

Eosinophilic Enteritis: Efficiency of the ^{13}C -Acetate Breath Test for Assessing the Disease Activity

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Abstract

Few clinical studies have so far focused on gastrointestinal motility in patients with eosinophilic gastroenteritis. A 29-year-old man was evaluated for epigastralgia of unknown origin. A histopathological examination of biopsy specimens from the duodenum revealed numerous eosinophilic infiltrations. Eosinophilic enteritis was therefore diagnosed. The patient received oral prednisolone and his symptoms improved. Both at the onset and at relapse of the disease, the maximal $^{13}\text{CO}_2$ excretion time (T_{\max}) of ^{13}C -acetate breath test was noted to have increased levels of excretion. Recovery of this parameter was observed in parallel with clinical improvements after treatments. This is the first report of a case of eosinophilic enteritis in which the ^{13}C -acetate breath test was effective for assessing the disease activity and evaluating the effectiveness of treatment.

Key words: eosinophilic gastroenteritis, gastric emptying, ^{13}C -acetate breath test

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Introduction

Eosinophilic gastroenteritis was first described in 1937 by Kaijser et al. (1) as an unusual inflammatory disease characterized by eosinophilic involvement of the gastrointestinal tract. The clinical features of eosinophilic gastroenteritis depend on the extent of the disease and the particular layers of the digestive tract that are involved (2). Although some clinical studies on eosinophilic esophagitis have demonstrated that many patients with this condition have an abnormal esophageal motility (3, 4), few clinical studies have so far focused on gastrointestinal motility in eosinophilic gastroenteritis.

In this report, we present a case of eosinophilic enteritis in which the use of the ^{13}C -acetate breath test was effective for both assessing the disease activity and evaluating the effectiveness of treatment.

Case Report

A 29-year-old man was evaluated at our hospital for epigastralgia of unknown origin that had been ongoing for a duration of two months. Esophagogastroduodenoscopy (EGD), abdominal ultrasonography, and computerized tomography at another hospital revealed normal findings. The patient had also previously experienced allergic dermatitis.

On physical examination, the patient's abdomen was soft, with tenderness in the epigastric region. Laboratory studies showed normal hemoglobin (13.3 g/dL) and a white blood cell count of 6,500/mm³ with slightly elevated eosinophils (11%). The total serum protein level was slightly decreased (6.4 g/dL with 3.6 g/dL albumin), while the C-reactive protein level was not elevated (0.2 mg/dL). A microscopic examination of the patient's feces revealed no parasite eggs.

Because we suspected functional dyspepsia, the ^{13}C -acetate breath test was performed to evaluate gastric emptying. T_{\max} was decreased, thus suggesting delayed gastric emptying. However, the administration of mosapride citrate

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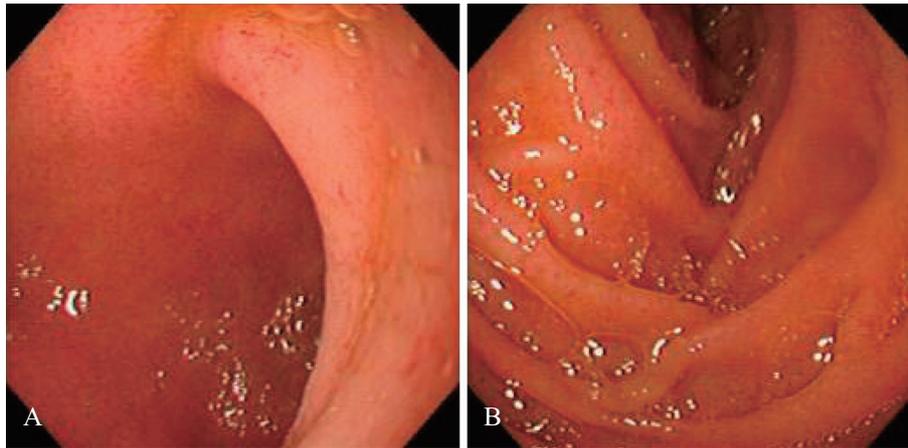


Figure 1. Esophagogastroduodenoscopy showed dilated capillary vessels in both the mucosa at the bulbs (A) and in the second portion (B) of the duodenum.

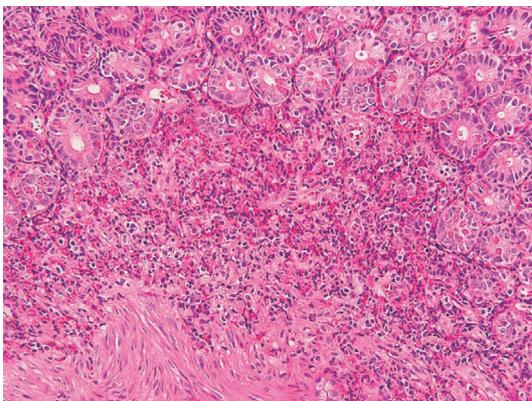


Figure 2. A histopathological section of biopsy specimens from the second portion of the duodenum revealed numerous areas of eosinophilic infiltration in the muscularis mucosae (Hematoxylin and Eosin staining).

for delayed gastric emptying failed to relieve the patient's symptoms. Although EGD at another hospital found no abnormal findings, we performed EGD for histological assessment (Fig. 1). A histopathological examination of biopsy specimens from the second portion of the duodenum revealed numerous eosinophilic infiltrations on the muscularis mucosae (Fig. 2). Based on these findings, eosinophilic enteritis was diagnosed.

The patient was treated with 30 mg of oral prednisolone, and his symptoms immediately and dramatically improved. The dose of prednisolone was gradually reduced, and the patient was weaned off the drug over a period of five months. A histopathological examination of duodenal mucosa samples did not reveal any residual eosinophilic infiltration. Four months after termination of the steroid treatment, the epigastralgia reappeared. Although a histopathological examination of the duodenal mucosa samples revealed only mild eosinophilic infiltration, the patient's symptoms were similar to the first episode, and a relapse of the eosinophilic enteritis was assumed. The patient was again treated with 20 mg of oral prednisolone, and the

symptoms immediately showed improvement. He was again weaned off steroid treatment over a period of five months. At the last follow-up visit at 35 months after termination of the second treatment, the patient was in good condition with no evidence of recurrence.

Analysis of gastric emptying using the ^{13}C -acetate breath test

Because the patient's gastric emptying was delayed before treatment, this was followed up during the clinical course.

Methods: The patient's gastric emptying was measured using the ^{13}C -acetate breath test, in which the patient ingests a liquid meal (OKUNOS-A; 200 kcal/200 mL; Forica Foods, Niigata, Japan) labeled with 100 mg of sodium ^{13}C -acetate (Sodium Acetate (1- ^{13}C , 99%); Euriso-Top, Saint-Aubin, France). Breath samples are then collected in air bags at baseline (before test meal) and at 10 minutes intervals for 2 hours after intake of the test meal for $^{13}\text{CO}_2$ measurements. An analysis of isotopic enrichment is performed using an isotope ratio mass spectrometer with an online gas chromatographic purification system (UBiT-IR200; Otsuka Pharmaceuticals, Tokyo, Japan). The T_{\max} , which is the time of maximal $^{13}\text{CO}_2$ recovery in the breath samples, is calculated.

Results (Fig. 3): The T_{\max} at the time of diagnosis was 2.09 hours, which was a remarkable delay compared with normal controls (0.94 ± 0.3 h) assessed in a previous study (5). After termination of the first treatment, the T_{\max} had decreased (0.88 h). However, at relapse of the disease, the T_{\max} was noted to be elevated (1.57 h). The T_{\max} again decreased after termination of the second treatment (1.17 h).

Discussion

Dysphagia is one of the primary symptoms in patients with eosinophilic esophagitis and it is known to be associated with esophageal dysmotility. Abnormal esophageal manometry was found in 41% of the patients who underwent stationary manometry (3). Martin Martin et al. (4) evaluated

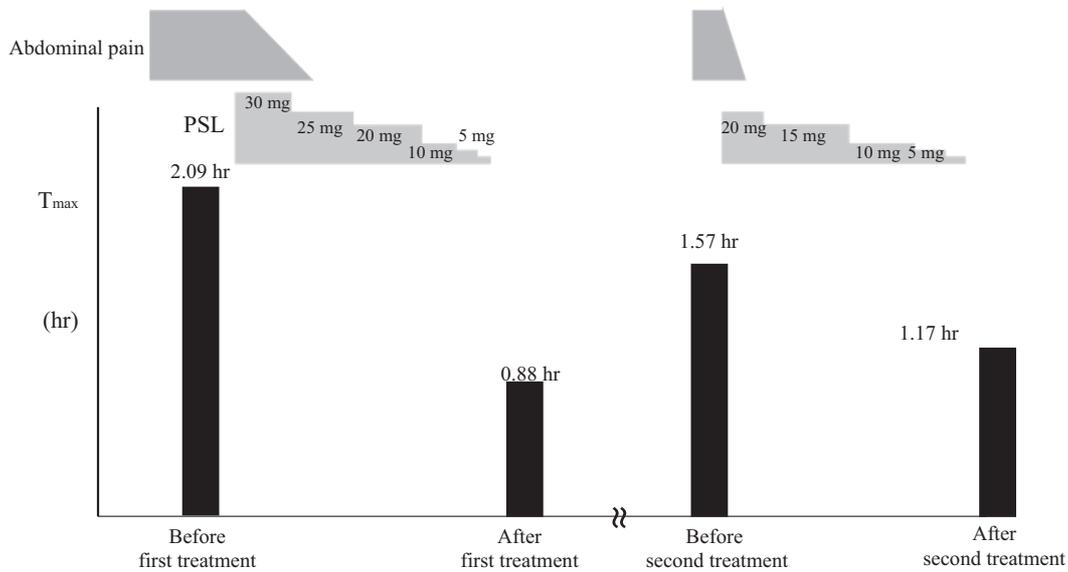


Figure 3. Gastric emptying, as measured by the ¹³C-acetate breath test during the patient's clinical course. The black columns show the T_{max} at each point during the clinical course. PSL: prednisolone

esophageal motility using high-resolution manometry, and motor abnormalities, such as pan-esophageal pressurization and peristaltic dysfunction, were observed in 76% of the patients with eosinophilic esophagitis. Although dyspepsia, bowel obstruction and diarrhea suggest abnormalities of gastrointestinal motility in patients with eosinophilic gastroenteritis (6), few clinical studies have so far focused on this condition.

Walker et al. (7) observed subtle duodenal eosinophilia in about half of a group of patients with functional dyspepsia and speculated that eosinophil infiltration may be associated with symptoms of dysmotility. Hogan et al. (8) demonstrated, in a murine model of eosinophilic gastroenteritis, that eosinophils are involved in gastric dysmotility, gastromegaly and cachexia through an eotaxin-dependent response. Eosinophils are also known to interface directly and indirectly through the eosinophil-mast-cell axis with the enteric nerves and smooth muscle, and have been suggested to be involved in disorders of gastrointestinal motility (9). The increased T_{max} observed in the present case may therefore reflect delayed gastric emptying due to eosinophilic infiltration into the gastrointestinal tract, and monitoring of the T_{max} measured by the ¹³C acetate breath test may be a useful tool for assessing the disease activity and for evaluating the efficacy of treatment.

The ¹³C acetate breath test was developed as a nonradioactive alternative for the measurement of gastric emptying, and has been confirmed to correlate well with gastric scintigraphy (10). However, this test is also influenced by the rate of absorption of ¹³C acetate from the duodenal mucosa. Since intestinal malabsorption is one of the symptoms of eosinophilic enteritis, the increased T_{max} in the present study may reflect delayed gastric emptying, as well as impairment of absorption from the duodenal mucosa. An analysis of

gastric emptying in additional cases by gastric scintigraphy is necessary to determine the relationship between eosinophilic infiltration and gastrointestinal dysmotility in eosinophilic gastroenteritis.

In the present case, epigastralgia correlated with the T_{max}, but other dysmotility symptoms, such as early satiation or postprandial fullness, were not present in this patient. It is therefore possible that severe epigastralgia masked the other symptoms or that the patient perceived these vague symptoms as epigastralgia. Devanarayana et al. (11) reported a significant correlation between both the severity of abdominal pain and delayed gastric emptying in children with functional abdominal pain. They speculated that the increase in gastric wall tension associated with delayed gastric emptying activated both tension and pain receptors in the stomach.

The endoscopic features of eosinophilic enteritis are non-specific, and include erythema, edema, hyperemia, friability and superficial ulcerations (12). In the present case, dilated capillary vessels were seen in the duodenal mucosa, and even though this was uncharacteristic for the mucosa, no diagnosis was made. Based on the endoscopic appearance and increased T_{max}, the patient was presumptively treated with a prokinetic agent for functional dyspepsia; however, this strategy was not successful. Similar to our case, eosinophilic enteritis may be overlooked in patients with intractable functional dyspepsia. Because the endoscopic appearance of eosinophilic enteritis may look normal, the microscopic evaluation of endoscopic biopsy samples is therefore essential for obtaining a differential diagnosis. In the present case, a histopathological examination of the duodenal mucosa at the time of relapse did not reveal any remarkable eosinophilic infiltration. However, an increased number of biopsies would have likely been beneficial in that scenario, because multiple biopsies have been suggested as a standard to re-

duce sampling errors when diagnosing eosinophilic esophagitis or gastroenteritis (9).

The authors state that they have no Conflict of Interest (COI).

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