Should Intussusception in Children Prompt Screening for Celiac Disease?

*Norelle R. Reilly, †Kathleen M. Aguilar, and †Peter H. Green

ABSTRACT

Objectives: An association between adult celiac disease (CD) and intussusceptions (ISs) has been described. Although more common among children, intussusception has not been linked with childhood CD aside from isolated case reports. Our aim was to investigate the frequency of IS among children with CD.

Methods: A patient database containing children with biopsy-proven CD was reviewed, in addition to radiology records contained in a hospital-maintained clinical data repository.

Results: Of 254 children with biopsy-proven CD and complete records available for review, abdominal imaging was performed in 21%, mainly because of abdominal pain. Among children with CD, 1.2% experienced an IS <9 months before their diagnosis with CD. Among children seen at our institution in the same time period, 0.07% experienced an IS. The majority of those children with CD who were found to have IS had no evidence of nutritional deficit at the time of IS. IS was not identified in any children with CD who had been treated with a gluten-free diet.

Conclusions: IS was far more common among children in our cohort with untreated CD than in the general pediatric population simultaneously seen at our center. The diagnosis of CD should be considered in children with IS, even in the absence of signs of nutritional compromise.

Key Words: abdominal pain, celiac disease, children, intussusception

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Intussusception (IS) is the second most common cause of gastrointestinal obstruction in young children, and the most common cause of small bowel obstruction in children ages 3 months to 5 years with an approximate incidence of 22 to 56 cases per 100,000 per year (1–3). Occasionally, a lead point such as Meckel diverticulum or lymphoma may be found, but in 90% to 95% of pediatric cases, no cause can be identified (1,4). Despite the fact that IS is relatively rare beyond childhood (5–7), an association with celiac disease (CD) has been described in adults (8–11). In contrast, descriptions of ISs in children suspected to have been caused by underlying CD are limited to case reports (12–16). There are, however, no studies determining how frequently ISs occur among children with CD. Our aim was, therefore, to determine whether the frequency of ISs in children with known CD is greater than that among our pediatric population.

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From the *Division of Pediatric Gastroenterology, Columbia University Medical Center, and the †Department of Medicine, Celiac Disease Center, Columbia University Medical Center, New York, NY.

Address correspondence and reprint requests to Norelle Rizkalla Reilly, MD, Celiac Disease Center at Columbia University, 180 Fort Washington Ave, Suite 934, New York, NY 10032 (e-mail: nr2268@columbia.edu).

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METHODS

We reviewed the records of 318 patients contained in a registry of children with biopsy-proven CD seen at our center from 2000 to 2010. These records were reviewed for abdominal imaging studies (ultrasound, magnetic resonance imaging, computed tomography [CT], or small bowel series) and we noted those patients whose imaging revealed an IS. Using a clinical data repository maintained by our hospital, we also identified children ages 6 months to 18 years who were diagnosed with IS at our center during the same period. A cutoff of 6 months of age was used because of the typical start of grains in the infant diet at this age in the United States. We reviewed these patients' records for a diagnosis of CD preceding or following the IS, as well as for histologic or serologic evidence of possible CD (increased liver function tests; iron-deficiency anemia; hypoalbuminemia; and/or positive tissue transglutaminase IgA, anti-endomysial IgA, or anti-gliadin IgA/IgG). These records were further reviewed for recurrent presentation to the emergency department or pediatrician for abdominal pain.

Exact 95% binomial confidence intervals were calculated for each IS prevalence value. The present study was approved by the institutional review board of Columbia University Medical Center.

RESULTS

Patients With IS

For the 303,612 pediatric patients (mean age 7 ± 6.2 years) seen at our center from January 1, 2000 to January 1, 2010, 23,692 abdominal radiographic studies (CT, sonogram, magnetic resonance imaging, barium enema, small bowel series) were performed for children ages 6 months to 18 years, identifying 226 cases of IS in 216 patients. This translated into ISs diagnosed in 0.07% of children seen at our center during this time frame (95% CI 0.06%–0.08%). In 210 cases (200 patients), the IS was idiopathic. In the remainder of cases, a potential underlying cause or complicating factor was identified (Meckel's diverticulum [3], rotavirus infection [2], inflammatory bowel disease [3], Henoch-Schönlein purpura [1], Peutz-Jegher syndrome [1], jejunostomy/gastrojejunostomy [2], nasoduodenal tube [1], history of prior abdominal surgery [3]).

Thirty patients diagnosed with idiopathic IS returned to the emergency department or primary care office for evaluation of abdominal pain following their initial IS. In 10 cases of returning patients (33%), a second IS was identified and treated. Three patients without confirmed IS recurrence returned 2 or more times with abdominal pain. When we reviewed the laboratory tests of patients experiencing IS, we identified 11 patients with iron-deficiency anemia, 2 of which had return visits for abdominal pain.

Testing for CD with serology or esophagogastroduodenoscopy was performed for 4 of 200 patients with idiopathic IS: 1 patient with pain recurrence, and 3 patients with no apparent

additional risk factors. All of the 4 patients' celiac tests were negative. None of the patients with CD and ISs were tested, nor were patients with a history of IS and additional findings of iron deficiency anemia.

Patients With Known CD

Of the 318 patients with biopsy-proven CD in our registry, 53 had undergone a total of 77 abdominal imaging studies (Table 1) (1–3,5–9,17). The majority of those imaged (66%) were girls. Abdominal pain was the indication for 75% of studies; nearly half of these studies (48%) were performed before a diagnosis of CD was established. All of the episodes of IS were identified by ultrasound. IS represented the most frequent abnormal sonographic diagnosis among patients in the cohort (12.7%).

Four patients of 254 with complete records available (mean age 8.6 ± 4.9 years) had a history of IS (6 episodes total) (Table 2). All of the 4 patients experienced an IS before being treated for CD. In 3 patients, the IS prompted workup for CD and preceded the diagnosis by 9 months or less. The fourth patient was diagnosed with IS at age 5 months and was excluded from data analyses because it could not be ascertained whether he had been introduced to gluten at the time of his IS. Considering the remaining 3 patients, 1.2% of our cohort of children with CD experienced a known IS (95% CI 0.2–3.4).

Only 1 patient had laboratory abnormalities aside from positive celiac serologies (hypoalbuminemia and iron-deficiency anemia); the other 2 had no laboratory evidence of nutritional deficits. Normal body mass index (BMI) z scores were noted for patients with IS and available data. No patients with CD were diagnosed with an IS following treatment with a gluten-free diet.

DISCUSSION

Approximately 1200 to 1400 cases of IS occur annually in children in the United States alone (18). Although the majority of ISs in children are believed to be idiopathic, those with known etiologies are caused by lesions such as tumors or Meckel diverticula as well as associated conditions such as Henoch-Schönlein purpura (19), viral infections (20), and receipt of past versions of the oral rotavirus vaccine (21). There may be an increased risk among patients with Crohn disease, in whom case reports of ISs have been described (22), whereas in 1971, Holsclaw et al (23) described a 1% prevalence of IS among approximately 2200 patients with cystic fibrosis.

TABLE 1. Abdominal imaging studies performed for children with celiac disease

Study	No. studies	Findings
SBS	14	Normal (9)
		Thickened duodenal folds (3)
		Duodenal ulcer/malrotation (1)
		Narrow/irregular TI concerning for Crohn (1)
Ultrasound	47	Normal (17)
		Intussusception (6)
		Hepatomegaly (5)
		Splenomegaly (1)
		Pancreatic cyst (1)
		Splenic cleft (1)
		Possible gallbladder polyp (1)
		Hydronephrosis (1)
CT scan	16	Normal (8)
		Ileus (2)
		Splenomegaly (2)
		Prominence of jejunal folds (1)
		Nonspecific small bowel gas and fluid distension (1)
		Pneumonia (1)
		Mild fullness of renal pelvis (1)

Number of patients in parentheses. CT = computed tomography; SBS = small bowel series; TI = terminal ileum.

In the present study, we report that >1% of children with CD experienced a known IS before treatment with a gluten-free diet. This was similar to recent documentation of the prevalence among adults with CD (1.6%) (10). Given that not all of the children with CD and abdominal pain underwent abdominal imaging, this estimate refers only to cases clinically significant enough to warrant medical attention. The true prevalence of IS in this population may exceed this figure if one assumes that many patients with comparatively mild abdominal symptoms may have had transient, undiagnosed ISs. ISs among patients in our cohort of children with CD exceeded recent reports of the overall prevalence in American children (up to 0.037%) (3), as well as at our institution (approximately 0.07%).

An association between transient, nonobstructive ISs and CD has been described in the adult literature for >30 years, (24) some studies citing the prevalence of transient ISs among adults with CD and malabsorptive symptoms at 20% (8). One case report documents an IS in a women who underwent laparotomy because of a presumed tumor, who was later diagnosed as having mesenteric lymphadenopathy and underlying CD (8). Among adults, IS may also occur in the setting of type II refractory CD and is less common in uncomplicated CD (25). Transient small bowel ISs have been noted in children (26,27), although the association between these and CD is not well described to date in the pediatric literature.

The reason for the lack of pediatric data on this subject may be attributed to the fact that IS is a rare finding among adults, so an etiology may be sought more vigorously. In their recent 25-year review of adult patients diagnosed with IS, Onkendi et al (28) studied 196 patients with IS, 60% of which underwent CT scanning, and 61% of which required surgical management. Malignancy was found to be the cause in 22% of cases; CD accounted for 4%. In contrast, ISs are comparatively common in children, and usually considered to be idiopathic (1,4). Pediatricians may not feel compelled to probe further into predisposing factors of a child who otherwise appears healthy.

Data regarding an association between ISs and childhood CD have been limited to case reports and cite transient small bowel-small bowel ISs not requiring intervention (12–14,16). In our patient series, 1 child manifested multiple small bowel-small bowel and ileocolic ISs, whereas the other lesions were purely ileocolic. Furthermore, all of the cases of IS occurred in children with untreated CD, and in 3 of 4 cases IS was a presenting complaint prompting further evaluation. With the exception of 1 patient diagnosed as having CD at age 11 years whose IS occurred in infancy, all of the others were diagnosed as having CD weeks to months after the IS. The close temporal relationship of most cases with the patients' diagnoses with CD suggests more than a coincidental association. In addition, the absence of IS among children treated for CD in our cohort should be noted; similarly, 64% of adult patients with CD and IS in a recent study were shown to have been diagnosed with an IS soon before or after diagnosis with CD (10).

Among patients diagnosed with IS at our institution, only 2% were tested for CD, including 1 patient with recurrent episodes. Our data have demonstrated that evidence of nutritional deficiencies, such as iron-deficiency anemia and low albumin, need

TABLE 2. Characteristics of children with celiac disease and intussusception history

Patient	Age of IS/CD diagnosis	Symptoms preceding CD diagnosis	BMI z score at diagnosis	IS location (treatment)	Histological severity	Follow-up (duration)
A*	5 mo/11 y	Abdominal pain	1.57	NA (surgical reduction)	PVA	GF, doing well (4 y)
B	11 y/12 y	IS, abdominal pain	Not available	Ileocolic (surgical reduction)	PVA	GF, doing well, (3 y)
C	2.5 y/2.5 y	IS, vomiting	−0.48	Ileocolic (surgical reduction)	''Consistent with celiac sprue''	GF, doing well (8 y)
D	2 y/2.5 y	Recurrent IS, abdominal pain	−0.4	Ileocolic x 1/SB-SB x multiple (self-limited)	STVA	Not available

CD = celiac disease; GF = gluten-free; IS = intussusception; PVA = partial villous atrophy/mild enteropathy (Marsh II–IIIa); SB-SB = small bowel-small bowel; STVA = subtotal villous atrophy/severe enteropathy (Marsh IIIb–IIIc).
* Patient A was excluded from data analysis.

not be present for a child with IS and CD. In addition, all of the patients with IS who were later diagnosed as having CD demonstrated normal growth patterns. Although red flags such as recurrent small bowel-small bowel ISs, failure to thrive, and nutritional deficiencies may facilitate a diagnosis of CD, an index of suspicion for CD should be maintained in the setting of IS despite absence of these criteria.

Whether transient ISs underlie some complaints of chronic or recurrent abdominal pain in children with CD is not known, nor is it known how often ISs underlie pediatric complaints of recurrent abdominal pain in general. Abdominal pain is a frequent presenting complaint in children diagnosed as having CD (25,27,29–31), although the etiology of the pain is unclear. Three of the 4 patients with IS had complained of chronic abdominal pain, which resolved following dietary treatment. Additionally, abdominal pain was the indication for 75% of abdominal imaging studies performed; however, the majority of patients in our cohort who had abdominal pain did not undergo radiologic imaging (62.5%). Prospective studies are warranted to investigate the etiology of abdominal pain in children with untreated CD, as well as in patients compliant with dietary therapy.

Limitations of the present study include its retrospective nature. A prospective design may better approximate the rate of ISs among children with CD, perhaps capturing some that are transient. Additionally, complete radiology records were not available for all of patients in our cohort. Finally, although the frequency of ISs at our institution was close to the prevalence in the United States, because ours is a quarternary care medical center, the experiences of our patients may differ from those of patients elsewhere in the United States or in other countries.

In conclusion, we describe a greater frequency of IS among children with CD than in a general pediatric population. CD may be an underlying cause of IS and should be considered even in well-appearing children, although particularly if nutritional deficiencies or growth failure are also seen or in the setting of baseline abdominal complaints. IS may be a cause of recurrent abdominal pain in children with CD; however, it does not recur after diagnosis and treatment of CD with a gluten-free diet. Prospective studies are required to further explore the relation of abdominal pain, IS, and CD.

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