Case report

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Role of ultrasound in the diagnosis of very early-onset inflammatory bowel disease in children: a report of three cases

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Abstract

Very early-onset inflammatory bowel disease (VEO-IBD) is defined as IBD onset before 6 years of age and some cases are caused by unique monogenic disorders that require specific treatments such as stem cell transplantation. We identified three children with VEO-IBD of whom two had monogenic disorders. In cases 1 and 2, ultrasound revealed isolated colonic distribution and the loss of wall stratification. In case 3, mesentery inflammation was evident. Bowel ultrasound showed variable findings due to differences in the inflammation distribution within the bowel. In order to diagnose VEO-IBD, sonographers should carefully evaluate the intestinal wall thickness and stratification and the distribution of inflammation in the intestine and mesentery. These findings may aid the diagnosis of VEO-IBD.

Keywords: inflammatory bowel disease; very early-onset inflammatory bowel disease; immunodeficiency; ultrasound; children; monogenic

Introduction

Inflammatory bowel disease (IBD) is quite frequent in children and the incidence approaches the incidence and prevalence of adult IBD [1-6]. IBD with onset at <6 years of age was defined as very early-onset IBD (VEO-IBD) [7]. Furthermore, the type of IBD is generally classified into ulcerative colitis (UC), Crohn's disease (CD), or unclassified (IBD-unclassified) [8]. In children with VEO-IBD, IBD-unclassified is reportedly more common than older-onset IBD [9]. Recently, some cases of VEO-IBD have been included as a monogenic disorder in a unique category of IBD that accompanies immunodeficiency syndromes, hematological disorders or other genetic diseases [6,9-12]. This category is more resistant to conventional therapy and requires specific treatments such as stem cell blood transplantation [3,5,6].

Endoscopic examination is needed to diagnose VEO-IBD; however, this examination typically requires general anesthesia and can be technically difficult in children [13]. Clinically, ultrasound (US) is performed as the first examination in children with various symptoms such as diarrhea, abdominal pain or bloody stool and it is important to differentiate IBD from other diseases, such as infectious enterocolitis, owing to the high incidence of these diseases in pediatric patients [7,14].

Although US examination is recommended for the initial evaluation for IBD [13], to the best of our knowledge, no reports have focused on the US findings of VEO-IBD. The purpose of this case report was to explore the US findings related to VEO-IBD in children.

Case report

Table I summarizes the three patients' characteristics and US findings.

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Table I. Patient characteristics and ultrasonographic findings

Case	Age	Sex	Diagnosis	Symptoms	Sonographic findings			Endoscopic examination	Clinical diagnosis
					Bowel wall thickness	Bowel wall stratification	Distribution of inflammation		
1	3 years	M	Wiskott-Aldrich syndrome	Abdominal pain, bloody stool	>4 mm	Destruction	Left sided large colon	Colonoscopy	VEO-IBD
2	2 years	M	XIAP	Severe diarrhea, weight loss	>4 mm	Destruction	Left sided large colon	Colonoscopy	VEO-IBD
3	1 year	M	Unknown	Abdominal distention, weight loss	<4 mm	Preserved	Small bowel Mesentery	Colonoscopy, Capsule endoscopy	VEO-IBD

F, female; M, male; VEO-IBD, very early-onset inflammatory bowel disease; XIAP, X-linked inhibitor of apoptosis protein.

Case 1: Three-year-old boy with Wiskott-Aldrich syndrome

This patient was a 3-year-old boy, previously diagnosed with Wiskott-Aldrich syndrome. He had experienced abdominal pain and bloody stools for 2 weeks. US showed a bowel wall thickness of >4 mm from the rectum to the transverse colon, loss of wall stratification at the sigmoid and transverse colon and normal ascending colon. Echogenicity around the colon was high and lymphadenopathy was detected (fig 1). The small intestines were normal. Colonoscopy revealed multiple ulcers from the rectum to the transverse colon. The pathological findings were compatible with VEO-IBD. Finally, UC-like VEO-IBD by Wiskott-Aldrich syndrome was diagnosed. The symptoms persisted regardless of immunosuppressive treatment; therefore, stem cell blood transplantation was performed.

Case 2: Two-year-old boy with X-linked inhibitor of apoptosis protein

This patient was a 2-year-old boy with a 2-month history of severe diarrhoea and weight loss. The patient had a recurrent anal fistula. The wall thickness of the sigmoid colon was >4 mm. Echogenicity in this area was high owing to inflammation. Lymph node swelling was also evident and the wall stratification was destroyed in the transverse colon. The wall thickness of the ascending colon, terminal ileum, and small intestines was normal (fig 2). Colonoscopy revealed multiple longitudinal ulcers from the rectum to the transverse colon, and the ulcer type was similar to CD. The terminal ileum and ascending colon were normal. The pathological findings were consistent with VEO-IBD. The anal fistula and longitudinal ulcers were CD-like lesions; therefore, enteral nutrition and tumour necrosis factor-α therapy were selected, and monogenic VEO-IBD was suspected. During treatment, X-linked inhibitor of apoptosis protein (XIAP) deficiency was diagnosed. Stem cell blood transplantation was planned.

Case 3: One-year-old boy with VEO-IBD still not diagnosed as monogenic disorder

This patient was a 1-year-old boy with a 2-month history of abdominal distention and weight loss. US revealed an enlarged mesenteric lymph node and high echoic change in the mesentery, normal small bowel (wall thickness 2.7 mm), preservation of bowel wall stratification (fig 3) and normal colon and rectum. Cap-

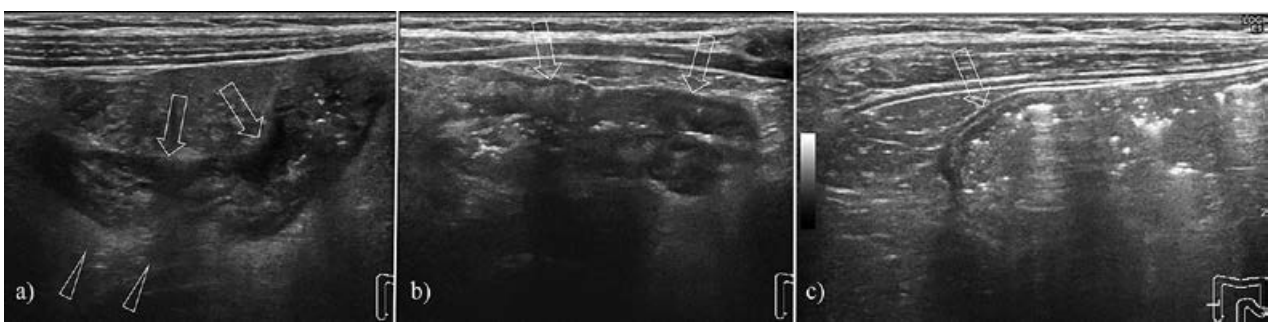

Fig 1. Three-year-old boy with Wiskott-Aldrich syndrome: a) the bowel wall thickness was >4 mm on the side of the sigmoid colon (arrow). Wall stratification disappeared at the sigmoid colon. Echogenicity around the colon was high and lymphadenopathy was detected (arrowheads); b) wall stratification also disappeared at the transverse colon and the wall thickness was >4 mm (arrow); c) normal ascending colon (arrow).

Fig 2. Two-year-old boy with X-linked inhibitor of apoptosis protein: a) the wall thickness was >4 mm on the sigmoid colon (arrow), echogenicity around the sigmoid colon was high and lymph node swelling was evident (arrowhead); b) wall stratification was destroyed in the transverse colon, the wall thickness was >4 mm (arrow) and echogenicity around the sigmoid colon was high (arrowheads); c) normal ascending colon (arrow).

sule endoscopy indicated multiple ulcers in the small intestine and colonoscopy revealed erosion at the terminal ileum. The pathological finding from the terminal ileum was compatible with VEO-IBD. Laboratory data associated with immune-dysfunction and hematologic disorder were normal and physical examination findings such as extraintestinal manifestation and family history of autoimmune disease were not detected. A gene panel for VEO-IBD was not performed. Therefore, this patient is yet to be classified into the monogenic IBD group. Because VEO-IBD was diagnosed, enteral nutrition was selected for treatment, which resulted in weight gain and the disappearance of the abnormal US findings.

Discussion

We herein reported three cases of children with VEO-IBD. Bowel US showed variable findings due to differences in the inflammation distribution and components within the bowel. These findings could vary according to the severity and type of disease and the timing of the examination. To suggest a diagnosis of VEO-IBD, a sonographer should carefully evaluate the intestinal wall thickness and stratification, as well as the distribution of inflammation in the intestine and mesentery.

Although not specific to VEO-IBD, the following factors were important indicators of an IBD diagnosis: 1) bowel wall thickness and its stratification and 2) the distribution of inflammation [15-18]. Regarding the bowel wall thickness and its stratification, the cut-off value of bowel wall thickness was reported to be ≤3 mm (2-2.5 mm) [15-24]. Pathological inflammation mainly involves the mucosa and superficial submucosa in UC and all bowel wall layers from the mucosa to the serosa in CD [14]. Therefore, the increased wall thickness may be caused by the thick mucosa and superficial submucosa in UC. In CD, bowel wall stratification may disappear [16]. In the pathological findings of cases of VEO-IBD, severe chronic architectural changes and small intestine villous blunting have been reported [25]. Therefore, destruction of the bowel wall stratification can be detected in cases of VEO-IBD. Regarding the distribution of inflammation, in cases of VEO-IBD with CD characteristics, ileitis and terminal ileum narrowing were not common [25]. Therefore, in cases with sonographic findings that indicate the destruction of bowel wall stratification, such

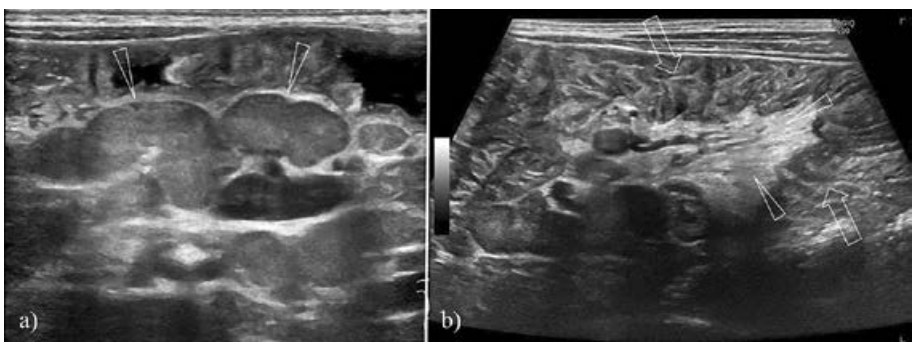

Fig 3. One-year-old boy with very early-onset inflammatory bowel disease not associated with a monogenic disorder: a) enlarged mesenteric lymph node (arrowheads); b) high echoic change in the mesentery (arrowheads), small bowel was not distended (arrow), wall thickness was 2.7 mm and wall stratification was preserved.

as in CD, and an inflammation distribution atypical of CD, VEO-IBD should be considered. In our cases 1 and 2, the distribution of inflammation was similar to that of UC, but the wall stratification was lost, unlike that in UC. According to the clinical information and endoscopic and pathological findings, monogenic VEO-IBD was suspected and these cases were diagnosed with Wiskott-Aldrich syndrome and XIAP.

In case 3, inflammatory change was noted in the mesentery and high echogenicity around the mesentery was detected by US. This finding was reported to indicate inflammation [19]. In this case, however, US did not show a bowel wall thickness of >3 mm or loss of the wall stratification and VEO-IBD was diagnosed based on the endoscopic and pathological findings. Therefore, US findings of inflammation in the mesentery may necessitate further examinations to diagnose VEO-IBD.

In cases 1 and 2, the symptoms such as bloody stool or diarrhoea might have been associated with US findings of the colonic inflammation distribution and the loss of wall stratification [10]. In contrast, in case 3, US did not reveal abnormal bowel wall thickness and the loss of wall stratification. Therefore, the primary symptoms of this case were abdominal distention and weight loss rather than bloody stool or diarrhoea.

In conclusion, the US findings of VEO-IBD include various degrees of inflammation (isolated colonic inflammation distribution, loss of wall stratification or inflammation of the mesentery). and if these findings are detected, the clinical information and family history should be checked, and VEO-IBD should be considered.

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