



Crohn's disease: a case presentation

Austin L. Jones, DO,^a Kenneth E. Jones, DO^b

From the ^aDepartment of Radiology, University of Missouri-Kansas City School of Medicine, Kansas City, MO; and the ^bDepartment of Radiology, Golden Valley Memorial Hospital, Clinton, MO.

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Crohn's disease is one of the two major types of idiopathic, chronic intestinal inflammation known as inflammatory bowel disease. It is a significant disease process, especially in populations of Northern European ancestry, of chronic relapsing disease along with an increased risk of mortality in long-standing and extensive cases. The clinical presentation of Crohn's disease depends on the anatomical regions affected and the type of inflammation present. The diverse presenting symptoms overlap several disease processes, which necessitates a high degree of suspicion to make the diagnosis. In this case study, a 26-year-old Caucasian male with abdominal pain, nausea, and vomiting provides an excellent example of a challenging initial clinical presentation and workup of Crohn's disease. A number of therapies are useful for induction and maintenance of remission, along with an enhancement in quality of life. Obtaining the diagnosis of Crohn's disease in a quick, efficient manner and a rapid application of therapy can potentially reduce the associated morbidity and mortality. Therefore, it is imperative that physicians maintain a high degree of suspicion for Crohn's disease in the appropriate settings, and that they stay current with screening and treatment guidelines.

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Introduction

The clinical presentation of Crohn's disease depends on the anatomical regions affected and the type of inflammation present. The diverse presenting symptoms of Crohn's disease overlap several disease processes, which require a high degree of suspicion to make the diagnosis. Although Crohn's disease is a challenging diagnosis to make at initial presentation, quick elucidation of this disease process and proper application of therapy has the potential to reduce both morbidity and mortality for these patients.

History and review of systems

T.J., a 26-year-old Caucasian male, presents to the emergency department with a chief complaint of abdominal pain. His symptoms began two days earlier, with abdominal pain that is mostly diffuse but seems to be more intense in the

right lower quadrant. He rates the pain as an 8 on a scale of 1 to 10. He also has had associated anorexia, nausea, vomiting, diarrhea, fatigue, weakness, and shortness of breath. The diarrhea is described as watery, nonbloody, and occurring approximately 10 times per day, without bowel incontinence and hematechezia. He describes the nausea as occasional, with two episodes of vomiting that day. The patient has never had this type of pain or combination of symptoms before. The remaining components of a 10-point review of systems are negative.

The patient's past medical history is significant for cervical spine fracture and phrenic nerve damage seven years ago. He denies taking any medications in the past month, but does admit to a Sulfa drug allergy. Past surgical history is unremarkable. The family history is significant for hypertension. T.J. is a Christian minister who lives with his pregnant wife and their two-year-old female child. He has a five pack-year smoking history, with smoking abstinence for the past five years. He denies alcohol or illicit drug use, or any recent travel history or contact with individuals with similar gastrointestinal symptoms. He also denies unsanitary living and working conditions.

Corresponding author: Dr. Austin Jones, Department of Radiology, University of Missouri-Kansas City, St. Luke's Hospital, 4401 Wornall Road, Kansas City, MO 64111.

E-mail address: ajones@atsu.edu.

Physical findings

Physical examination reveals a height of 5 feet, 10 inches, weight of 200 lbs, body mass index of 29, blood pressure of 108/70, heart rate of 90 bpm, respiratory rate of 20 breaths per minute, and a temperature of 98.6 °F. The patient appears appropriate for his stated age, and is alert and oriented to person, place, and time. Skin is found to be pale, warm, and dry, without edema present. There is poor capillary return at greater than 2 seconds refill time in the fingernail beds. Head, eyes, ears, nose, and throat reveal no abnormalities. Pulmonary and cardiovascular systems are within normal limits. The abdomen is observed to be flat and tense with no masses or organomegaly; bowel sounds are present. Diffuse tenderness to palpation is present, with the greatest tenderness in the right lower quadrant. Tenderness is elicited over McBurney's point along with rebound tenderness in the right lower quadrant. Murphy's sign is absent and Lloyd's sign is negative. No hernias are palpated. Rectal examination reveals no fistulas or fissures. There is good anal sphincter tone, no palpable masses, and no occult blood. The genitourinary system is within normal limits. There are no gross neurological or musculoskeletal deficits. The osteopathic structural examination is significant for acute tissue texture changes consisting of hot erythematous skin, paraspinal muscle spasm, and edematous subcutaneous tissues in the cervical, thoracic, lumbar, sacrum, and abdominal diaphragm. The following segmental somatic dysfunction is observed: occipitoatlantal joint flexed, rotated left, and sidebent right; C3-5 extended, sidebent right, and rotated right; T10-12 neutral, sidebent right, and rotated left; L1 flexed, sidebent left, and rotated left; abdominal diaphragm rotated left, sidebent left, and extended; and right unilateral sacral flexion.

Initial differential diagnosis and initial plan

The initial differential diagnosis includes: acute appendicitis, viral enterocolitis, bacterial enterocolitis, parasitic infection, irritable bowel syndrome, Crohn's disease, ulcerative colitis, nonspecific enterocolitis, diverticulitis, lower-lobe pneumonia, urinary tract infection, and dehydration. The initial plan is to obtain a complete blood count (CBC); comprehensive metabolic panel (CMP); stool examination for ova, parasites, *Clostridium difficile* toxin, and bacterial pathogens; two-view chest radiographs; and computed tomography (CT) of the abdomen and pelvis with contrast. These tests can quickly assess the patient's current status, more completely rule out conditions that are less likely after history and physical examination, and direct further assessment and treatment.

Laboratory, x-ray, and diagnostic findings

The CMP was found to be unremarkable, with results within normal limits. The CBC revealed leukocytosis at 18,000/ μ L and all other components within normal limits. The chest radiographs revealed no acute cardiopulmonary process, unchanged from the previous study. Computed tomography of the abdomen and pelvis revealed: (1) thickening of bowel at the illeocecal and sigmoid areas, suggestive of inflammatory bowel disease; and (2) normal appendix observed without acute inflammatory changes. These results narrowed the differential diagnosis to Crohn's disease, infectious enterocolitis, and nonspecific enterocolitis, along with the associated dehydration.

Stool studies were negative for ova, parasites, *C. difficile*, and other bacterial pathogens. This narrowed the differential diagnosis to Crohn's disease, viral enterocolitis, and other noninfectious enterocolitis. However, the presumptive diagnosis of Crohn's disease was tentatively assessed based on historical information, physical examination, and previously stated diagnostic testing. A colonoscopy with lesion biopsy was recommended for further diagnostic clarification. However, a colonoscopy was determined to be contraindicated during the acute inflammation period and deferred to a later time. Therefore, attention was focused on management of the acute inflammatory stage of the presumptive diagnosis.

Final diagnosis and management plan

To reach a final diagnosis, resolution of the acute gastrointestinal inflammation was necessary to obtain a more definitive diagnosis via colonoscopy. The initial management plan included intravenous fluid rehydration with normal saline to run at 250 mL/hour, along with recording accurate daily inputs and outputs. The plan also included intravenous metronidazole 500 mg every 6 hours and intravenous methylprednisolone 125 mg every 12 hours. Adjunctive osteopathic manipulative treatment (OMT) was also provided to address specific somatic dysfunctions, provide somatic pain relief, and enhance homeostatic mechanisms. With resolution of symptoms, the intravenous fluid therapy was changed to oral fluids and the patient was advanced to a normal diet. Also, the intravenous medications were discontinued and changed to oral administration as follows: metronidazole 500 mg every 6 hours and prednisone 40 mg daily to be taken until outpatient follow-up appointment approximately one week after discharge. At the follow-up appointment, medication prescription would be reassessed.

With the reduction in acute inflammation, a colonoscopy was performed. Colonoscopic findings indicated aphthoid ulcerations, cobblestoning, and skip lesions in the sigmoid and illeocecal areas, as well as histologic findings of transmural inflammation and granulomas consistent with Crohn's disease. The diagnosis of Crohn's disease was confirmed. The management plan included follow-up to confirm complete resolu-

tion of symptoms and reassessment of medical therapy. The plan also included thorough patient education on Crohn's disease, treatment risks and benefits, prognosis, and risk factors.

Discussion

Crohn's disease is one of the two major types of idiopathic, chronic intestinal inflammation considered to be a type of inflammatory bowel disease (IBD). The disease is named after Burrill B. Crohn, MD, who, with colleagues, published a landmark paper describing the disease entity of regional ileitis based on 14 cases in 1932.¹ Over time, Crohn's disease has been determined to have involvement in any portion of the gastrointestinal tract and can also have a number of associated extraintestinal manifestations. The incidence of Crohn's disease differs by geographic region and by ethnicity with the highest incidence in northern countries and populations of Northern European ancestry. The incidence rate in the United States is estimated to be 7 in 100,000 individuals.² The prevalence of Crohn's disease in North America is estimated to be between 400,000 and 600,000 patients.³ There are two peak ages of onset, with a major peak in the second and third decades of life and a second peak in the seventh and eighth decades.^{2,3} The cause of Crohn's disease is presently unknown, although current evidence supports a multifactorial etiology consisting of inappropriate immune system functioning with associated genetic predisposition and environmental factor influence.^{2,4}

There are a number of common clinical presentations of Crohn's disease that depend on the anatomical regions affected by the inflammatory process and the type of inflammation present. The most common presenting complaints include diarrhea, abdominal pain, weight loss, and fatigue.² The most common site of inflammation is the terminal ileum, generally termed *regional enteritis*. Duodenal involvement can also be seen early in the course of this disease and may be the only area of involvement. The presence of skip lesions is a hallmark of Crohn's disease. Sometimes the initial presentation of regional enteritis can closely imitate acute appendicitis, with focal right lower quadrant pain, fever, and leukocytosis.² The diverse presenting symptoms and imitation of other disease entities makes it imperative that clinicians maintain a high degree of suspicion to make the diagnosis of Crohn's disease.

In T.J.'s case, he presented in his third decade of life with right lower quadrant pain, rebound tenderness, diarrhea, fatigue, and leukocytosis, which strongly suggested the presence of acute appendicitis. In the process of ruling out this disease process with CT of the abdomen and pelvis with oral and intravenous contrast, inflammation was observed in the ileocecal region, leading to a strong suspicion of IBD and, more specifically, Crohn's disease. Obtaining CT imaging of the abdomen is consistent with appropriateness guidelines set for acute right lower quadrant pain and possible appendicitis in an adult.⁵ The studies obtained are also

similar to guidelines for imaging of an adult with an initial presentation of suspected Crohn's disease, which is described as CT of the abdomen and pelvis with neutral oral and intravenous contrast material (CT enterography).⁶ The combination of neutral oral contrast and iodinated intravenous contrast allow visualization of the bowel wall to assess for radiographic changes of IBD. However, neutral oral contrast is not currently used in all imaging centers. Consultation with the local radiologist is recommended for determination of the most optimal imaging procedure in each individual practice setting (Figure 1).

The diagnosis of Crohn's disease is based on the combination of clinical history; physical examination; and endoscopic, radiologic, histologic, and laboratory findings.^{2,4} In T.J.'s case, a presumptive diagnosis of Crohn's disease was reached before endoscopic and histologic investigation. To procure a final diagnosis colonoscopy and lesion biopsy was performed; however, clinical judgment at the time of presentation suggested that colonoscopy should be withheld during the severe, acute stage of inflammation. The use of colonoscopy and mucosal biopsy for differentiating forms of gastrointestinal inflammation along with deferment of the procedure during severe colitis is supported in the literature.⁷ However, contrary to T.J.'s case, expert opinion suggests that in the presence of a contraindication to colonoscopy, flexible sigmoidoscopy may provide an adequate diagnosis.⁷ Although flexible sigmoidoscopy may have provided a diagnosis in T.J.'s case, because he had a representative lesion in the sigmoid colon, it would not be an appropriate substitute for colonoscopy because it would not adequately stage the extent and severity of the colitis. Also, many experts would pursue a colonoscopic diagnosis instead of empiric therapy in the acute setting regardless of colonic inflammation, because an accurate diagnosis can best direct definitive therapy.

There are a number of endoscopic and histological findings that support the diagnosis of Crohn's disease. Crohn's disease can affect any portion of the gastrointestinal tract and is generally segmental, with nonaffected regions separating pathological lesions. Endoscopy findings include aphthous ulcerations in mild disease and stellate ulcerations in more active disease (Figure 2).^{2,7} A cobblestone appearance caused by areas of pathology surrounded by normal mucosa is a frequent observation, and pseudopolyps can be present.⁷ Adhesions and fistula formation can be present, generally in more longstanding disease.² Histological findings include aphthoid ulcerations, noncaseating granulomas in all layers of the bowel wall, submucosal or subserosal lymphoid aggregates, gross and microscopic skip areas, and transmural inflammation.² Endoscopy and biopsy can also be useful in following the course of disease progression and remission.⁷ In T.J.'s case, colonoscopic findings of aphthoid ulcerations, cobblestoning, and skip lesions, along with histologic findings of transmural inflammation and granulomas were consistent with a diagnosis of Crohn's disease.

After obtaining an accurate diagnosis, treatment options can be provided to the patient. The long-term management of

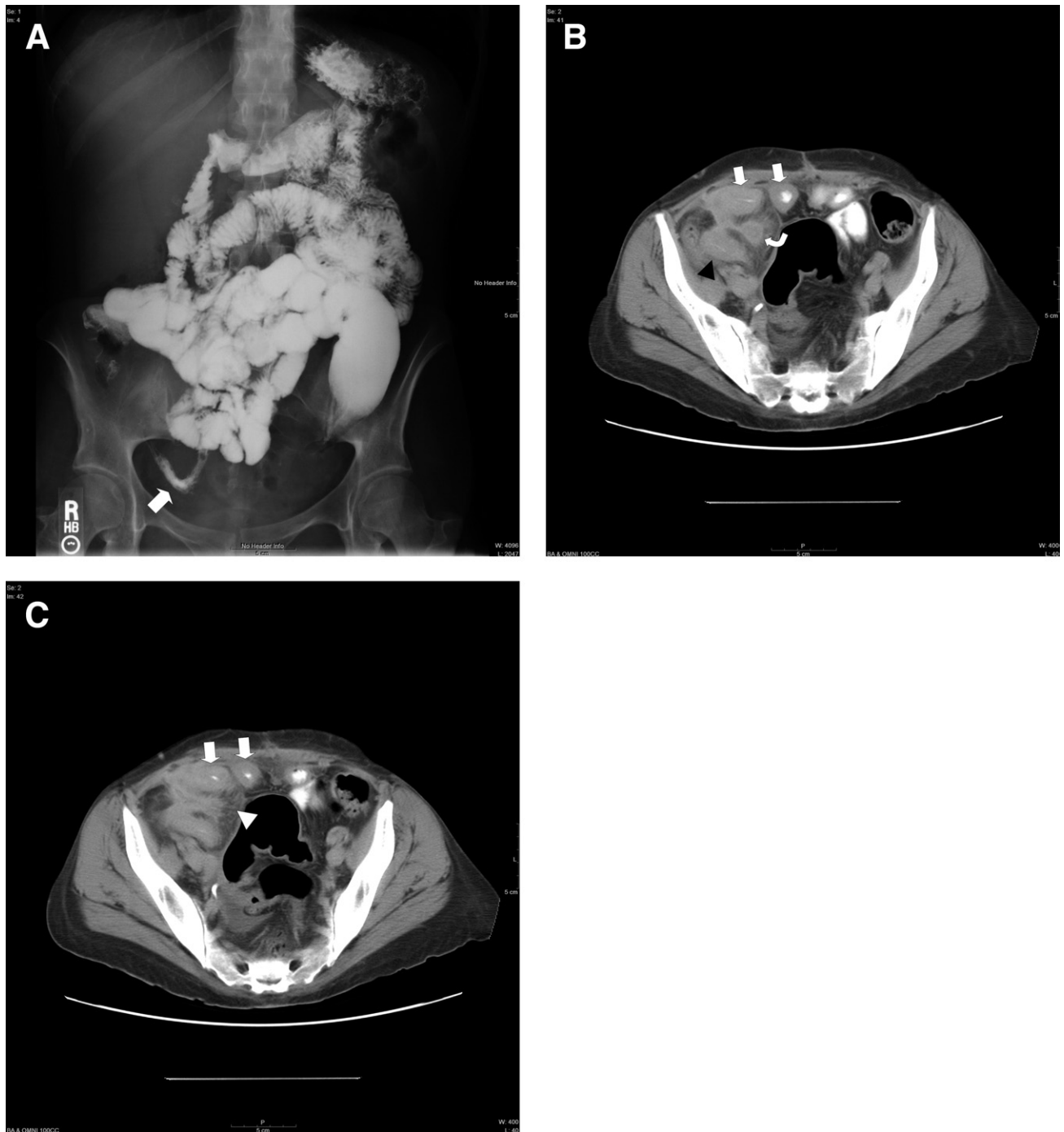


Figure 1 (A) Frontal abdominal radiograph after a single-contrast barium small bowel follow-through (SBFT). Contrast material is present in all segments of the small intestine except for the terminal ileum; contrast has advanced into the colon as well. This image demonstrates narrowing of the lumen of the distal ileum and separation of this loop from the remainder of the small bowel (*arrow*) secondary to mucosal thickening and surrounding edema. This constellation of findings, although nonspecific, is consistent with the confirmed diagnosis of Crohn's disease. The SBFT is commonly used to assess Crohn's disease and is given an appropriateness rating of 7 on the ACR Appropriateness Criteria[®] for evaluation of an initial presentation of suspected Crohn's disease. (B) Contrast-enhanced axial CT image of the same patient through the pelvis at the level of the terminal ileum demonstrates mucosal thickening (*white arrows*) of several segments of visualized small bowel. There is no contrast in the lumen at the terminal ileum; however, mucosal thickening is identified in this region (*black arrowhead*). There are associated inflammatory changes of the mesentery surrounding the distal ileum, terminal ileum, and cecum. There is also a small abscess in the surrounding mesentery (*white curved arrow*). This imaging correlation demonstrates that CT is excellent at documenting extraluminal manifestations of Crohn's disease. CT of the abdomen and pelvis with positive oral and intravenous contrast has an appropriateness rating of 7 on the ACR Appropriateness Criteria[®] for evaluation of an initial presentation of suspected Crohn's disease. (C) Contrast-enhanced axial CT image of the same patient through the pelvis inferior to the level of the terminal ileum demonstrates contrast-filled distal ileum with mucosal thickening (*arrow*) and mesenteric inflammatory changes (*arrowhead*). These correlate directly with the visualized distal ileum on the SBFT examination. Images courtesy of Kenneth E. Jones, D.O., Golden Valley Memorial Hospital, Clinton, Missouri.

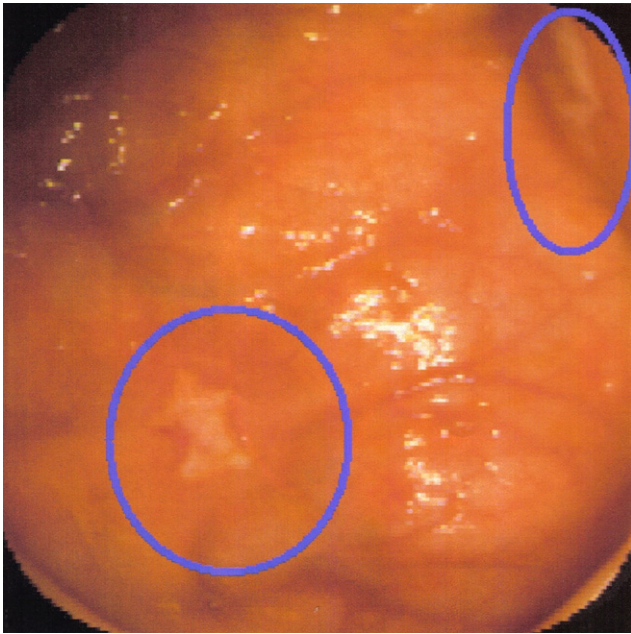


Figure 2 Single image obtained during colonoscopy of a different patient with known Crohn's disease demonstrates colonic ulcerations (*circled regions*). Image courtesy of Rob Wetzel, M.D., Golden Valley Memorial Hospital, Clinton, Missouri.

Crohn's disease usually requires a multifaceted approach including specific therapy for the inflammatory process along with adjunctive care to minimize symptoms and comorbidities.⁴ The most common medications used in Crohn's disease therapy include 5-aminosalicylic acid (5-ASA), corticosteroids, antibiotics, immunosuppressive agents, and biologic agents that are chimeric monoclonal antibodies.^{2,4,8,9} 5-ASA is commonly a first-line agent in Crohn's disease.^{2,4,9} A by-product of the 5-ASA agent sulfasalazine contains a sulfa moiety that can be harmful in patients with a sulfa allergy.² However, the 5-ASA agent mesalamine does not contain a sulfa moiety and therefore can be used in sulfa-allergic patients. The only 5-ASA therapy available in T.J.'s case was sulfasalazine and was contraindicated because of his sulfa allergy. Most experts would agree with the empiric use of metronidazole in T.J.'s case because it is well established in the treatment of Crohn's disease and is consistent with treatment of recent onset diarrhea, which is considered infectious until proven otherwise. However, many would object to the empiric use of steroid therapy because it has no value in the treatment of infectious diarrhea and may obscure endoscopic findings, making a definitive diagnosis more difficult. Overall, given the final definitive diagnosis of Crohn's disease, the therapy given to T.J. in this case is compatible with the current literature based on his drug allergy profile, his presenting symptoms requiring intravenous therapy, and a transition to oral therapy at the earliest availability.^{8,9}

Medical therapy in Crohn's disease is individualized based on the patient's disease location, extent, and response to therapy.^{10,11} An acute flare of disease activity requires initiation of induction therapy that is eventually followed by

chronic maintenance therapy, if it is necessary. There has been debate in the literature regarding a "step-up" versus "step-down" approach to medical therapy in the treatment of Crohn's disease.¹¹ In general, a step-up approach has been traditionally used with medical therapy instituted for several weeks, followed by disease reassessment and further therapy based on the findings.¹⁰ The decision to use maintenance therapy is based on the individual patient's disease process. Once it is determined that maintenance therapy is necessary, the specific agent used depends on the individual needs of the patient and their disease process. When using this step-up approach, biologic agents are used for cases refractory to other forms of maintenance therapy. In T.J.'s case, a step-up approach was used. This author is not aware of the patient's need for maintenance therapy because the patient transferred care, and therefore follow-up was not possible. A step-down approach would use biologic agents initially and then scale down to other agents based on the patient's disease characteristics over time. Controversy still exists regarding the best approach to medical therapy in Crohn's disease and is generally guided by the needs of each individual patient. General treatment guidelines, medication descriptions, and treatment algorithms can be found in the current literature.^{10,11}

Nutrition is very important in the treatment of Crohn's disease because the symptoms and pathophysiology can lead to dehydration, malnutrition, and vitamin deficiencies. In T.J.'s case, nutrition was addressed through fluid resuscitation and providing a well-balanced diet as tolerated. Several different malabsorption syndromes can occur based on the location and extent of intestinal involvement. Nutritional support should be patient specific, based on the nature of their disease and directed by the patient's physician, with possible dietician consultation. In many cases, patients require vitamin and mineral supplementation including vitamin B₁₂, folic acid, fat soluble vitamins, and calcium. Periodic checks of nutritional status may also be required.¹⁰

The use of osteopathic manipulative treatment (OMT) as an adjunctive therapy in the abdominal pathology setting is reasonable and well established in medical literature. Diagnosis and treatment of somato-visceral reflexes, viscerosomatic reflexes, lymphatic dysfunction, and specific segmental somatic dysfunction is a rational approach to the patient with IBD and provides an added value to the services provided by osteopathic physicians.^{12,13} Indications for OMT include the presence of somatic dysfunction and, based on evaluation of the patient, the presence of a need to support homeostasis. The patient received soft tissue, indirect balanced ligamentous tension, myofascial release, direct articulatory, direct muscle energy, rib-raising, and paraspinal muscle inhibition techniques. OMT was provided daily as indicated during hospitalization and was well tolerated, without complication, and improved the patient's functional status as well as his overall sense of well-being and pain level.

There are a number of complications that may occur with Crohn's disease including: stenosis of the small intestine or colon and associated comorbidities including obstruction;

extensive ileal mucosal damage and associated malabsorption syndromes; fistulas; urinary calcium oxalate stones; gastrointestinal hemorrhage; and colorectal cancer, especially in long-standing disease.¹⁴ Appropriate follow-up, multidimensional therapeutic interventions, and appropriate screening can potentially provide optimal patient outcomes and a reduction in morbidity and mortality.^{4,7,14}

Crohn's disease is a significant disease entity, especially in specific populations including northern countries and people of Northern European ancestry. The heterogeneity of presenting symptoms based on disease location and extent of inflammation, along with the similarity of presenting signs with other disease processes, makes it imperative that clinicians maintain a high degree of suspicion to make the diagnosis of Crohn's disease. Current data describes a natural history of chronic relapsing disease for the majority of Crohn's disease patients and an increased risk of potentially fatal complications including colorectal cancer in long-standing disease.^{2,3,7} There are a number of medications that are useful for induction and maintenance of remission, along with adjunctive therapies to optimize patient quality of life.^{2-4,8,9} The proper, early diagnosis of Crohn's disease can lead to a more rapid institution of therapy, which has a great deal of potential to reduce both morbidity and mortality associated with this disease process. Therefore, it is imperative that physicians maintain a high degree of suspicion for Crohn's disease, with appropriate patient presentations, and that they stay informed on current screening guidelines and treatment options for the common, preventable comorbidities.

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