A 7-Year-Old Male with Ulcerative Colitis and Rectal Stump Bleeding

Robert Listernick, MD

A 7-year-old male was diagnosed with ulcerative colitis (UC) 3 years previously at age 4 years. He has a complicated medical history. At age 4 months, he developed hematochezia associated with breast-feeding. His mother tried various elimination diets, but the hematochezia persisted. He was started on an elemental formula at age 5 months. The hematochezia resolved at age 13 months.

At age 2.5 years he had occasional loose stools without blood. He was tested for allergies with skin tests but they were negative. Blood with stools returned at age 4 years and was associated with abdominal pain and loose bowel movements up to 30 times daily. Ultimately, he underwent upper and lower endoscopy. There were no abnormalities on the upper endoscopy. On the lower endoscopy the terminal ileum was normal, but the entire colon demonstrated mild active colitis. He received the diagnosis of UC.

Initially, he was treated with prednisone and mesalamine. Prednisone was tapered and treatment continued with mesalamine; however, diarrhea returned several months later. He was hospitalized and treated with 6-mercaptopurine as well as intravenous prednisolone. This is just a piece of his complicated course. Eventually, bloody diarrhea returned and infliximab was started. He required multiple transfusions due to ongoing rectal bleeding. Eventually, he underwent laparoscopic subtotal colectomy with end ileostomy leaving a rectal stump remnant.

Colon pathology showed severe active UC; the terminal ileum was normal. There were no granulomas or evidence of dysplasia.

Over the next few months he continued to have rectal stump bleeding despite medical therapy. His ileostomy bag is emptied 5-6 times during the day and 1-2 times at night. The consistency is brown applesauce-like without blood. He has bloody, mucousy discharge from his anus once daily.

His birth history is unremarkable. His father was diagnosed with UC at age 22 years, his maternal grandmother was diagnosed with UC at the age 17 years, and two children of his father’s first cousin have Crohn’s disease (CD).

On physical exam, his weight was in the 90th percentile and height in the 45th percentile. He had a marked cushingoid habitus and an ileostomy bag in place. In all other respects, his exam was normal.

Robert Listernick, MD, moderator: What’s up with this family history?

Jeffrey Brown, MD, pediatric gastroenterologist: We’ve recognized for a long-time that there’s a strong genetic component to inflammatory bowel disease (IBD). Genome-wide association studies have identified over 100 susceptibility loci for UC and CD. As far as single gene disorders go, several examples exist, including mutations in genes encoding the interleukin (IL)-10 receptor subunit proteins, which have been shown to be responsible for very early-onset colitis.

Dr. Listernick: Does knowing that a particular patient has a single-gene disorder responsible for IBD change one’s approach to treatment?

Dr. Brown: Definitely, depending on the particular mutation. For example, the standard of care for patients who have the IL-10 receptor defect is stem cell transplant.

Dr. Listernick: OK, so now let’s discuss how one distinguishes pathologically between CD and UC? Can we see his original pathology?

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Jonathan Bush, MD, pediatric pathologist: No surprises. The colon demonstrated features of chronic active colitis with neutrophilic infiltration of the crypts. No granulomas were seen. The final diagnosis was IBD.

Dr. Listerick: Not UC? How difficult is it to arrive at a final diagnosis of either UC or CD in cases of colitis?

Dr. Bush: It can be quite tricky if the disease is limited to the colon. Classically, UC is diffuse, continuous, and limited to the mucosa, whereas CD is deeper with transmural inflammation, crypt abscesses, “skip lesions,” and granulomas. Even experts agree at a final diagnosis at best 65% of the time, so there is considerable overlap. At least 15% of the time, we’re left with a diagnosis of “indeterminate colitis.” It’s extremely important to correlate the pathologic diagnosis with the clinical information in order to arrive at a final diagnosis.

Hector Melin-Aldana, MD, pediatric pathologist: It becomes even more confusing at times. UC can produce glandular damage that destroys crypts, releasing mucin that may produce a granulomatous reaction. Pathologists have to distinguish between a true granuloma seen in CD from this granulomatous reaction seen in UC.

Dr. Brown: Another caveat should be that granulomas don’t always mean CD. For instance, we see granulomatous colitis in children with chronic granulomatous disease.

Dr. Listerick: Any more twists and turns in our pathologic highway?

Dr. Brown: Unfortunately, yes. Theoretically, UC limited to the colon might actually be CD. That’s always a concern when recommending total colectomy. Some centers specifically put this into the informed consent prior to colectomy. There have been definite cases of pancolitis without any evidence of small intestinal disease and all the pathologic features of UC in colectomy specimens who have returned years later with classic CD.

Dr. Listerick: How should pediatricians evaluate children in whom they suspect IBD? Should they just refer to a gastroenterologist without any evaluation?

Dr. Brown: Besides the obvious labs (complete blood count, albumin, inflammatory markers), I don’t think there’s much use in performing X-rays. In unusual cases in which these blood tests are normal and the patient has less common symptoms (eg, growth failure without abdominal symptoms, isolated digital clubbing), stool calprotectin can be quite helpful. Calprotectin is a protein found in large amounts in neutrophils and is a highly sensitive and specific marker for intestinal inflammation.

Dr. Listerick: OK. Let’s take for granted that he has UC. In general, what is the medical approach?

Dr. Brown: Mesalamine, an aminosalicylate, is our first-line drug for induction and maintenance of remission in mild to moderately symptomatic patients. As opposed to adults, most children are sicker at presentation and require corticosteroids to control disease activity. We continue steroids for 1-2 months, and if the patient is in remission we would wean the steroids. If the child remains dependent on steroids in order to maintain remission, we add an immunomodulator such as 6-mercaptopurine. If that fails, our last line is either infliximab, a monoclonal antibody against tumor necrosis factor-alpha, or a calcineurin inhibitor such as cyclosporine.

Dr. Listerick: When the time comes, what’s the role of surgery in the management of UC?

Tim Lautz, MD, pediatric surgeon: Once the decision has been made, the operation of choice is total proctocolectomy with creation of a J-pouch.

Dr. Listerick: Can you explain what a J-pouch is?

Dr. Lautz: Often, this is performed in two or three stages. Initially, the colon is removed so that the active inflammation can subside while performing an end ileostomy and leaving in the rectal pouch. After everything “cools off,” in a second procedure the remaining rectum is removed and the ileum is folded upon itself in order to create a larger reservoir for stool. Generally, these children have somewhere in the range of 5-6 watery and thick bowel movements each day.

Dr. Listerick: Are there occasions when you would do this all in one operation?

Dr. Lautz: Absolutely. It depends on how sick they are. We try to not create a J-pouch when there’s active inflammation. Essentially, you only have one chance to create it. The more times you dissect through the anal sphincters, the worse their long-term outcome is going to be.

Dr. Listerick: How does the possibility of CD enter into this decision?

Dr. Lautz: A discussion at the American Pediatric Surgical Association 2014 national meeting that reviewed the use of J-pouches for UC suggested that as many as 10% of children will be diagnosed as having CD at some point in the future. The classic teaching has always been that one should not create the chance to create it. The more times you dissect through the anal sphincters, the worse their long-term outcome is going to be.

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a J-pouch in patients with CD colitis. However, that concept is changing, and as many as 50% of children with CD colitis who receive a J-pouch will do well as long as they don’t have ileal disease.

Marleta Reynolds, MD, pediatric surgeon: The family has to make a decision. The two choices are (1) proctectomy and creation of a permanent ileostomy or (2) performing a “pull-through” operation and creation of a J-pouch. The “pull-through” may be extremely difficult due to previous surgeries and the theoretical risk of CD. If that happens, the patient will undoubtedly wind-up with an ileostomy regardless and he’ll have lost some of the ileum necessary for creation of the ileostomy.

Dr. Listernick: Moving on, there’s even more to discuss. Over the last several years, the patient has had what has been best described as IBD-associated reactive arthritis characterized by pain and swelling of multiple joints. Recently, he mentioned that his left foot hurt while playing soccer. Four nights prior to presentation, he awoke crying because of pain in his left knee and ankle and was not able to walk. Because of persistent pain and the development of fever, his mother brought him in for further evaluation. There were no obvious physical findings at that time. Inflammatory markers were very elevated. It was thought that he was having an IBD-associated arthritis flare and he was given intravenous pulse steroids. The pain resolved only to recrudesce 2 weeks later. At that time, he had erythema of his right thenar eminence with warmth, tenderness, and swelling. In addition, he had tenderness and swelling of his right lateral ankle. Over the next several hours, he developed increasing erythema and swelling over both knees. At the time, his laboratory test results were hemoglobin 10.5 g/dL, white blood cell count 14,000/mm³ with 82% neutrophils, erythrocyte sedimentation rate 98 mm/hour, and C-reactive protein 20 mg/dL. What do we know about IBD-associated arthritis?

Dr. Brown: Depending upon the study you look at, it occurs in 5%-50% of patients. Arthritis is more likely to occur in patients with colonic disease (whether from CD or UC) or in patients who have complications such as intraabdominal abscesses, uveitis, or erythema nodosum. Spondylitis or sacroilitis occurs in as many as one-quarter of the patients, and in boys more often than girls. IBD-associated arthritis is nondeforming. Finally, arthritis and sacroilitis are strongly associated with specific CARD15 polymorphisms as well as human leukocyte antigen (HLA)-B27.

Dr. Listernick: Because at this point his course and physical exam seemed unusual for IBD-associated arthritis, imaging was performed on admission.

Mary Wyers, MD, pediatric radiologist: Plain X-rays were normal. Magnetic resonance imaging of the distal tibia and ankle demonstrated extensive bone marrow edema with extensive contrast enhancement. There was a large fluid collection involving the ankle joint extending into the soft tissues. There were very similar findings in the hand, with extensive bone marrow edema within his first metacarpal and thumb with a large fluid collection in the soft tissues around the metacarpal. These findings are highly suggestive of an infectious process.

Leena Mithal, MD, pediatric infectious disease physician: Once the imaging was obtained, noninfectious etiologies such as chronic recurrent multifocal osteomyelitis seemed much less likely. Both fluid collections were aspirated; the hand yielded frank pus whereas the ankle fluid was serosanguinous. Both cultures were negative. Polymerase chain reaction testing for bacterial 16S rRNA was also negative. He was continued on levofloxacin and slowly improved.

Dr. Listernick: So I assume he’ll be treated for chronic bacterial osteomyelitis?

Dr. Mithal: We have to treat him as if he has chronic osteomyelitis given his course. Remember, it is even more
Firm Rounds

Key Learning Points

1. Genome-wide association studies have identified dozens of susceptibility loci for ulcerative colitis (UC) and Crohn's disease (CD). Mutations in genes encoding the interleukin-10 receptor subunit proteins have been shown to be responsible for very early-onset colitis.

2. Classically, colonic UC is diffuse, continuous, and limited to the mucosa, whereas colonic CD is deeper with transmural inflammation, crypt abscesses, “skip lesions,” and granulomas. However, there’s considerable overlap if the disease is limited to the colon.

3. Even if a child has pancolitis with classic UC pathology without small intestinal involvement, there is a small chance that a child subsequently may develop CD. Patients and families need to be aware of this risk when considering total colectomy.

4. Inflammatory bowel disease-associated arthritis is more likely to occur in patients with colonic disease whether from CD or UC, or in patients who have complications such as intraabdominal abscesses, uveitis, or erythema nodosum. Spondylitis or sacroiliitis occurs in as many as one-quarter of the patients, and in boys more often than girls.

complicated because he had been receiving large doses of corticosteroids for treatment of presumed IBD-associated arthritis. Treatment of chronic osteomyelitis usually entails use of intravenous antibiotics for 4-6 weeks followed by a long course of oral antibiotics, generally 4-6 months. The long course of oral antibiotics is necessary to kill any slowly replicating organisms that remain in the bone in very small numbers.

Dr. Listernick: Thank you everybody.