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# Initial Presentation of a Pediatric Intestinal Pseudo-Obstruction Episode After SARS-CoV-2 Virus (COVID-19) Infection

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## INTRODUCTION

Pediatric intestinal pseudo-obstruction (PIPO) is an umbrella term describing disorders characterized by gastrointestinal (GI) dysmotility with variable course, severity, and onset. PIPO may account for up to 15% of pediatric intestinal failure cases, which can lead to use of parenteral nutrition (PN) supplementation, intestinal transplantation, and sometimes intestinal resection or the creation of ostomies (1,2). Patients present with symptoms of bowel obstruction in the absence of a mechanical etiology (3). Children with PIPO may also have involvement of smooth muscle viscera, including megacystis with polyhydramnios. The ESPGHAN consensus statement on diagnosis of PIPO requires at least 2 of the following 4 criteria: objective measure of small intestinal neuromuscular involvement, recurrent or persistently dilated loops of small intestine with air-fluid levels, genetic abnormalities, and the inability to maintain adequate nutrition or growth with enteral feeding (4,5). Recent advances in whole-exome sequencing have identified several mutations that can be pathogenic, commonly including the *ACTG2* gene (1,3).

Viral infections may alter the integrity of the enteric neuromuscular system and play a role in the development of pseudo-obstruction (6). Several case reports over the last 2 decades have reported Epstein-Barr, cytomegalovirus, varicella-zoster, and John Cunningham viral illnesses to be the causal agent of PIPO episodes, possibly due to acquired hypoganglionosis, myopathy, or neuropathy (7,8). While it has been suggested that infections, general anesthesia, psychologic stress, and poor nutritional status may serve as precipitating factors to exacerbations, triggers are largely unpredictable and unknown (9). The novel severe acute respiratory syndrome coronavirus 2 or COVID-19, is a single-stranded RNA virus with emerging evidence for significant GI involvement. Several recent publications have found that 9%–20% of COVID-19 patients experience nausea, vomiting, diarrhea, anorexia, hepatic inflammation, or abdominal pain (10). We believe this virus may also represent a potential trigger for PIPO episodes.

## CASE REPORT

We present the case of a 7-month-old male with history of megacystis, bilateral hydronephrosis, and constipation who presented with acute onset of abdominal distension and bilious emesis. Due to concern for bowel obstruction, he underwent an exploratory laparotomy which did not demonstrate a mechanical etiology. Abdominal radiograph comparison with previous imaging showed persistently dilated bowel loops (Figs. 1 and 2). Barium enema was normal and without evidence of microcolon. Upper GI with small bowel follow-through demonstrated significant delayed emptying of contrast from the small bowel. Rectal biopsy was negative for Hirschsprung's disease.

There were no prenatal anatomic abnormalities or polyhydramnios. There was no history of delayed passage of meconium. He developed constipation at 4 months of age, requiring 2 admissions for bowel clean-out in the setting of abdominal distention. Work up for diabetes and thyroid disease were unremarkable.

Approximately 1 month before this presentation, the patient and his family tested PCR positive for COVID-19. Repeat PCR testing at time of admission was also positive. The patient did not develop any extraintestinal symptoms while his family members experienced fever, anosmia, nausea, vomiting, and abdominal pain.

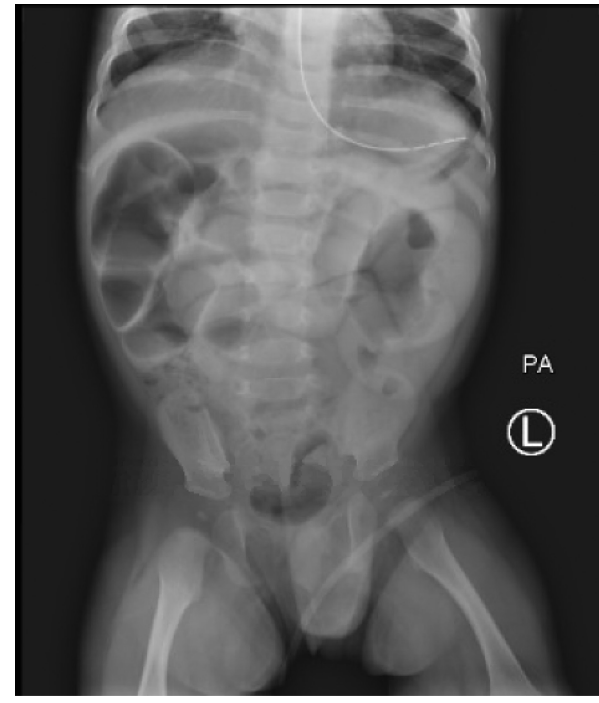


**Figure 1.** Abdominal X-ray showing distended loops of bowel before admission (during a constipation episode at 5 months of age).

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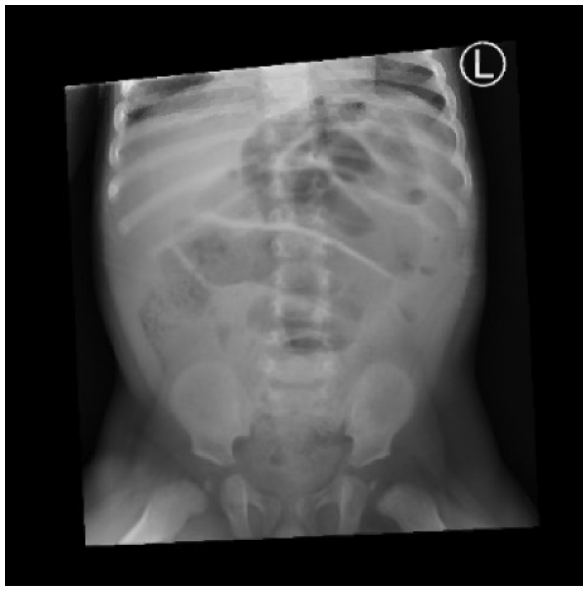

**Figure 2.** Repeat abdominal X-ray on admission showing persistently dilated bowel loops (7 months of age).

The patient underwent medical management with nasogastric and rectal decompression and ten days of PN support. With improvement of abdominal distention, he tolerated nasogastric breast milk and hypoallergenic formula feeds. Erythromycin was started for prokinetic properties and polyethylene glycol 3350 powder was started to produce softer, more frequent bowel movements. Enteral feeds were advanced and patient was weaned off of PN before discharge within 2 weeks. There was development of oral aversion during hospitalization, so patient went home with oral and gavage nasogastric feeding regimen. After 3 weeks of outpatient follow-up, he resumed all per oral feeding and is gaining weight, but has ongoing issues with constipation. He requires daily erythromycin, polyethylene glycol 3350, and as needed glycerin suppositories to ensure appropriate movement of intestinal contents.

An intestinal pseudo-obstruction panel collected during his 2-week hospitalization was positive for *ACTG2* gene mutation. There was no family history of chronic GI disorders in the family and parents are currently undergoing testing for the *ACTG2* mutation.

Based on his previous medical history, radiologic evidence of persistently dilated loops of bowel, genetic testing, feeding intolerance requiring PN, and obstructive presentation with lack of mechanical etiology on exploratory laparotomy, this patient met diagnostic criteria for PIPO with his first crisis presenting in association with a recent COVID-19 infection.

## DISCUSSION

This case is the first known pediatric description of pseudo-obstruction crisis caused by COVID-19.

Previously published data suggest viral illnesses may alter the integrity of the enteric neuromuscular system leading to episodes of pseudo-obstruction. Our patient's acute initial presentation after COVID-19 infection provides additional evidence that viral infections may contribute to the development of PIPO episodes in a person with an underlying predisposition, such as an *ACTG2* mutation. Interestingly, previous case reports of PIPO viral triggers have all been related to double-stranded DNA viral infections (Epstein-Barr, cytomegalovirus, varicella-zoster, John Cunningham virus), while the structure of COVID-19 is single-stranded RNA.

Whole-exome sequencing has identified *ACTG2* genetic mutations as one of the mutations responsible for PIPO. *ACTG2* mutations cause visceral myopathy responsible for a spectrum of disease ranging from Megacystis-Microcolon-Intestinal-Hypoperistalsis Syndrome to milder forms of myopathy with varying presentations of GI and urinary system abnormalities due to abnormal folding of the gamma 2 actin protein, a critical part of smooth muscle filaments and contraction (3).

Continued research is required to evaluate contributing factors to PIPO. While there is growing evidence of genetic mutation predisposition in patients with this disorder, it will be important to further evaluate triggers of obstruction. Future research should investigate the role of viral infections, including COVID-19, and their impact on the enteric nervous system.

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