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Urticaria due to polyethylene glycol-3350 and electrolytes for oral solution in a patient with jejunal nodular lymphoid hyperplasia

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Abstract

Both jejunal nodular lymphoid hyperplasia (NLH) and polyethylene glycol (PEG)-3350 hypersensitivity are extremely rare. We describe a 30-year-old female who had previously taken a PEG-3350 bowel preparation without adverse effects, and presented for evaluation of chronic diarrhea. An upper and lower gastrointestinal endoscopy, and small bowel series were scheduled. PEG-3350 and electrolytes for oral solution was prescribed for bowel cleansing. During consumption of the bowel preparation she developed urticarial hypersensitivity. An alternative bowel preparation was used. Colonoscopy and upper endoscopy were normal, but small bowel series revealed innumerable sand-like lucencies in the jejunum. NLH was confirmed on biopsy from antegrade enteroscopy. This is the first case report on the pathological jejunal NLH in association with the PEG-3350 urticarial hypersensitivity. The potential pathophysiological etiology of this association is discussed.

Keywords Bowel preparation solutions, hypersensitivity, jejunal nodular lymphoid hyperplasia, polyethylene glycol-3350

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Introduction

Polyethylene glycol (PEG)-3350 and electrolytes for oral solution (GoLYTELY®, Braintree Laboratories, Inc., Braintree, MA, USA) was developed by Davis *et al* [1] in 1980 to overcome large fluid and electrolyte shifts seen with other bowel preparations. GoLYTELY® contains 236 g PEG-3350, 22.74 g sodium sulfate, 6.74 g sodium bicarbonate, 5.86 g sodium chloride, and 2.97 g potassium chloride. The powder is dissolved in 4 L of water to form an iso-osmotic solution. The benefit of this lavage solution is minimal water and electrolyte absorption or secretion across the intestinal mucosa with sodium sulfate as the predominant salt. Besides the salty taste, the most common adverse events are mild and include nausea, vomiting, abdominal pain, and bloating. Rare case reports of urticaria, dermatitis, and anaphylaxis exist and have been attributed to PEG [2,3] though the mechanism of the GoLYTELY® hypersensitivity has not been explored.

Nodular lymphoid hyperplasia (NLH) of the small intestine represents a rare disease grossly characterized by the presence of numerous mucosal lymphoproliferative nodules. It has been suggested that NLH is a risk factor for both intestinal and extraintestinal lymphoma. There is also an association with immunodeficiency syndromes and Giardiasis [4]. Its etiology is unknown.

The jejunum differentiates from the rest of the small intestine by its larger diameter, thicker wall, more plicae circulares, much longer villi (which largely increase the absorptive surface area), and the absence of Brunner's glands or Peyer's patch.

Both jejunal NLH and GoLYTELY® hypersensitivity are extremely rare. We report the first case of jejunal NLH in association with GoLYTELY® hypersensitivity. The potential pathophysiological etiology of this association is discussed.

Case report

A 30-year-old Caucasian female, with a history of hypersensitivity to radiocontrast media and sulfa drugs and who had previously taken a PEG-3350 bowel preparation without adverse effects, presented for evaluation of chronic diarrhea. An upper and lower gastrointestinal endoscopy,

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and small bowel series were scheduled. GoLYTELY® was prescribed prior to colonoscopy for bowel cleansing. Within a few minutes of taking the bowel preparation, her throat became itchy, followed by generalized pruritus, and chest pressure. She presented by car to the emergency department. On examination there were symmetric erythema of the forearms and hives on the chest. The symptoms completely resolved after administration of an antihistamine and oral corticosteroid. Due to concern for hypersensitivity to PEG-3350, the patient was discharged with new bowel lavage instructions that included a regimen of magnesium citrate and Gatorade® (The Gatorade Company, Chicago, IL). The alternative bowel preparation was well tolerated and resulted in adequate bowel cleansing.

Colonoscopy and upper endoscopy were normal, but small bowel series revealed innumerable sand-like lucencies in the jejunum that became less prominent distally (Fig. 1). These findings were concerning for NLH as seen with giardiasis, histoplasmosis, Whipple's disease, mastocytosis, immunodeficiency syndromes, lymphoma, and early occult Crohn's disease. Wireless capsule endoscopy confirmed jejunal nodularity biopsied on antegrade enteroscopy (Fig. 2). The mucosal biopsy also showed pathologic NLH involving the jejunum.

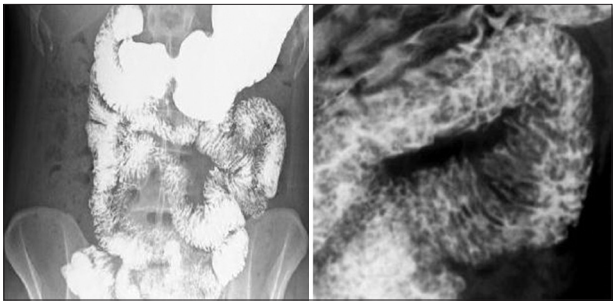

Figure 1 Small bowel series showed many sand-like lucencies in the jejunum less prominent distally

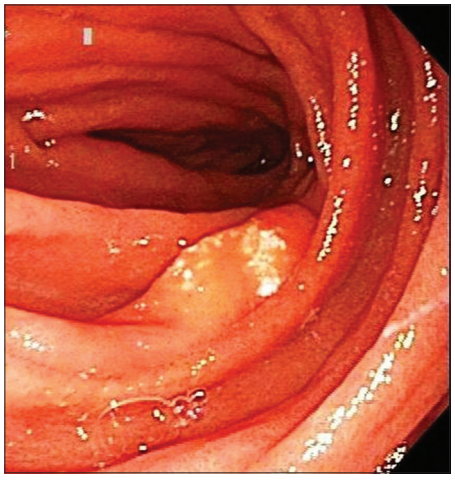

Figure 2 Antegrade enteroscopy showed jejunal nodularity in the jejunum which was biopsied

Discussion

PEG is used extensively in a wide variety of substances and medications. Although high-molecular-weight PEG (>1000 g/mol) solutions are believed to be poorly absorbed, 0.06% of the mean PEG load was recovered in the urine of normal subjects, and 0.09% was recovered in patients with inflammatory bowel disease [5]. It was suggested that loss of mucosal integrity could promote the systemic absorption of PEG-3350 [2]. Chronic diarrhea is one of the most common gastrointestinal conditions that can impact a patient's nutritional status due to the remarkably impaired efficiency of the gut to absorb nutrients and, the patient's decreased appetite and reduced nutrient intake out of fear of exacerbating the symptoms; and so chronic diarrhea can cause impaired normal function of the mucosal recovery and mucosal barrier of the intestine and therefore lead to increased systemic absorption of PEG-3350 in our patient.

It should be noted that the mucosal breaks may also be associated with the pathophysiology of NLH. The defects in the gastrointestinal mucosal surface caused by chronic diarrhea in our patient may lead to chronic antigen exposure, host immunological stimulation, and subsequent formation of NLH.

Mast cells (MCs) are concentrated in the areas of lymphoid storage and their proliferation dependents on T-cell growth factor. MCs are also the major modulator of the lymphoid cell immune function and regulate the proliferation of the lymphoid cell [6]. Lee *et al* [7] reported that intestinal lymphoid cells could differentiate into MCs. However, MCs are difficult to identify via standard hematoxylin and eosin staining. They can be seen when stained with metachromatic dyes such as toluidine blue or Giemsa stain. It is believed that many patients with MC-associated diseases may be missed if these dyes are not used. We certainly missed the opportunity to repeat the jejunal mucosa biopsy with these unique dyes in our patient. However, Nicolov *et al* [8] found there were extremely increased numbers of mucosal MCs in the jejunal NLH.

We therefore hypothesize that in the jejunal NLH, the concentrated lymphoid cell-associated cytokines and the increased MC-associated IgE responses contribute to the hypersensitivity reaction to an unusual antigen, such as GoLYTELY®. The unique anatomy and histology of the jejunum probably also contribute to this association of GoLYTELY® hypersensitivity with jejunal NLH.

In our patient, the mucosal breaks associated with her jejunal NLH placed her at increased risk for systemic exposure to luminal antigens and hypersensitive reaction to GoLYTELY®, otherwise typically localized within the bowels. What is unclear, however, is the immune-stimulating antigen which induced the GoLYTELY® hypersensitivity. The patient reported a known drug allergy only to sulfonamides and radiocontrast media. It is necessary to clarify that sulfonamide or "sulfa" allergies present as a common hypersensitivity to drugs with a sulfonamide (SO_2NH_2) moiety. The allergy-inducing ingredient is thought to be the aromatic amine group at the N4 position [9]. Sulfonamides are not the same as sulfate (SO_4^{2-}), and hence,

sulfa allergies should not be mistaken for sulfate allergies [10]. Hence the sulfate component of the bowel preparation is less likely to be the hypersensitivity inducing agent.

In conclusion, this case report emphasizes the need for physicians to be aware of GoLYTELY® hypersensitivity, as PEG-3350 is commonly thought to be localized only within the lumen of the bowel and also because GoLYTELY® hypersensitivity can potentially be severe [2,3]. Increased caution should be warranted in cases where defects in mucosal integrity are suspected.

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