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Allergic colitis: a mimic of Hirschsprung disease

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Abstract *Background.* Allergy to cow milk protein is a common cause of gastrointestinal symptoms in infancy. Milk allergy is usually a clinical diagnosis, and thus there have been few reports of the radiographic findings.
Objective. To describe the barium enema findings of allergic colitis and differentiate them from Hirschsprung disease.
Materials and methods. Four infants (age range 7 days–5 weeks) with constipation underwent barium enema to exclude Hirschsprung disease. Radiographic findings were correlated with the pathologic specimens from suction rectal biopsy.
Results. All enemas revealed irregular narrowing of the rectum and a transition zone. Rectal biopsies in each case demonstrated ganglion cells and evidence of an allergic colitis, with inflammatory infiltrates in the lamina propria. A diagnosis of milk allergy colitis was made and symptoms resolved after removal of milk from the diet.
Conclusions. Milk allergy is common in infancy. The rectum is a primary target organ, with allergic colitis often diagnosed on clinical grounds alone. However, a child with allergic colitis may be referred to radiology for barium enema, especially if constipation is present. The radiologist should be aware of the unique imaging findings of allergic colitis, so as to avoid confusion with Hirschsprung disease and perhaps an unnecessary rectal biopsy.

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Introduction

Cow milk protein intolerance is a broad term encompassing the signs and symptoms related to multiple organ systems after the introduction of cow milk into the diet [1]. The diagnosis of milk allergy enteropathy is usually made on clinical grounds alone [2]. On occasion, the clinical history, signs, and symptoms can be nonspecific and resemble Hirschsprung disease, with the patient referred to radiology for imaging of the lower gastrointestinal (GI) tract. We have encountered four patients who underwent imaging of the lower GI tract and were initially diagnosed with Hirschsprung disease. Subsequent rectal biopsies revealed an allergic colitis

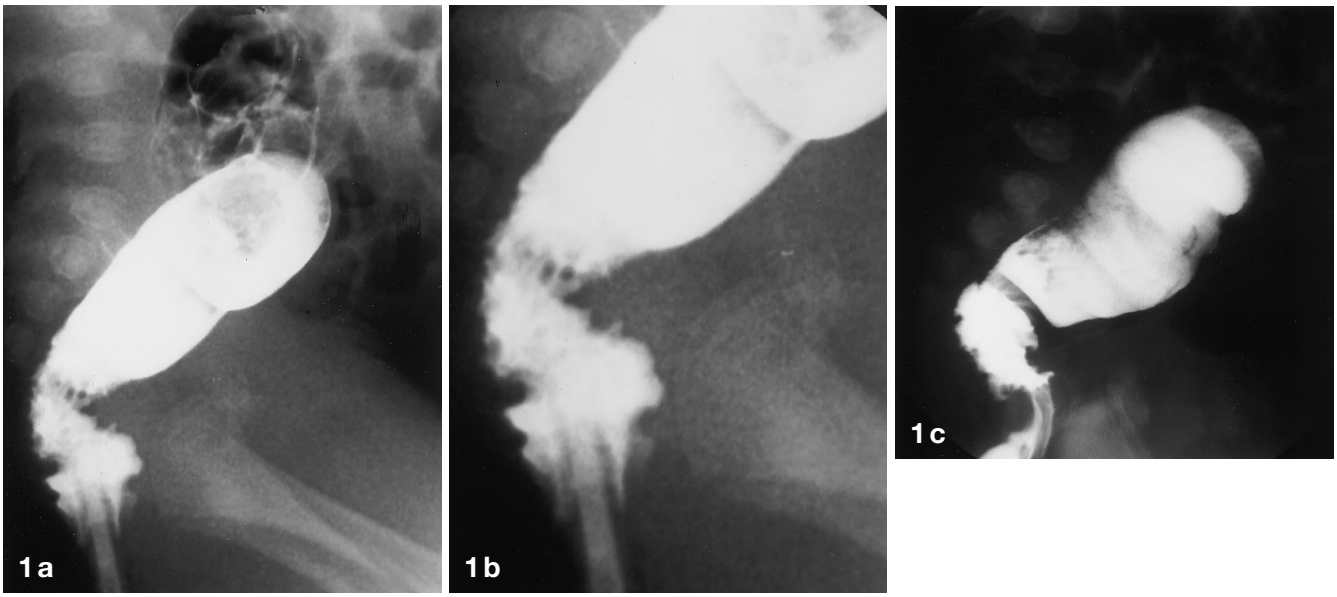

Fig. 1 **a** Lateral view from a barium enema in a 3-week-old with bloody stools and perirectal abscess, demonstrating thickened, irregular folds and a narrowed rectum. There is a transition to dilated sigmoid colon. **b** Magnified view of **a,** with better delineation of the mucosal fold thickening. **c** Lateral view from a barium enema in a 5-week-old, with an apparent transition zone in the mid rectum and even greater sigmoid dilatation as compared to **a**

and all patients responded to elimination of cow milk from their diets. It is important for the practicing radiologist to be aware of this entity and to try to distinguish allergic colitis from Hirschsprung disease based on the radiographic and clinical findings.

Materials and methods

A retrospective study was performed on four newborns (age range 7 days–5 weeks, 2 female/2 male) who presented with signs and symptoms related to the GI tract. Two of the four children had abdominal distention, and all four presented with decreased stool output. Irritability and failure to thrive was noted in one patient. A 3-week-old boy developed a perirectal abscess, diagnosed on physical examination and treated successfully with medical management. Two of the patients had occult blood in their stool. No extraintestinal signs or symptoms were identified. Each had normal prenatal and perinatal courses, and were referred to radiology for barium enema to exclude Hirschsprung disease. All four contrast studies were performed by two of the authors (DAB, CB).

The barium enemas were performed with a small end-hole catheter placed into the distal rectum, just past the anal verge. The contrast material was instilled under gravity. Imaging was begun in lateral projection during early filling. AP and various oblique views were also obtained prior to a postevacuation film. All patients tolerated the procedure well.

Based on the radiographic findings, the four children were referred to gastroenterology or general surgery for suction rectal biopsy. Adequate specimens were obtained in all patients. Clinical follow-up was possible in each case by chart review and consultation with the referring physicians.

Results

All four enemas revealed narrowing and mucosal irregularity of the rectum with an abnormal rectosigmoid index (sigmoid colon diameter greater than rectal diameter) (Fig. 1 a–c). The thickened and irregular folds of the rectum were in sharp contrast to the dilated sigmoid colon above, which demonstrated a normal mucosal fold pattern (Fig. 2). A radiologic diagnosis of Hirschsprung disease was made in each case.

The rectal biopsies showed ganglion cells in all four patients. There were inflammatory infiltrates within the lamina propria in each case, including eosinophils in three of four patients (Fig. 3). Stool cultures were negative. The clinical, radiologic, and pathologic findings for the patients are summarized in Table 1. Based on these results, a diagnosis of allergic colitis was made in each patient.

All four children were treated for allergic colitis by elimination of cow milk from the diet. In patient 1, who was solely breast-fed, the mother initially eliminated cow milk from her diet but reintroduced dairy products on her own several months later. This resulted in recurrence of the patient's symptoms, including abdominal bloating, low stool output, and guaiac-positive stools. No further symptoms occurred once the cow milk was eliminated for the second time. Patients 2 and 3 did well when switched from cow milk formula to (Nutramigen Mead Johnson Evansville, Indiana) Patient 3 was rechallenged with cow milk at 11 months of age, with re-

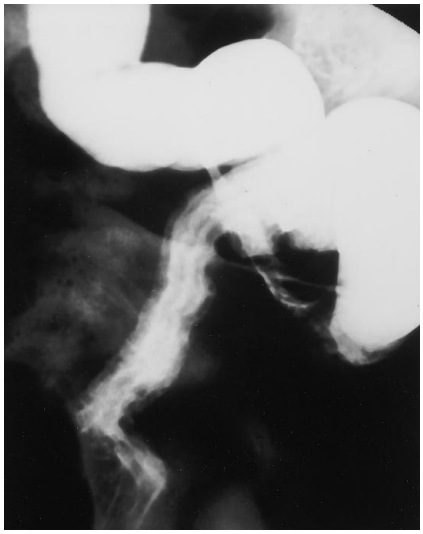

Fig. 2 Three-week-old with guaiac-positive stools and constipation. Note the significant mucosal abnormality of the rectum, with intact sigmoid mucosa

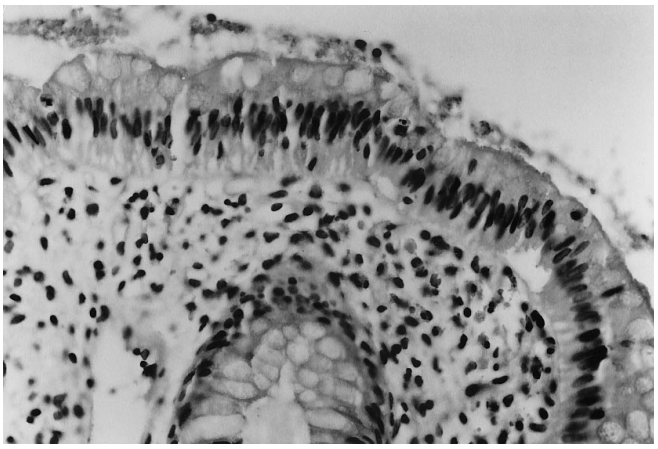

Fig. 3 Suction rectal biopsy specimen, low power hematoxylin and eosin stain. There is a significant inflammatory response within the submucosa and lamina propria, including abundant eosinophils. Ganglion cells were present in other sections (not shown)

current irritability, poor feeding, and guaiac-positive stools. A second challenge at 14 months of age showed resolution of all symptoms. Both dietary challenges were done on an outpatient basis under the supervision of the referring pediatrician and gastroenterologist. Patient 4 has done well on a diet free of cow milk.

Discussion

Cow milk protein allergy usually affects newborns, infants, and young children, especially those with other allergies or a family history of allergies [3]. Specific symptoms will depend on the part of the GI tract involved. There are frequently associated respiratory and skin manifestations, such as asthma and atopic dermatitis [3].

Cow milk contains many antigenic proteins, with whey protein (beta-lactoglobulin) the most common offending agent [2–4]. These low-molecular-weight proteins are usually glycoproteins or acid proteins resistant to various forms of denaturation [2]. Soy protein has also been shown to possess antigenic properties both in vivo and in vitro [2]. Approximately 10–30 % of children with cow milk allergy are also sensititve to soy protein [2, 3, 5].

Allergic colitis, a specific form of cow milk protein intolerance, is an immune-mediated event resulting in an inflammatory response within the colon (especially the rectosigmoid) and gastrointestinal symptoms [1, 2]. Allergic colitis is probably the most common cause of colitis in the first year of life [6]. The antigenic proteins are found in commercially available formulas and breast milk, depending on the maternal diet [2, 7, 8]. Symptoms are protean, but commonly include failure to thrive, constipation, rectal bleeding or guaiac-positive

Table 1 Patient summary

Patient	Age	Clinical symptoms	Radiographic findings	Pathology
1	7 days	Abdominal distention, low stool output, guaiac-negative stool	Abnormal rectosigmoid index, narrowed and irregular rectum with transition zone	+ ganglion cells
2	3 weeks	Constipation, history of bloody stools, perirectal abscess, guaiac-positive stool	Same as #1	+ ganglion cells + eosinophils
3	3 weeks	Irritable, poor feeding, constipation, guaiac-positive stool	Same as #1	+ ganglion cells + eosinophils
4	5 weeks	Abdominal distention, decreased stool output, nonbilious emesis, guaiac-negative stool	Same as #1	+ ganglion cells + eosinophils

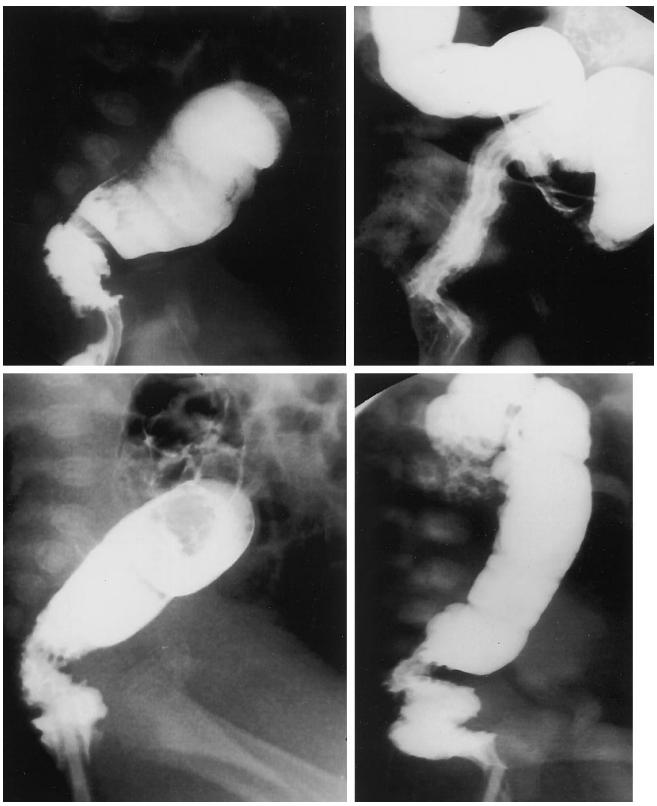

Fig. 4 All four patients demonstrate the striking similarity of each barium enema

stools, and abdominal distention with or without pain [2, 9].

With time, tolerance to these proteins develops. Few children past the age of two have clinical symptoms of cow milk protein allergy [1, 2, 6]. An immature intestinal barrier and alterations in gastrointestinal immunity have been postulated as predisposing factors to the development of allergic colitis [1, 2]. Rectal bleeding and diarrhea often dominate the clinical picture, with the child otherwise looking relatively well. This is in contrast to other causes of colitis, such as infection, Hirschsprung disease, and necrotizing enterocolitis, where significant constitutional signs and symptoms will be part of the clinical picture [2]. In general, allergic colitis has a more insidious onset.

The diagnosis of allergic colitis is usually made on clinical grounds alone. If confirmation is needed, peripheral eosinophilia and eosinophils in stool samples or mucosal biopsies are identified [1, 2, 10]. After elimination of cow milk (or soy) from the diet, there is usually clinical improvement, confirming the diagnosis. If symptoms persist, other causes of colitis should be excluded by stool culture and rectal biopsy.

Allergic colitis can affect any part of the colon, but the rectosigmoid is often the primary segment involved [1, 2, 10]. The mucosa is friable, with foci of erythema and skip areas of normal-appearing colon. Erosions and ulcerations can simulate an infectious etiology [2, 10]. Hirschsprung colitis can look similar, but the presence of ganglion cells will exclude this diagnosis. Microscopic sections in cases of allergic colitis reveal normal architecture and infiltration of the mucosa, submucosa, and lamina propria by eosinophils [2, 10]. Crypt abscesses will contain eosinophils as well as neutrophils [2, 10].

Treatment is primarily eliminating the offending antigen from the diet. Currently, this requires changing to a hydrolyzed casein or elemental formula [1, 4]. However, even casein formulas have been shown to be immunogenic [11]. Since patients with cow milk allergy can also be sensitive to soy protein, the introduction of soy protein-based formulas must be done with caution. Breast-feeding can usually continue with elimination of cow milk from the maternal diet. In most cases, cow milk or soy protein can be safely reintroduced into the diet by 1–2 years of age [2]. It is important to note that severe anaphylactic reactions can occur when the child is challenged with the antigen, necessitating careful monitoring when the challenge is to occur [1, 2].

There has been very little written about the radiographic findings of allergic colitis. One can see mucosal edema and narrowing of the colonic lumen on barium enema [12, 13]. Upper gastrointestinal findings include fold thickening of the small bowel, with the potential for a small-bowel obstruction [13, 14]. To our knowledge, there have been no reports of allergic colitis as a clinical and radiologic mimic of Hirschsprung disease.

The patients in our series were all referred to radiology to exclude Hirschsprung disease. Although allergic colitis usually presents with bloody diarrhea, our patient population was identified by a clinical history suspicious for Hirschsprung disease. It is unclear why these four children developed constipation and not more typical symptoms. Two of the four patients also had guaiac-positive or bloody stools, raising the question of a superimposed enterocolitis. One newborn developed a perirectal abscess prior to barium enema, which based on the clinical findings was thought to be related to an ongoing proctocolitis. The radiographic findings were virtually identical in all cases, with Hirschsprung disease the preliminary diagnosis (Fig. 4). Biopsy made the final diagnosis of allergic colitis in all patients. This was confirmed by clinical improvement after appropriate intervention, as well as long-term follow-up.

The distinction between allergic colitis and Hirschsprung disease by barium enema may be difficult. However, differences do exist that can help the radiologist make the correct diagnosis. In allergic colitis, pronounced mucosal fold thickening and irregularity, reflecting the inflammatory response of the rectum to the antigenic proteins, are a constant finding [12, 13]. Large

rectal ulcers may also be seen [2, 12]. In comparison, the rectal mucosa in Hirschsprung disease is usually intact, with the serrated appearance of the contrast column due to intermittent spasm and not inflammation [15–17]. We have also observed that the duration of rectal spasm appears to be greater in cases of allergic colitis. With Hirschsprung disease, the rectal spasm can easily be overcome by continued retrograde filling during barium enema [15]. This was not the case in our patients.

In addition, the location of the mucosal abnormality was atypical for Hirschsprung enterocolitis, in which edematous mucosa and submucosa is identified predominantly above the level of the transition zone [15, 16]. In our cases of allergic colitis, the dilated bowel above the narrowed rectum demonstrated intact mucosa. Finally, the radiographic findings were, for the most part, out of proportion to the relatively mild clinical symptoms of these patients. In essence, the enemas looked terrible but the patients looked reasonably well.

In conclusion, newborns and infants with allergic colitis may be referred for barium enema to exclude possible Hirschsprung disease. It is important for the radiologist to understand that allergic colitis may mimic the radiographic findings of Hirschsprung disease, but that radiographic differences can be appreciated and help to avoid any diagnostic confusion. When the clinical and radiographic findings of allergic colitis are identified, consultation with the referring pediatrician or gastroenterologist may allow a trial of diet modification before suction rectal biopsy is undertaken.

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