Clinician's Corner

A 5-month-old boy with bloody stools

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Speciality Area: Paediatric Medicine, Gastroenterology, Nutrition

A 5-month-old previously healthy boy presented with bloody, loose green stools for 2 days. He was mostly breastfed with occasional dairy protein formula supplementation. His mother consumed an unrestricted diet. There was no history of vomiting, cellulitis, joint swelling, or eczema.

The child was born at term by vaginal delivery. His birth weight was 3.77 kg (80th %) and height was 51 cm (60th %). He received antibiotics for presumed sepsis after prolonged maternal rupture of membranes. His parents were nonconsanguineous and of European background. His grandmother had irritable bowel syndrome.

He appeared well, active, and not toxic. His weight was 6.5 kg (20th %) and height was 65 cm (50th %). His temperature was 37.5°C, heart rate was 120/minute, and blood pressure was 88 mmHg systolic. His perfusion and hydration were good.

Abdominal, skin, mucous membrane, and perineal examinations were normal.

Investigations showed a leukocytosis of $20.3 \times 10^9/L$ (reference 5.0 to $15.0 \times 10^9/L$) and normal haemoglobin, albumin, and platelet counts. His stool smear demonstrated red and white blood cells. Stool culture, electron microscopy for virus, and abdominal radiograph and ultrasound were unremarkable.

A provisional diagnosis of cow's milk protein allergy was made. His mother was instructed to eliminate dairy from her diet with continuation of breastfeeding and elemental formula supplementation. Attempts to introduce soy formula and cow's milk at 7 and 16 months of age, respectively, resulted in recurrence of bloody stools. Subsequent investigations established the diagnosis.

CASE DIAGNOSIS: VERY-EARLY-ONSET INFLAMMATORY BOWEL DISEASE

At 24 months of age, colonoscopy and upper gastrointestinal contrast with follow through (UGIFT) studies were performed.

Biopsy and UGIFT revealed moderate colitis throughout the entire colon confirming the diagnosis of very-early-onset inflammatory bowel disease (VEOIBD). His immunological workup was unremarkable. His course was complicated by extra-intestinal manifestations including a perianal abscess, arthritis, and eczema. At 10 years of age, his growth remained delayed (weight and height 5th %).

Inflammatory bowel disease (IBD) is characterized by chronic inflammation of the gastrointestinal tract and is commonly categorized into Crohn's disease (CD), ulcerative colitis (UC), and IBD unclassified (IBDU). Crohn's disease involves transmural lesions affecting any segment of the gastrointestinal tract while UC has mucosal lesions affecting the large intestine. Whereas, IBDU presents with overlapping features of CD and UC. Children account for approximately 25% of IBD cases with the majority presenting during teenage years (1). Recent studies show a decrease in age of IBD onset over the past 10 years, with children as young as 2 years old presenting with typical IBD (2). Symptoms of paediatric IBD are similar to those seen in adults, including abdominal pain, weight loss, and diarrhoea (3). Additional findings include symptoms refractory to dietary changes, positive family history, and extra-intestinal manifestations (skin rashes, mucosal ulcers, arthralgia, uveitis, and perianal involvement) (4). Failure to consider IBD in childhood may delay diagnosis and treatment with negative impacts on growth, puberty onset, and global development (3,4).

Very-early-onset inflammatory bowel disease (VEOIBD) is defined as paediatric IBD diagnosed under 6 years of age. This includes infantile IBD (<2 years of age) (3). VEOIBD often has a phenotype of pancolitis with limited or no small bowel involvement, making it challenging to distinguish between CD and UC. Further, the colitis phenotype often is resistant to standard treatment and has a stronger association with underlying immune deficiencies (1) (Table 1). Children with VEOIBD are more likely to have a positive IBD family history through monogenic inheritance (1) as identified in 31% of infantile IBD patients (3). The polymorphism identified in our patient (e.g., *NCF2* mutation) affects components of phagocyte NADPH oxidase, which is associated with immunodeficiency and intestinal inflammation resembling IBD (4).

In patients where IBD is suspected, standard investigations including biopsy would rule out allergic and infectious colitis. Given the higher risk of underlying immunodeficiencies in the VEOIBD population, patients should have additional screening including serum immunoglobulin levels, flow

Table 1. Differences between VEOIBD and paediatric IBD

	VEOIBD	Paediatric IBD
Disease distribution	Predominantly colonic Rarely ileal	Ileal and colonic
Genetic distribution	Common, low-impact variants Rare, loss of function mutations	Common, low-impact variants
UC colectomy rate	Low	High
CD intestinal resection rate	Low	High

VEOIBD, Very early onset inflammatory bowel disease. IBD, Inflammatory bowel disease. UC, Ulcerative colitis. CD, Crohn's disease. Adapted from (1).

cytometry analysis, and analysis of neutrophil oxidative burst (4). Comprehensive immunological and genetic screening is recommended for patients with infantile IBD given the prevalence of monogenic disease (3). Common laboratory abnormalities in VEOIBD may include anemia, hypoalbuminaemia, thrombocytosis, or inflammatory changes in C-reactive protein and erythrocyte sedimentation rate (3).

This child had a novel *NCF2* gene polymorphism and Crohn's disease phenotype. Medical management including immunosuppressants and intermittent antibiotics (ciprofloxacin, metronidazole) were tailored with good response.

CLINICAL PEARLS

- 1) Although uncommon, VEOIBD should be considered in recurrent bloody stools of early childhood when symptoms are refractory to dietary modifications and extra-intestinal manifestations evolve.
- 2) Very-early-onset inflammatory bowel disease (VEOIBD) is typically pancolonic, resistant to standard therapy and may be associated with underlying immunodeficiency.
- 3) Patients with VEOIBD have higher likelihood of a family history of IBD. Monogenic diseases that mimic IBD in this population (i.e., *NCF2* mutation) are more common and may lend well to precision medicine.

Keywords: Crohn's disease; Inflammatory bowel disease; Ulcerative colitis

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