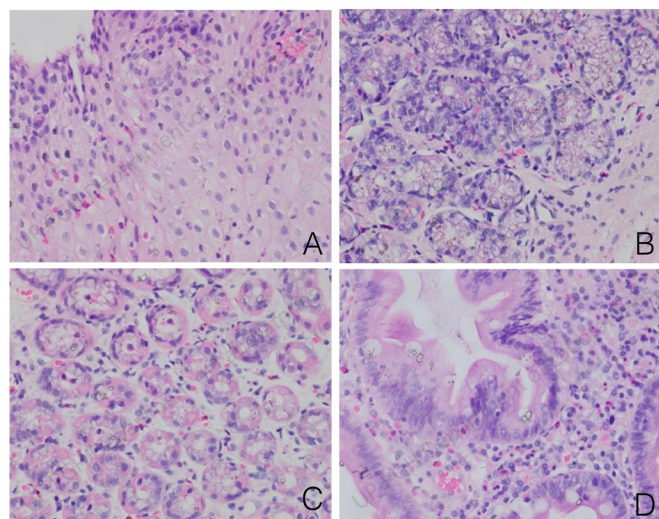


Figure 2 Biopsy of the gastrointestinal tract shows eosinophil counts within normal values: (A) oesophagus with 5–10 eosinophils/high power field (hpf), (B) antrum of the stomach with 5–10 eosinophils/hpf, (C) body of the stomach with 3–5 eosinophils/hpf, (D) duodenum with 25–28 eosinophils/hpf.

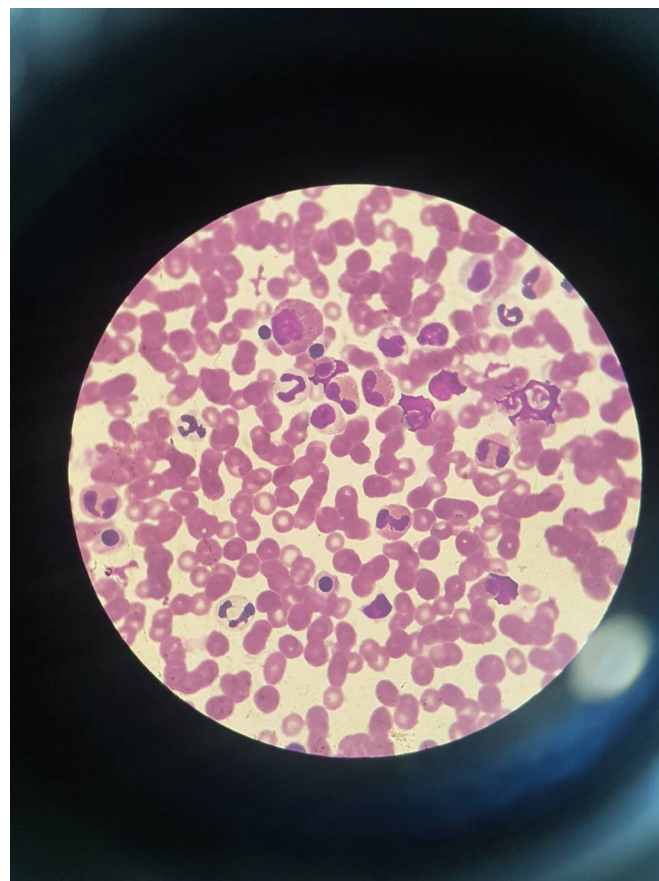


Figure 3 Bone marrow aspiration shows multiple eosinophilic precursors.

levels, skin test to food allergens, and urine, stool and peritoneal fluid acid fast bacilli smear were all normal.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis for his case included tuberculosis of the gastrointestinal tract, partial gut obstruction from adhesions, parasitic infection of the gastrointestinal tract, hypereosinophilic syndrome, inflammatory bowel disease, haematologic malignancy, food allergy and IgA vasculitis.

TREATMENT

He was diagnosed to have eosinophilic gastroenteritis. He was started on prednisone at 0.85 mg/kg/day, with resolution of clinical symptoms. His AEC dropped to 25 after 2 weeks of steroids. Steroids were tapered gradually.

OUTCOME AND FOLLOW-UP

Our patient has been on regular follow-up for the past 7 months, with no recurrence of symptoms so far. He is on close monitoring with his paediatric rheumatologist to monitor for possible evolution of other autoimmune diseases, such as systemic lupus erythematosus. His general paediatrician and subspecialty doctors continue to coordinate to provide holistic and optimal management for this patient.

DISCUSSION

Eosinophilic gastroenteritis is an inflammatory disorder that predominantly affects the stomach and small intestine. In the USA, the prevalence is 5.1 per 100 000.⁵ Prevalence data among

Asian countries is lacking.⁶ It is more common among the paediatric population than the adult population, with recent epidemiological data showing a shift from male to female predominance.² Our patient first manifested with symptoms at the age of 16 years.

The widely used criteria for diagnosing eosinophilic gastroenteritis are as follows: (1) the presence of gastrointestinal symptoms; (2) histological demonstration of eosinophilic infiltration of the gastrointestinal tract or presence of eosinophilia in ascitic fluid; and (3) exclusion of other causes of tissue eosinophilia. Common differential diagnoses include intestinal parasitism, food allergy, adverse drug reactions, protein-losing enteropathy from intolerance to cow milk protein and malignancy.¹²

Eosinophilic gastroenteritis can be classified into mucosal, muscular or serosal, based on the extent of eosinophilic infiltration. The mucosal type is most common, accounting for 57%–100% of cases. Patients with mucosal eosinophilic gastroenteritis manifest with abdominal pain, nausea, vomiting, dyspepsia and diarrhoea. The muscular type occurs in 30%–70% of cases, manifesting as bowel-wall thickening, intestinal obstruction, caecal mass or intussusception. The serosal type is the least common, occurring in 4.5%–9% of cases in Japan and 13% of cases in the USA. This type manifests as eosinophilic ascites which may be accompanied by eosinophilic pleural effusion, as well as abundant peripheral eosinophilia, peritonitis or perforation.¹⁷ Our patient can be classified as the serosal type due to eosinophilic ascites and abundant peripheral eosinophilia in the absence of significant mucosal infiltration of eosinophils. The increased eosinophils in the omentum and a dramatic response to corticosteroid therapy are also consistent with the serosal type of eosinophilic gastroenteritis.^{5,8,9}

Patients with eosinophilic gastroenteritis have concomitant allergic diseases in 45%–63% of cases. Family history of atopy is reported in 64%. Food allergy is commonly associated with eosinophilic gastroenteritis, and it is postulated that food allergens may trigger the recruitment and activation of eosinophils in the gastrointestinal tract.⁸ Our patient had persistence of symptoms despite being on prolonged fasting, making food allergy unlikely.

There are also reports of association of eosinophilic gastroenteritis with autoimmune conditions such as coeliac disease, ulcerative colitis and systemic lupus erythematosus.² A 2015 systematic review on patients with eosinophilic gastrointestinal disorders and autoimmune diseases found 20 published cases. Systemic lupus erythematosus was the most prevalent autoimmune disease, accounting for 35% of the reports. This was followed by rheumatoid arthritis in 20%, systemic sclerosis in 15%, inflammatory myositis in 15%, and Sjogren's syndrome, scleromyositis, and overlapping systemic lupus erythematosus and systemic sclerosis (5% each). Although eosinophilic oesophagitis is more common than eosinophilic gastroenteritis in general, this systematic review reported that 95% of patients had eosinophilic gastroenteritis.¹⁰ A proposed mechanism for the association of eosinophilic gastrointestinal diseases and autoimmune disease is a common genetic cause, since genomic studies identified loci for eosinophilic gastrointestinal diseases that are also associated with autoimmune diseases. These loci are the thymic stromal lymphopoietin/WD repeat domain 36 (TSLP/WDR36), chromosome 11 open reading frame 30 (c11orf30) and signal transducer and activator of transcription 6 (STAT6).¹¹ Another possible mechanism is that effector functions of eosinophils can contribute to autoimmune inflammation. Eosinophils may initiate autoimmune responses by presenting antigens and activating T cells. Eosinophils may also cause antibody-dependent

cellular cytotoxicity of host cells that express autoantibodies. Furthermore, eosinophils release cytokines and chemokines that can initiate or perpetuate inflammation.¹²

Our patient did not have any allergic disease or family history of atopy. However, he was previously diagnosed with chronic bullous disease from age 3 to 12 years old by a dermatologist. Chronic bullous disease, also known as linear IgA dermatosis, is a rare vesiculobullous autoimmune disease characterised by IgA anti-basement membrane zone antibodies. It is exceptionally responsive to dapsone. Spontaneous remission usually occurs within 2–4 years.¹³ The positive ANA result of this patient could be correlated with this autoimmune disease; however, positive ANA at 1:160 dilution may also be observed in 5% of the normal population.¹⁴ To date, this is the first case report of a patient with eosinophilic gastroenteritis and chronic bullous disease.

The pathophysiology of the possible association of eosinophilic gastroenteritis and chronic bullous disease is not established. The characteristic histopathological finding in chronic bullous disease is linear IgA deposition with neutrophil-predominant inflammation of the dermis. One case report described an adult female with linear IgA dermatosis whose skin biopsy revealed neutrophil-rich and eosinophil-rich inflammation.¹⁵ This report illustrates the potential role of eosinophils in the pathogenesis of both inflammatory conditions. Another case report described an adult male with eosinophilic gastroenteritis–serosal type who had positive autoantibodies. The patient tested positive for rheumatoid factor, ANA and perinuclear anti-neutrophil cytoplasmic antibody (p-ANCA), but did not have autoimmune disease manifestations. The authors explained that eosinophilic gastroenteritis could be associated with autoantibody positivity, and suggested an autoimmune pathogenesis for eosinophilic gastroenteritis.¹⁶

This patient underwent two surgical interventions due to the initial suspicion of an acute abdomen. Similar to this case, there have been published reports on patients manifesting severe abdominal pain, vomiting and diarrhoea who underwent laparotomy. They were eventually diagnosed to have eosinophilic gastroenteritis after documentation of tissue eosinophilic infiltration.¹⁷ This highlights the importance of prompt recognition of the diagnosis to avoid unnecessary invasive interventions. Important clues to the diagnosis are the presence of abdominal symptoms and peripheral eosinophilia.

Patient's perspective

I am hopeful that my symptoms will not recur. If it recurs, it makes me calm that my doctors are closely following my condition.

Learning points

- ▶ Eosinophilic gastroenteritis is a rare but treatable disorder that affects children and adults.
- ▶ Although rare, this diagnosis should be suspected among patients who have abdominal symptoms and peripheral eosinophilia.
- ▶ Important to the diagnosis is the histologic demonstration of eosinophilia in the gastrointestinal tract or ascitic fluid.
- ▶ Prompt recognition and provision of appropriate management will greatly improve the quality of life of patients.

Case report

The mainstay of therapy is corticosteroids. The appropriate duration of therapy is unknown, with most patients showing improvement with 2–6 weeks of prednisone at a dose of 1–2 mg/kg/day.^{1 5} Other therapeutic options include dietary modifications, leukotriene inhibitors, mast cell stabilisers, immunomodulators such as 6-mercaptopurine and azathioprine, and biologic agents such as reslizumab, infliximab and omalizumab.¹ Our patient was given prednisone 1 mg/kg/day for 2 weeks, with dramatic improvement in symptoms and AEC.

The natural course of eosinophilic gastroenteritis is variable. A study among 10 adult patients with eosinophilic gastroenteritis who were observed for at least 1 year reported that 70% experienced chronic disease or multiple flares. All of these patients had a history of allergy. Among the three patients who experienced a single flare-up without relapse, two had no history of allergy while one had food allergy.¹⁸

Acknowledgements The authors would like to thank Dr Faustine Richelle C Ong and Dr Mae Ferrollyn Q San Pedro for their help in managing the patient and reviewing the manuscript.

Contributors CSCT-L: conceptualisation, writing, review and editing. JMM: data gathering and review. MSR: conceptualisation, review and editing. MARC: conceptualisation, review and editing.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests MSTR serves in the advisory board of A Menarini, Abbott Nutrition and Sanofi Aventis; a speaker for A Menarini, Abbott Nutrition, Abbott Pharma, Nutricia, RB Mead Johnson, Kalbe, Glenmark, Leo pharma, Mylan, Bayer, Natrapharm, AstraZeneca and Galderma; and received research grants from Galderma and Novartis. MARC served as a speaker and facilitator for a series of research workshop sponsored by Wyeth.

Patient consent for publication Parental/guardian consent obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iDs

Carol Stephanie C Tan-Lim <http://orcid.org/0000-0001-8815-4191>

Mary Anne R Castor <http://orcid.org/0000-0003-2291-4615>

REFERENCES

- 1 Sunkara T, Rawla P, Yarlagadda KS, *et al.* Eosinophilic gastroenteritis: diagnosis and clinical perspectives. *Clin Exp Gastroenterol* 2019;12:239–53.
- 2 Abou Rached A, El Hajj W, Rached AA. Eosinophilic gastroenteritis: approach to diagnosis and management. *World J Gastrointest Pharmacol Ther* 2016;7:513–23.
- 3 Collins MH, Capocelli K, Yang GY. Eosinophilic gastrointestinal disorders pathology. *Front Med* 2017;4:251.
- 4 Burks AW, Holgate ST, O'Hehir RE. *Middleton's Allergy Principles and Practice*. Philadelphia: Elsevier, 2020: 1075–84.
- 5 Mansoor E, Saleh MA, Cooper GS. Prevalence of eosinophilic gastroenteritis and colitis in a population-based study, from 2012 to 2017. *Clin Gastroenterol Hepatol* 2017;15:1733–41.
- 6 Wong G-W, Lim KH, Wan WK, *et al.* Eosinophilic gastroenteritis: clinical profiles and treatment outcomes, a retrospective study of 18 adult patients in a Singapore tertiary hospital. *Med J Malaysia* 2015;70:232–7.
- 7 Uppal V, Kreiger P, Kutsch E. Eosinophilic gastroenteritis and colitis: a comprehensive review. *Clin Rev Allergy Immunol* 2016;50:175–88.
- 8 Melboucy-Belkhir S, Khentache R, Andre-Ledun L, *et al.* Eosinophilic ascites, a challenging diagnosis. *Int Arch Intern Med* 2018;2:009.
- 9 Bleibel F, Fragoza K, Faller GT. Acute eosinophilic ascites in a middle-aged man. *Case Rep Gastrointest Med* 2012;2012:1–4.
- 10 Lecouffe-Desprets M, Groh M, Bour B, *et al.* Eosinophilic gastrointestinal disorders associated with autoimmune connective tissue disease. *Joint Bone Spine* 2016;83:479–84.
- 11 Ishihara S, Kinoshita Y, Schoepfer A. Eosinophilic esophagitis, eosinophilic gastroenteritis, and eosinophilic colitis: common mechanisms and differences between East and West. *Inflamm Intest Dis* 2016;1:63–9.
- 12 Diny NL, Rose NR, Čiháková D. Eosinophils in autoimmune diseases. *Front Immunol* 2017;8:484.
- 13 Barnett CN, Fong M, Rosario-Collazo JA. Linear IGA Dermatitis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, 2020. Available: <https://www.ncbi.nlm.nih.gov/books/NBK526113/>
- 14 Kavanaugh A, Tomar R, Reveille J, *et al.* Guidelines for clinical use of the antinuclear antibody test and tests for specific autoantibodies to nuclear antigens. American College of pathologists. *Arch Pathol Lab Med* 2000;124:71–81.
- 15 Fulton E, Jan F, Zimarowski MJ. Flame figures in linear IgA bullous dermatitis: a novel histopathologic finding. *Dermatol Online J* 2017;23.
- 16 Fonseka CL, Nanayakkara S, Singhapura SDAL, *et al.* Eosinophilic gastroenteritis with a relapsing and remitting course with presence of autoimmune antibodies. *Case Rep Med* 2020;2020:1–5.
- 17 von dem Borne PA, Kramer MH, Vermeijden JR. Acute abdominal pain and eosinophilia, two cases of eosinophilic gastroenteritis. *Neth J Med* 1999;54:197–201.
- 18 Sato H, Honma T, Owaki T, *et al.* Clinical and pathological profile of eosinophilic gastroenteritis. *Eur J Gastroenterol Hepatol* 2019;31:157–62.

Copyright 2021 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <https://www.bmj.com/company/products-services/rights-and-licensing/permissions/>
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

Customer Service

If you have any further queries about your subscription, please contact our customer services team on +44 (0) 207111 1105 or via email at support@bmj.com.

Visit casereports.bmj.com for more articles like this and to become a Fellow