

Teenager With Abdominal Pain and Decreased Appetite

John Clore, MD, Shelly Dean, MSN, Abigail V.W. Kumral, MD, Eva Manthe, RDN, CNSC, Serwa Ertl, MD

A 16-year-old girl presented to her primary care physician with a one-month history of decreased appetite and abdominal pain. She had normal bowel movements and no vomiting, but her periumbilical pain limited her ability to finish most meals. She had gradual weight loss over the previous 2 years, and during the previous 4 years, she intermittently received counseling for depression after the loss of her mother. Her initial physical examination and laboratory evaluation were unremarkable. She was referred to a nutritionist, adolescent medicine, and pediatric gastroenterology. Her presentation evolved over time, which ultimately led to a definitive diagnosis.

abstract

CASE INTRODUCTION AND INTERVIEWS

Dr John Clore (Pediatric Resident)

The patient is a 16-year-old previously healthy girl who presented to her primary care physician with a one-month history of decreased appetite and abdominal pain. She described intermittent periumbilical discomfort and pressure throughout the day and particularly at night when going to sleep. She reported feeling hungry and early satiety with the inability to finish most meals, with greasy foods eventually causing more severe symptoms. Her father noticed her eating pattern and encouraged her to take Ensure supplements, which she tolerated. She reported soft, daily bowel movements and denied nausea or vomiting. Per the patient and by chart review, she had a gradual 20-lb weight loss over the previous 2 years. She continued to have regular menstrual periods. At the time of presentation, the patient was struggling with depressed mood characterized by low energy, low motivation, anhedonia, and irritability but no suicidal ideation or sleep disturbance. This had been a concern for 4 years, since her mother died

of renal cancer. She intermittently received counseling for depression over that time period, but she was never prescribed medications. Specifically, she received initial grief counseling when she lost her mother, and she restarted counseling 2 years ago. She reported dissatisfaction with her thin appearance and denied intentional weight loss, fear of weight gain, purging behaviors, or laxative use. Her physical examination was normal, with the exception of left upper quadrant tenderness.

Dr Kumral, how did you approach this patient with concern for gradual weight loss, generalized abdominal pain, and decreased appetite?

Dr Abigail Kumral (Primary Care Physician, General Pediatrics)

When I first met this patient, she had a one-month history of abdominal pain and early satiety. She also had a prolonged history of gradual weight loss and depressed mood over the past 2 years. My initial assessment of a patient with recurrent abdominal pain includes a physical and mental health evaluation and initial laboratory studies (Table 1). I think it is important to discuss mental health in the first visit

Department of Pediatrics, University of Virginia, Charlottesville, Virginia

The authors obtained written consent from the family to publish this article.

All authors drafted and edited the content of the manuscript, approved the final manuscript as submitted, and agree to be accountable for all aspects of the work.

DOI: <https://doi.org/10.1542/peds.2019-2233>

Accepted for publication Jan 6, 2020

Address correspondence to Serwa Ertl, MD, Division of General Pediatrics, Department of Pediatrics, School of Medicine, University of Virginia, 1204 W Main St, PO Box 800386, Charlottesville, VA 22908. E-mail: sertl@virginia.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

To cite: Clore J, Dean S, Kumral AVW, et al. Teenager With Abdominal Pain and Decreased Appetite. *Pediatrics*. 2020;145(5):e20192233

for chronic issues because it normalizes the relationship between mental and physical health. If there are red flag symptoms suggestive of a particular diagnosis, I sometimes make a referral as well. It is important to balance cost-effectiveness and hassle for the family in choosing when to get specialized testing and referrals. As we manage patients for chronic issues over time, the need for these referrals often becomes clearer. In this patient with normal stools, regular menses, and a lack of skin findings, I did not think an urgent gastrointestinal (GI) referral was needed at initial presentation.

Dr Clore

It appeared difficult to distinguish her physical health from her mental health. Given that the patient's symptoms evolved over the preceding 2-year period, in what way was her growth chart used?

Dr Kumral

In a patient who regularly comes to the clinic, the growth curve can be helpful when evaluating a chronic issue. I first saw her at point A (Fig 1). This patient's linear growth was complete, and her pubertal stage was Tanner stage 5, so the length curve was only helpful insofar as her linear height was essentially in line with predicted midparental height (165.7 cm vs 167.5 cm predicted). Her weight curve was concerning because she had crossed 2 percentile lines (~75th to the 25th percentile) but was again suggestive of a gradual, chronic process. The slow and steady weight loss also correlated by history with the patient's reported worsening depression.

Dr Clore

What were your differential diagnoses for this patient, and how did that guide you in choosing her laboratory evaluation?

TABLE 1 Patient's Initial Laboratory Evaluation

Laboratory Component	Result	Reference Range
WBC count, μ L (thousand)	4.58	4.40–8.10
RBC count, μ L (million)	4.70	4.20–5.20
Hemoglobin, g/dL	12.0	12.0–16.0
Hematocrit, %	37.5	35.0–47.0
MCV, fL	79.8 (low)	83.0–95.0
MCH, pg	25.5 (low)	28.0–32.0
MCHC, g/dL	32.0	32.0–36.0
RDW, %	13.4	11.0–14.0
MPV, fL	8.9 (low)	9.0–12.0
Platelet count, μ L (thousand)	505 (high)	150–450
Lymphocytes, %	19.7	15.0–45.0
Monocytes, %	13.5 (high)	2.0–12.0
Eosinophils, %	5.7	0.0–6.0
Basophils, %	1.3	0.0–2.0
Nucleated RBC, %	0.0	—
Neutrophils, % calculated	59.8	47.0–82.0
Sodium, mmol/L	138	136–145
Potassium, mmol/L	4.0	3.4–4.8
Chloride, mmol/L	104	98–107
CO ₂ , mmol/L	24	20–28
SUN, mg/dL	7 (low)	8–21
Creatinine, mg/dL	0.7	0.6–0.9
Glucose, mg/dL	90	74–99
Calcium, mg/dL	9.3	8.5–10.5
Total protein, g/dL	6.6	6.0–8.0
Albumin, g/dL	3.5	3.2–5.2
Total bilirubin, mg/dL	0.7	0.3–1.2
Alkaline phosphatase, U/L	89	40–150
AST, U/L	13	<35
ALT, U/L	9	<55
Anion gap, mmol/L	10	5–15
Transglutaminase IgA, U/mL	<0.5	<15.0
Deaminated gliadin IgA, U/mL	0.3	<15.0
Free T ₄ , ng/dL	1.2	0.8–1.4
IgA, mg/dL	130.1	68.0–378.0
TSH, mIU/L	0.99	0.47–3.41

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CO₂, carbon dioxide; IgA, immunoglobulin A; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean cell volume; MPV, mean platelet volume; RBC, red blood cell; RDW, red cell distribution width; SUN, serum urea nitrogen; TSH, thyrotropin; T₄, thyroxine; WBC, white blood cell; —, not applicable.

Dr Kumral

My initial differential was broad and included celiac disease, thyroid disease, inflammatory bowel disease (IBD), depression, avoidant-restrictive food intake disorder (ARFID), and superior mesenteric artery syndrome. Initial screening laboratory tests included a complete blood cell count (CBC) with differential, a comprehensive metabolic panel, thyroid studies, and celiac screening laboratory tests. When working up a patient for chronic abdominal pain, I find these laboratory tests are a good starting point; I then will see the patient back

frequently and potentially get additional studies down the line. Although superior mesenteric artery syndrome was on my initial differential, the weight loss had been so gradual at that point that I thought it less likely than other diagnoses, so I decided not to do initial imaging. In this patient with gradual, chronic weight loss and no symptoms of malabsorption, and with familial concern over the cost of laboratory studies, I did not initially obtain inflammatory markers; however, after worsening acute weight loss and increased frequency of visits over the next several weeks, inflammatory markers were obtained.

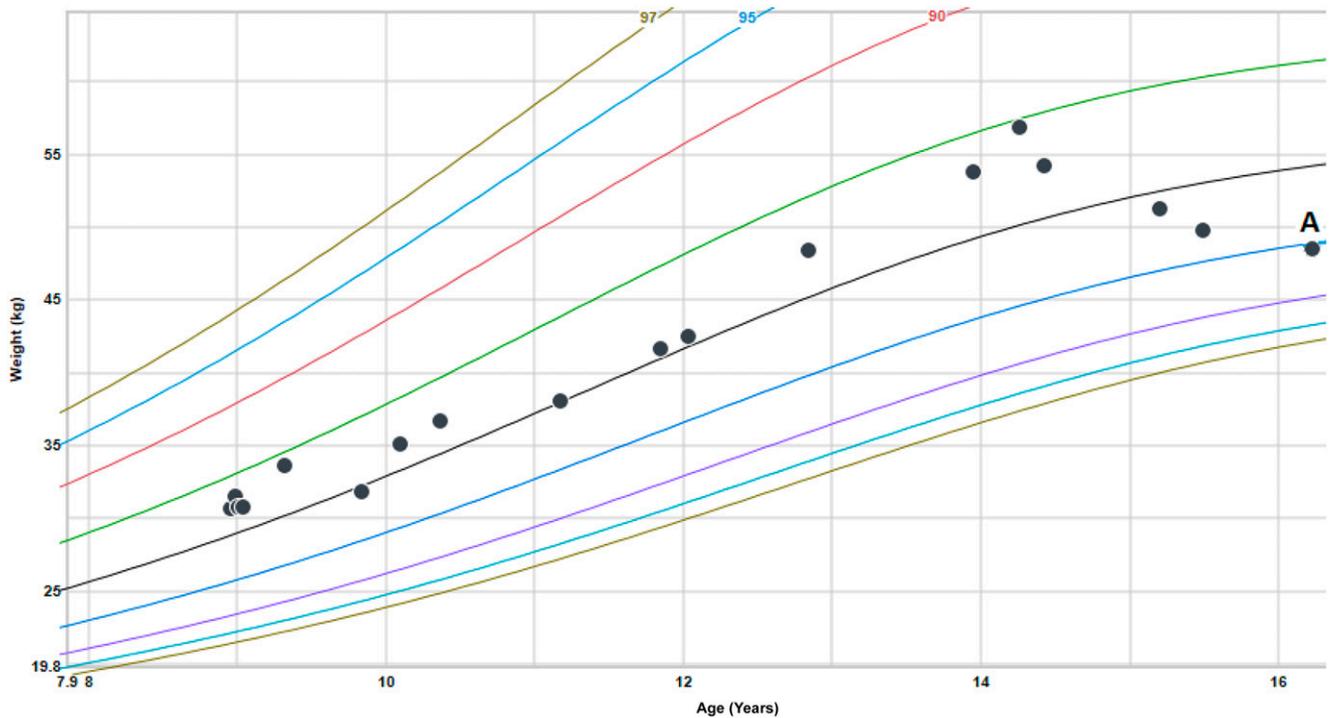


FIGURE 1
Growth curve demonstrating weight loss over time. A, first visit to Dr Kumral.

After I got the laboratory results back, I was more concerned about a possible ARFID in the setting of underlying depression. Although laboratory studies alone cannot rule out all organic etiologies, they were reassuring that I likely had some more time to figure out the etiology while trying to optimize her mental health. I referred the patient to nutrition as a first step and recommended she make a follow-up appointment with her psychologist. At her initial follow-up appointment, her affect had worsened, and I started her on a low dose of fluoxetine (10 mg) and continued to follow her closely for medication management. Both the patient and her father reported finding the guidance from the nutritionist helpful.

Dr Clore

Eva Manthe, how did you approach this patient with weight loss?

Eva Manthe, Registered Dietitian (Pediatric Clinical Dietitian)

Initially, we explored what factors may have led to her weight loss. The

patient denied any intentional changes to promote weight loss or worries about weight gain, but both she and her father reported challenges with appetite and pickiness overall, which had resulted in her skipping meals at times or not eating much of a meal. Initially, there were not certain foods that the patient or father could identify that led to more abdominal pain than others; therefore, we did not focus on any food eliminations. We reviewed general nutrition education topics, including the importance of adequate nutritional intake (especially during adolescence), the food groups, and macronutrients and micronutrients and why each is important. Throughout our first few visits, we worked together to brainstorm ways to improve her intake, but we ultimately reviewed a more structured meal plan that her father would help implement at home.

Dr Clore

When should a patient with weight loss be referred to nutrition?

Eva Manthe

Each case is unique; however, generally, if weight loss has been identified, the family and patient indicate struggles with eating, and a medical workup to rule out organic reasons for the challenges has been completed, then a dietitian assessment (or a registered dietitian assessment as part of a multidisciplinary team) that includes evaluation of current intake with nutrition education, goal setting, and monitoring should be pursued.

Dr Clore

What interventions did you recommend to this patient?

Eva Manthe

When first meeting the family, the patient's intake was rather variable (as with many teenagers); on the basis of her own report, she was often skipping meals or eating inadequate portions. Her reasons for skipping meals were usually related to timing in the morning or not feeling hungry

at lunch during the school week. Her intake on weekends was improved. At our initial visit, I strived to partner with her to review general meal planning strategies, how to balance her meals with the various food groups, and how to estimate appropriate portions for her needs. Given her pickiness, we reviewed new recipes to try at home. At our second visit a month later (first follow-up), they reported that there were not many changes made, and she was interested in additional support. We reviewed therapy as an option because her depression may have been challenging for her, and depression can often impact appetite and nutritional intake. We also reviewed trying a more structured meal plan with set goals within each food group to provide certain nutritional intake each day.

Dr Clore

After seeing the patient, what made you refer to adolescent medicine?

Eva Manthe

We had 2 visits before my recommendation of referring to adolescent medicine, and although she denied body image concerns and worries about weight gain, I did have concerns that her psychological state (especially depression) was playing more of a role in her eating patterns than I alone could address. Her father was also struggling to support her eating at home; therefore, we agreed that expanding her support team to include a medical provider who specializes in the adolescent population and has expertise in eating struggles, psychological concerns, and malnutrition in this population would be a beneficial next step.

Dr Clore

Dr Ertl, on the basis of her initial history and examination findings, could this patient have had an eating disorder?

Dr Serwa Ertl (Adolescent Medicine)

When the patient presented to our first visit, both an eating disorder and disordered eating secondary to depression were on my differential diagnosis. Initially, she had decreased appetite, abdominal pain, and the inability to meet her nutritional requirements, which resulted in significant weight loss over a gradual period of time. She lost almost 18 lb within the past 2 years, 5 lb of which came within the past 2 months. Her BMI was 16.6 (z score: -1.85) at our initial visit. Both her symptoms of decreased appetite and abdominal pain coincided with the loss of her mother and the development of depression. Therefore, my initial thought during our visit was that perhaps she was having disordered eating from depression and that treatment of her depression would result in increased nutritional intake. However, during our visit, she revealed that eating prompted the onset of abdominal pain, which prevented her from completing meals. The results of her initial evaluation for organic causes of her abdominal pain and weight loss were negative. Therefore, I was concerned that she could be restricting her nutritional intake because of her abdominal pain, which is more consistent with ARFID. With ARFID, restriction of food is not the result of body dysmorphism or fear of weight gain, as often seen in anorexia nervosa. Rather, it is the avoidance or restriction of food due to concern for aversive consequences such as abdominal pain after eating. Thus, ARFID as an eating disorder was at the top of my differential diagnosis as the potential cause of her restrictive eating and her significant weight loss.

Dr Clore

Although the patient continued to follow-up with you, what made you concerned for another potential cause for her weight loss?

Dr Ertl

After 3 visits within a one-month period, she was not having significant improvement in weight gain. She was on fluoxetine and seeing a school therapist for depression, which helped improve her mood. However, she continued to have poor appetite and minimal intake despite adequate management of her depression. Although she was continuing to have abdominal pain with meals, she was able to tolerate and eat through the discomfort she was having. Thus, her abdominal pain no longer appeared to be a significant cause of her decreased intake.

One month after our initial visit, she revealed that she had noticed intermittent bruising on her lower extremities for the last few weeks. She described the bruising as red, tender, and located from her ankles to her knees. After examination, the bruising was in fact erythematous, tender, nodules on her shins. On the basis of her examination, both Dr Clore and I were concerned for the onset of erythema nodosum. Now with the presence of erythema nodosum in the setting of weight loss, continued poor weight gain, and abdominal pain, there was even more concern for IBD as a potential cause for her symptoms.

Dr Clore

On the basis of her new physical examination findings, how did you decide on the next steps in her evaluation and management?

Dr Ertl

Her new onset of erythema nodosum and initial weight loss were concerning for IBD. Therefore, a laboratory evaluation for IBD was warranted. Her C-reactive protein (CRP) level was elevated (3.3 mg/dL), and her erythrocyte sedimentation rate (ESR) was 24 mm/hour. No prealbumin test was obtained. Her CBC revealed anemia, with a significant decline in hemoglobin

levels from 12.0 to 10.1 g/dL, hematocrit levels from 37.5% to 33.8%, and the mean corpuscular volume from 79.8 to 77.2 fL within 3 months. After the return of her laboratory tests, we had a higher suspicion for IBD. Therefore, we immediately contacted GI for an urgent referral and the likely need for an endoscopy and colonoscopy with biopsies for diagnostic confirmation of IBD.

Dr Clore

Shelly Dean, can you explain the biopsy results?

Shelly Dean, Nurse Practitioner (Pediatric Gastroenterology)

Her results were consistent with IBD, specifically Crohn's disease, because she had chronic active cryptitis with granulomas in her colon and terminal ileum.¹ Granulomas are only present in Crohn disease, not ulcerative colitis, and involvement of the terminal ileum makes the diagnosis even more concrete because there is small bowel involvement.¹ She had some inflammation in her duodenum on pathology, but an MRI of her small intestines revealed no stricture and no further small bowel involvement, making an argument that this is mostly isolated to her ileum.

Dr Clore

Could the patient's initial presentation have been consistent with IBD?

Shelly Dean

A small percentage of patients with Crohn's disease present with weight loss and/or slowing of their linear growth and few if any other symptoms along with normal routine laboratory studies.² This most typically occurs in patients with isolated terminal ileal Crohn's disease.² Several prospective studies have revealed that at the time of the diagnosis of IBD, ~20% of children have a normal CBC, normal serum albumin level, normal ESR, and

normal CRP level.³ Delay in the diagnosis is much more likely with ileal Crohn disease than with ulcerative colitis or Crohn's colitis because it is hard to ignore bloody diarrhea for long.⁴ Although the majority of children with weight loss and slow linear growth do not suffer from Crohn's disease, it is always important to keep this diagnosis in mind. This patient also presented with abdominal pain associated with meals, which can be a common manifestation of Crohn's disease. It is often difficult to discern between organic and psychosomatic causes of GI symptoms.³ Patients may have a primary GI disorder with resulting disordered eating or a primary eating disorder with resulting GI symptoms.³ Either may present with nonspecific symptoms such as abdominal pain, nausea, vomiting, altered bowel habit, anorexia, weight loss, and growth failure.³ A rectal examination is also useful in this setting because evidence of perianal inflammation with skin tags is almost pathognomonic of Crohn's disease.¹ Similarly, somewhere between 10% and 20% of children with IBD will have digital clubbing at the time of diagnosis that resolves with successful therapy.⁵

Dr Kumral, in retrospect, are there additional tests you might have added at the initial presentation?

Dr Kumral

In retrospect, I would have added an ESR as well and perhaps a CRP test. However, it is impossible to say if those studies might have been normal at the time. Given the cost (\$374 in our laboratory), I likely would not have started my workup with a fecal calprotectin study, but it would have been something to consider when symptoms did not improve and weight loss persisted.

Shelly Dean, is it unusual to have normal laboratory tests at the initial presentation, and if so, do laboratory

tests evolve on the basis of disease progression?

Shelly Dean

As stated previously, ~20% of children with IBD have normal routine laboratory tests, including ESR and CRP, at the time of diagnosis.⁶ Many children with ulcerative colitis persistently have a normal CBC, serum albumin level, ESR, and CRP level despite passing multiple bloody bowel movements each day. In children who have normal blood studies at the time of diagnosis, their blood studies may remain normal until they become ill.

Dr Kumral

Are there additional noninvasive tests that might have been helpful in this patient? What is the utility of a fecal calprotectin for IBD diagnosis, and when do you suggest it be ordered, especially in the primary care setting?

Shelly Dean

Calprotectin is a calcium-binding protein found in granules of neutrophils.⁷ Fecal calprotectin is a sensitive marker of intestinal inflammation, and it has become a common biomarker for IBD.⁷ In a number of prospective studies performed in different clinical settings, the sensitivity of a positive fecal calprotectin for IBD approaches 100%.⁸ If the fecal calprotectin level is low (<15.6), the negative predictive value for IBD approaches 100%.⁸ The specificity and positive predictive value of a positive test result is much lower because there are a variety of other etiologies for intestinal inflammation besides IBD. If the fecal calprotectin level is elevated, it is not diagnostic of IBD, but it should make one suspicious and consider further testing, most typically a colonoscopy. In a retrospective study of 898 patients, none of whom had a diagnosis of IBD and all of whom had fecal calprotectin measured in the primary care setting, 84% had normal calprotectin levels.⁸

None of these patients were diagnosed with IBD or any other GI disease in the following 12 months.⁸ These and other data suggest that fecal calprotectin is an excellent screening tool for IBD and can help avoid unnecessary referrals and endoscopies.

Dr Kumral, what are your thoughts on integrating fecal calprotectin into primary care practice?

Dr Kumral

I had not realized the high sensitivity and negative predictive value of fecal calprotectin. Given the high cost, I am not sure I would add it to my initial workup, but I think using this study if the weight loss has not improved at follow-up without clear etiology would be a reasonable choice and could help guide the decision of whether GI referral is needed. Although this patient ultimately developed a pathognomonic finding of IBD, most patients with IBD will not declare themselves as clearly, so it could be helpful.

CONCLUSIONS

This case exemplifies how difficult it can be to distinguish between the initial presentations of IBD, ARFID, and other etiologies of weight loss and abdominal pain in the adolescent. IBD can present in a variety of ways and can sometimes initially imitate other diagnoses. In this 16-year-old girl with weight loss, multiple aspects of her initial presentation were concerning for ARFID, and she did not have some of the clinical elements classically associated with IBD, such as diarrhea. Even in the setting of normal initial laboratory studies, she was followed closely by multiple providers who identified new and evolving symptoms as her course diverged from a typical ARFID presentation to her ultimate diagnosis of IBD. Her history of depression could have easily been determined as the sole contributor to her symptoms if not for an

interdisciplinary dialogue among her medical team, which may have caused a delayed or missed diagnosis. This scenario reveals the risks of an anchoring bias or effect, in which physicians rely too heavily on the first piece of information offered (the anchor) when making subsequent decisions.^{9,10} Aside from incorrect diagnosing, anchoring bias is also associated with therapeutic and management errors for patients.¹¹ Her history of depression could have easily become the anchor and been attributed to her disordered eating if not for an interdisciplinary dialogue among her providers. The medical team might have focused their recommendations on adequate therapy for the management of depression despite her continued weight loss with these therapies already in place. Thus, the previous case reveals the importance of clinician self-awareness of cognitive biases and the need for a comprehensive medical team with expertise with a unique patient population. Adolescents differ cognitively, physiologically, and socially from other age groups, yet a majority of adolescents receive ambulatory care from pediatricians or adult primary care physicians rather than adolescent medicine physicians.¹² This may contribute to a higher rate of adverse events, specifically diagnostic adverse events, in comparison with other age groups of children.¹¹

Although initial screening laboratory tests were normal, these can be normal in 20% of children at the time of diagnosis.⁶ Therefore, normal screening laboratory tests support alternative diagnoses, but they do not exclude IBD. Fecal calprotectin is a useful tool in assessing intestinal inflammation, and it has utility in both the primary care setting and the gastroenterologist's office.⁸ It is possible that the fecal calprotectin level would have been elevated at this patient's initial presentation;

however, given the lack of classic symptoms, this must be weighed in conjunction with the laboratory charge and the possibility that the laboratory would not be covered by insurance. Calprotectin would have been useful if her repeat laboratory tests were not concerning. Should all patients with disordered eating be screened with fecal calprotectin? To best answer this, a cost analysis is necessary. Regardless, performing a fecal calprotectin test in patients with disordered eating, weight loss, and abdominal pain has realistic benefits. In this case, a definitive diagnosis of Crohn's disease was made because of close follow-up with multiple providers over time. As soon as the diagnosis of IBD was made and appropriate therapy commenced, she had rapid restoration of her weight and resolution of her abdominal pain.

ACKNOWLEDGMENT

We thank Dr Rachel Moon (University of Virginia) for her encouragement in submitting this article and her assistance in editing initial drafts.

ABBREVIATIONS

ARFID: avoidant-restrictive food intake disorder
CBC: complete blood cell count
CRP: C-reactive protein
ESR: erythrocyte sedimentation rate
GI: gastrointestinal
IBD: inflammatory bowel disease

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Pediatrics 2020;145;

DOI: 10.1542/peds.2019-2233 originally published online April 29, 2020;

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DOI: 10.1542/peds.2019-2233 originally published online April 29, 2020;

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