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CASE REPORT
Enhanced therapeutic response with addition of loratadine in subserosal eosinophilic gastroenteritis

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ABSTRACT
A case of a 45-year-old Caucasian male initially reported with symptoms of acute intestinal obstruction was presented. Diagnostic tests revealed presence of eosinophilic ascites with marked peripheral eosinophilia, a significant thickening of stomach and intestinal wall and infiltration of gastric and duodenal mucosa with eosinophiles. Findings were conclusive with subserosal type of eosinophilic gastroenteritis and the patient’s treatment started with a combination of parenteral methylprednisolone and oral loratadine. A prompt clinical response was encountered after 5 days of treatment with complete resolution. 2011; 82:41-50.

Tupa povreda istmsusa torakalne aorte

INTRODUCTION
Eosinophilic gastroenteritis (EG) is characterized by eosinophilic infiltration of the gastrointestinal tract resulting in a variety of gastrointestinal symptoms such as abdominal pain, nausea, vomiting, and diarrhea, while patients with diffuse small bowel disease can develop malabsorption (1-2). It is a rare condition with around 280 cases described in worldwide literature since Kaijser described it first in 1937 (3).
There are three distinct types of EG with subserosal form of the disease being the rarest, since it accounts for only 10% of the reported cases in the literature (1,4).

Endoscopic ultrasound findings in EG have been described (5) but abdominal ultrasound findings in EG have never been portrayed before. Successful monotherapy of EG with antihistamine drug ketotifen has been reported on several occasions (6-8), however to our knowledge there are no reported cases of concurrent use of corticosteroids and antihistamines nor are there any reports of loratadine use in GE.

**CASE REPORT**

A 45-year-old Caucasian male was admitted to the Department of Surgery, University Clinical Center of Tuzla, Bosnia and Herzegovina, with symptoms suggesting acute intestinal obstruction. At the time of admission he complained of having strong periumbilical pain and strong sensation of nausea but without vomiting. He reported frequent dyspepsia and abdominal pain and cramps in the last 10 months with unintentional weight loss of 8 kg. He also reported that during that time he often had 3 to 4 loose, sometimes greasy, stools per day. He denied any history of fever or night sweating or recent respiratory or neurological problems. He was treated for facial eczema by a dermatologist 6 months before and while topical medications initially helped, rash sometimes came back without apparent provocative factor.

Initial physical findings revealed periumbilical tenderness, without abdominal guarding or rigidity. Plain abdominal X-ray obtained at the admission demonstrated several small gas-liquid levels. The patient was treated conservatively with incomplete resolution of symptoms. He continued having cramps and occasional nausea.

An abdominal ultrasound was performed revealing presence of large amounts of ascites and marked thickening of gastric (up to 10 mm) and intestinal wall (Figure 1 and 2). Signs of intestinal obstruction characterized with to-and-fro contraction and dilation of intestinal loops were also observed. Subsequent CT scan confirmed presence of large amounts of free intraperitoneal liquid, and thickening of stomach wall.

Complete blood count (CBC) with differential white blood cells (WBC) count demonstrated marked eosinophilia with WBC of 13.06 (10⁹/L) and eosinophile count of 7.05 (10⁹/L) or 54% in relative numbers. Hemoglobin level was 13.7 g/dL with normal renal function. Immunoglobulin E level was 354 IU/mL (ULN: 100 IU/mL). The patient was transferred to the Gastroenterology Department where additional tests were made. Albumin level was 28 g/L, with normal level of liver enzymes, lipoproteins and coagulation factors. Serology for all types of viral hepatitis was also negative as were other immunological markers such as antinuclear antibodies (ANA), autoantibodies to double-stranded DNA (anti dsDNA), perinuclear anti-neutrophil cytoplasmic antibody (pANCA), circulating anti-neutrophil

![Figure 1. Abdominal ultrasound demonstrating marked thickening of the wall of the gastric antrum (Salkić N, 2011)](image1)

![Figure 2. Abdominal ultrasound after 5 days of treatment with corticosteroids and loratadine demonstrating reduction in thickness of antral wall to normal values (Salkić N, 2011)](image2)
cytoplasmic antibody (cANCA) and anti-citrulline antibodies. Serological markers for celiac disease (antiendomysial and antigliadin antibodies) were also negative.

Analysis of ascitic fluid has shown ascitic glucose of 4.8 mmol/L, lactate dehydrogenase (LDH) 176 IU/mL, total ascitic protein 36.8 g/l, ascitic albumin level 21.6 g/L serum to ascites albumin gradient of 6.4 g/L and ascites/serum LDH ratio of 0.74. The total white cell count in ascites was 3.64 (10⁹/L) with striking ratio of 98% eosinophils, and remaining 2% of neutrophils.

Ascites fluid was sent for cytology for malignant cells, bacterial and fungal cultures, as well as cultures for *Mycobacterium tuberculosis* (TB) and all tests came back negative. Stool was negative for presence of ova and parasites, and serology was negative for *Echinococcus granulosus*, *Toxoplasma gondii* and *Toxocara canii*. Repeated sputum cultures were negative for TB, spirometry was also unremarkable. Echocardiography, electrocardiography and neurological examination also excluded presence of any overt cardial or neurological disease. Other than eosinophilia, peripheral blood smear was also unexceptional. Prick test for nutritional allergens was unavailable at the time.

The patient underwent upper GI endoscopy with findings suggestive for mild gastritis and patchy duodenitis. Numerous biopsy samples were obtained from several parts of stomach and duodenum. Subsequent histology demonstrated eosinophilic infiltration of gastric wall and duodenum with presence of free eosinophilic granules.

Since the patient did not give consent for colonscopy and bone marrow biopsy, we decided that, according to criteria suggested by Talley et al (1), the diagnosis of subserosal form of EG was most likely and started with five-day course of 40 mg of intravenous methylprednisolone combined with peroral loratadine 10 mg daily. The patient responded promptly with complete resolution of ascites as seen on the follow-up US six days after initiating the treatment and with reduction of gastric wall thickness to around 4 mm (Figure 2). The WBC count in peripheral blood also decreased to 7.05 (10⁹/L) with relative eosinophil number of 1.2% and what is also important, his subjective symptoms resolved entirely.

The patient was discharged in an excellent condition with continued treatment with 40 mg/day of oral prednisone only, tapering it quickly in the following 2 weeks to 10 mg/day. After additional 2 weeks of prednison treatment (10mg/day) the patient was gradually weaned off the prednison in the following 2 weeks. Six months after, the patient was without any signs of recurrence on subsequent follow-ups.

Eosinophilic gastroenteritis represents a member of a family of diseases that includes eosinophilic esophagitis, gastritis, enteritis, and colitis, collectively referred to as eosinophilic gastrointestinal disorders (EGIDs) (9). Klein et al. classified this disorder into three major pathological types: predominant mucosal layer type, predominant muscle layer type, and predominant subserosal layer type (10). Many patients have history of allergies and elevated IgE levels which suggest that the hypersensitivity response plays a major role in pathogenesis (11).

The subserosal form of EG occurs in a minority of patients with EG, and it is characterized by exudative ascites with marked eosinophilia of up to 88% in the ascitic fluid. Patients in this subgroup may have an allergic history and peripheral eosinophil counts as high as 8000 cells/μL and even an eosinophilic pleural effusion may also be present (1). When subserosal type of EG is present, it is not uncommon that biopsy samples taken during endoscopy do not show diagnostically sufficient degree of eosinophilic infiltration (>20 eosinophils/HPF); moreover, cases without mucosal involvement in subserosal type of EG have been described (12).

There are no standards for diagnosis of EG, however, the following criteria were suggested by Talley et al: the presence of gastrointestinal symptoms, histological demonstration of eosinophilic infiltration in one or more areas of the gastrointestinal tract or presence of high eosinophil count in ascitic fluid (latter usually indicates subserosal variety) and no evidence of parasitic or extraintestinal disease (1).

Diseases in which gastrointestinal symptoms are associated with peripheral eosinophilia usually can be distinguished from EG with simple
laboratory tests and/or endoscopic biopsies. EG can have the GI manifestation of connective tissue disorders, vasculitis, lymphoma, Crohn’s disease, parasitic infestations, and hypereosinophilic syndrome and we have managed to exclude these conditions in our case (13).

Eosinophilic gastroenteritis should be suspected in any patient with gastrointestinal symptoms associated with peripheral eosinophilia. Our patient additionally had a high count of eosinophils in ascitic fluid, which, combined with thickening of gastric and intestinal wall on abdominal ultrasound, made us consider the EG. A recent report demonstrated a significant thickening of antral and duodenal mucosal and submucosal layers on endoscopic ultrasound (5). However, demonstration of thickening of gastrointestinal wall on abdominal ultrasound in EG, to our knowledge, has never been described.

Corticosteroids have been the mainstay of therapy with improvement usually occurring within two weeks regardless of the layer of bowel involved (2,14). Steroids should be tapered rapidly over the next couple of weeks but some patients require more prolonged therapy (up to several months) until resolution of symptoms (14).

Ketotifen is an antihistamine drug that stabilizes mast cells and apparently inhibits eosinophil migration to target tissues. It has been used with success as a monotherapy in selected cases (6-8). On the other hand, loratadine is also an antihistamine drug but it does not have mast cell stabilizing properties. Yet, in vitro studies revealed that it may have a direct inhibitory effect on eosinophil activation and may reduce Inter-Cellular Adhesion Molecule 1 (ICAM-1) expression (15-16). It is also a safe and relatively inexpensive drug with very few side-effects. Since ketotifen is not available in our country we decided to co-administer loratadine with corticosteroids in order to produce a possible synergistic effect of both drugs.

Although it is extremely hard to make conclusions based on one case, accelerated response to the treatment (patient had as minimum as 2500 to 3000 ml of ascites before treatment to be reduced completely after 5 days of therapy) may at least suggest that simultaneous administration of corticosteroids and antihistamine drugs could produce both rapid and ample response in EG. It is also not easy to establish the role of loratadine and how much it actually added to the ultimate effect. But given the fact that it does have pharmacologic properties that are somewhat similar to ketotifen, the use of loratadine in EG may has its merits.

It is to be explored whether the monotherapy with loratadine may be a worthwhile alternative in cases when steroids cannot be administered and/or ketotifen is not available.

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TRANSPARENCY DECLARATION
Competing interests: none to declare

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Poboljšanje terapijskog odgovora s dodatkom loratadina u tretmanu subseroznog eozinofilnog gastroenteritisa

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SAŽETAK

Opisan je slučaj muškarca od 45 godina, koji se inicijalno prezentirao sa simptomima akutne intestinalne obstrukcije. Dodatni dijagnostički testovi otkrili su postojanje izraženog eozinofilnog ascitesa s naglašenom eozinofilijom u periferiji, kao i postojanje zadebljanja zida želuca i crijeva, uz biopsijski verificiranu infiltraciju mukoze želuca i duodenuma eozinofilima. Nalazi su bili u skladu sa subseroznim tipom eozinofilnog gastroenteritisa, te je pacijentu ordinirana kombinacija parenteralnog metilprednizolona i oralnog loratadina. Nakon 5 dana tretmana dolazi do potpunog kliničkog, biohemijskog i radiološkog odgovora.

Ključne riječi: eozinofili, antihistaminici, ultrazvuk, tretman

CASE REPORT

Pseudo-subarachnoid hemorrhage and death after a bee sting

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ABSTRACT

We report a case of a 33-year-old woman who developed severe brain edema and pseudo-subarachnoid hemorrhage (SAH) at 36-hour follow-up after successful cardiopulmonary resuscitation for anaphylactic shock as a result of a bee sting. The patient died on the sixth day of the follow-up due to multiple organ failure and brain herniation. Our case suggests that the SAH–like findings on computed tomography scanning were not a new complication (“real” SAH) arising from the bee sting; rather, it was a pseudo-SAH related to prolonged cardiopulmonary resuscitation).

Key words: pseudo-subarachnoid hemorrhage, bee sting, resuscitation

INTRODUCTION

Throughout the world, 9.3–28.5% of sensitization cases are known to be due to hymenoptera venoms (1). In this regard, the hyperalgesic and edematogenic effects of venoms of neotropical social wasps (Polybia paulista and Protonectaria sylveirae) and honeybees (Apis mellifera) were reported in a recent trial (1). Unusual and more serious complications may also be seen, such as anaphylactic shock, acute myocardial infarction, acute renal failure, acute pulmonary hemorrhage, acute hemorrhagic pancreatitis, and atrial fibrillation (2). Possible neurological complications