Residents’ Case Series

A 54-Year-Old Man With Arthritis and Diarrhea

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A 54-year-old Japanese man was transported to the emergency department by ambulance unable to walk and complaining of pain and swelling in his left ankle, left knee and right sternoclavicular joint. The patient had an episode of low back pain two months prior to admission and was seen by a chiropractor. During his treatments for low back pain, he noted slight left knee pain and swelling. Ten days before admission, the patient had up to five loose stools per day and at times watery diarrhea without melena or hematochezia. In the three days before his emergency room visit, low-grade fevers developed accompanied by a marked increase in the pain and swelling of the left knee which left him unable to ambulate. At this time, he also noticed new pain and swelling of the left ankle and right sternum. He had a recent ten-pound weight loss with minimal nausea, but denied emesis, skin lesions, rash, oral ulcers, penile discharge, chest pain, shortness of breath, or abdominal pain. The patient had a past medical history of adult onset diabetes mellitus and hypertension. He had not suffered from joint pains or effusions in the past. He did report a similar episode of diarrhea four months previously, but this resolved spontaneously without treatment. His medications included glyburide, metformin, indapamide, and recently celecoxib. He worked as a postal employee in an office and had a 50-pack-year smoking history, but had quit two years ago. He drank up to twelve beers every weekend. He had no recent pet or freshwater exposures, denied illegal drug use, had no recent foreign travel or extramarital sexual encounters.

Physical examination revealed a man in mild to moderate distress secondary to pain with a temperature of 99.2 degrees, a blood pressure of 130/80, a heart rate of 86 beats per minute, and a respiratory rate of 18 breaths per minute. The left knee had a significant effusion, mild warmth and erythema with tenderness at the medial aspect of the knee at the tibial plateau. The left ankle was warm with moderate effusion and tenderness, but no erythema. The right sternoclavicular joint had warmth, swelling, erythema and tenderness. The exam of the other joints and spine was unremarkable. Examination of his neurological, cardiovascular and respiratory systems was normal. His abdomen was soft, nontender and without organomegaly. Bowel sounds were present and the rectal exam was normal with guaiac negative stool.

Laboratory evaluation revealed hemoglobin of 13.2 g/dL, a leukocyte count of 19.7x10^9/L with 78% neutrophils, 13% bands, 4% lymphocytes, 4% monocytes, and 1% atypical lymphocytes. His abnormal chemistries (and normal values) were as follows: sodium 132 mEq/L (135-145), chloride 91 mEq/L (98-106), bicarbonate 31 mEq/L (22-29), glucose 308 mg/dL (70-115), albumen 1.5 g/dL (3.5-5.5), total protein 5.6 g/dL (6.0-8.0), alkaline phosphatase 233 U/L (38-126), iron 11 μg/dL (65-175), total iron binding capacity 79 μg/dL (250-450), iron saturation 14% (20-50), ferritin 526 ng/ml (20-250), prealbumin 6 mg/dL (>18) and erythrocyte sedimentation rate 48 mm/hr (<15). Synovial fluid from his left knee showed: RBCs 1113/ mm^3, WBCs 86250/mm^3 with 88% neutrophils, 2% lymphocytes and 10% monocytes without crystals or organisms seen by staining or culture. Evaluation of stool revealed no occult blood, WBCs or Clostridium difficile toxin and was negative for ova and parasites and pathogenic bacteria.

A bone scan after the administration of 25mCi of Tc-99m diphosphonate compound showed increased uptake in the left knee and ankle as well as the left sacroiliac joint. An In-111 labeled white cell study revealed intense left knee and ankle uptake and right proximal foot uptake. This scan also showed markedly increased and diffuse large bowel activity consistent with colitis.

A colonoscopy was then performed and showed cobblestoning, linear ulcerations and involvement of nearly the entire colon with some normal regions distally. Biopsy specimens of colonic mucosal fragments revealed areas of necrosis with acute and chronic inflammatory cells in the lamina propria. One section showed lymphoid aggregates, but crypt abscesses and granulomatous lesions were not seen. The patient was diagnosed with Crohn’s disease.

The patient was treated with steroids, azathioprine and mesalamine with resolution of his diarrhea and joint pain. His steroids were tapered and stopped as an outpatient. He was maintained on mesalamine and azathioprine and has generally been doing well. In the year since discharge, he has had three flares of his joint pain which were accompanied by diarrhea. This responded to a short course of steroids and increased doses of his other medications.

Discussion

This patient presented with joint pain and diarrhea suggesting an enteropathic arthropathy as the etiology of both complaints. Arthritis occurs in approximately 2% of patients with enteric infections such as Yersinia, Campylobacter, Shigella, Salmonella or Clostridium difficile. These infections can be detected by stool culture and a toxin assay for C. difficile. Whipple’s disease and Celiac disease can also be associated with arthritis, but these are primarily disorders of small bowel. Finally, inflammatory bowel disease such as ulcerative colitis and Crohn’s disease can have an associated arthritis in up to 20% of patients.

Drs. Crohn, Ginzburg and Oppenheimer described patients with regional ileitis in the Journal of the American Medical Association in 1932. Crohn’s disease has a prevalence of approximately 75/100,000 with a higher frequency in Caucasians and people of Jewish ancestry. In Hawaii, it is found in all ethnic groups with varying frequencies. The cause has not been fully elucidated. There is an abnormal activation of the immune system involving the gastrointestinal tract in patients who are genetically susceptible.

Family studies have supported a genetic component. Affected patients report a positive family history 10-20% of the time. Other studies have found at least one additional affected family member in about one third of cases. Concordance in monozygotic twins is approximately 40%. Two studies of dizygotic twins reported a concordance of 4% and 0%, respectively. Affected children are diagnosed 10-17 years before the age their affected parent was diagnosed. This may be due to ascertainment bias (heightened screening) or anticipation (earlier age of onset of genetic disorders.
in successive generations.)

Molecular studies have found a number of loci with significant linkage to Crohn's disease. This includes IBD1 on chromosome 16 and IBD2 on chromosome 12. Other genes under investigation include the mucin genes MUC2 and MUC3, and various HLA class 2 genes.

Crohn's disease often presents with diarrhea, abdominal pain and weight loss; however the presentation is variable and may be mild. This can lead to long period of time before a definitive diagnosis is made. Nonspecific laboratory findings may include leukocytosis, thrombocytosis, hypoalbuminemia and an elevated ESR. Other findings may include deficiencies in folate, iron and vitamin B12.

Antibody tests with varying sensitivities and specificities include antineutrophil cytoplasmic antibodies (pANCA), anti-Sacccharomyces cerevisiae antibody (ASCA IgA and IgG), ompC, PAB and I2.

The location of the gastrointestinal lesions is also variable and anywhere from the mouth to the anus can be affected. Isolated aphthous ulcers may be the only manifestation of disease. There are three common patterns seen at the time of presentation: ileum and cecum in 40%; small intestine in 30%; and colon in 25%.

Arthritis is the most common extraintestinal manifestation of Crohn's disease. Peripheral arthritis is most common in patients with disease confined to the colon. One study found arthritis in 16% of patients with Crohn's colitis, while only 4% of patients with ileitis or ileocolitis had arthritis.

The onset of arthritis is variable. It usually occurs after intestinal symptoms or simultaneously. Rarely, arthritis may clearly precede bowel symptoms. Exacerbations of arthritis and intestinal symptoms tend to recur together.

The affected joints typically have pain, erythema and swelling. The knees and the ankles are most commonly affected followed by the wrist, shoulder and elbow. Less commonly affected joints include the hips, proximal interphalangeal joints, metacarpophalangeal joints and metatarsophalangeal joints. Our patient had involvement of the sternoclavicular joint which is likely rare as it was not cited in two of the papers reviewed that included nearly 1000 patients with IBD.

References
5. Dubinski, M.C. Utility of Antibody Markers in the Diagnosis, Differentiation and Stratification in Inflammatory Bowel Disease (IBD). University of Hawaii Internal Medicine Grand Rounds. 4/24/01.

Editor's Comment
This commentary is a part of a collection of essays on "Healing in Clinical Practice," which was intergraded into a course "Medicine and Soul" at the Williams College in Williamstown, MA designed for aspiring medical professionals.

Dr. Barnett is now a Research Coordinator at the Cancer Research Center of Hawaii. When I first met her, she was a medical assistant to David Elpern MD, dermatologist at the Wilcox Clinic on Kauai. With the encouragement of David Elpern, she went on to get her PhD and is a frequent speaker at the Hotspots in Dermatology seminars held annually on our neighbor islands. Proud of you, Terriela and thank you David Elpern for encouraging her to continue her education.