CLINICAL VIGNETTE

Peripheral Arthritis as Extraintestinal Manifestation of Inflammatory Bowel Disease

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Case

A 30-year-old female with anxiety, depression and ulcerative colitis presented with bilateral ankle pain, swelling, and erythema for 3 days. Her symptoms initially were noted on the left ankle but also involved the right ankle. She denied joint trauma, but practiced yoga regularly. She was able to bear weight but noted certain movement would exacerbate the pain. One month prior, she was admitted for left ankle cellulitis, treated with vancomycin and discharged on doxycycline and cephalexin. Her recovery was slow with mild residual left ankle swelling. She made an appointment concerned that the new swelling was recurrent cellulitis. Her ulcerative colitis was diagnosed 8 months prior and involved her entire colon. She reported 4-5 episodes of diarrhea each day despite treatment with mesalamine.

On exam, she was afebrile with normal vital signs. Significant musculoskeletal findings included tenderness and swelling along the posterior and anterior talofibular ligaments bilaterally L > Rt. There was also mild erythema without nodules or ulceration along the left lateral malleolus. Her left Achilles tendon was also tender.

She was diagnosed with ankle sprain/ tendonitis likely from her yoga activities and treated conservatively with acetaminophen for pain, as she did not tolerate NSAIDS.

She returned 3 days later with worsening bilateral ankle pain, swelling and erythema especially on the right ankle. She also noted intermittent knee pain. She denied fever but still reported persistent daily diarrhea. She was started on empirical cephalexin for possible cellulitis pending labs which subsequently showed elevated wbc of 11.68, H/H 8/26.8, Platelet of 589, crp 6.7, esr 58 and low iron level of 18. The DDX included infectious vs. inflammatory etiologies related to UC.

After 5 days of antibiotics, patient returned with no improvement in the pain, swelling, and erythema of both ankles. She continued having 4-5 episodes of diarrhea per day. Because she was leaving for vacation she was started on methylprednisolone and was instructed to follow up with her GI physician for further management of her UC.

Patient returned for follow up and reported complete resolution of her ankle symptoms and improvement in general wellness shortly after starting steroids. She stopped her mesalamine and tried to modify her diet to control her UC. Unfortunately, her diarrhea worsened, with 15 episodes of diarrhea per day along with arthralgias. She was hospitalized with symptomatic anemia (hemoglobin of 6.3), transfused and restarted on corticosteroids. Colonoscopy showed severe active UC from the rectosigmoid to the hepatic flexure with sparing of the rectum, right colon and distal terminal ileum. She was also started on infliximab infusions every two weeks. Her UC improved dramatically with decreased diarrhea, resolution of anemia and improved energy and healthy weight gain. Her extra intestinal symptoms also resolved. She was able to sleep better and her depression and anxiety also improved.

Introduction

Inflammatory bowel disease is chronic relapsing inflammation of the digestive tract with two major types, Crohn Disease and Ulcerative Colitis. Gastrointestinal symptoms include abdominal pain and frequent diarrhea episodes with or without blood in stool. Extraintestinal manifestations (EIM) are common, in 25-40% of the patients with IBD.[1] EIM can involve multiple body systems including musculoskeletal, cutaneous, ocular, gastrointestinal (outside of bowel loop), renal, pulmonary and cardiac systems. EIM can be mild to severe and can significantly affect function. EIM can be categorized into four general groups. 1) Those directly related to gastrointestinal disease activity, including large and small joint arthritis and skin manifestations including pyoderma gangrenosum. 2) Genetically related illness complications or disease sharing common pathogenesis such as ankylosing spondylosis and primary sclerosing cholangitis. 3) EIM can occasionally result from chronic systemic inflammation outside of the GI system or from metabolic disease. 4) Finally some EIM are related to IBD treatment side effects including osteoporosis or drug induced hepatitis.[3] Skin, eyes and joints involvement is commonly associated with the degree of intestinal inflammation while other EIMs are not.[2,3] EIM can present before, during or after onset of GI symptoms. The development of EIM increases risk of developing other EIM.[4] Due to the wide range of EIM of IBD, these conditions can pose diagnostic and management challenges. We will focus on peripheral arthropathy as EIM of IBD.

Discussion

Musculoskeletal manifestations are the most common EIM and occur in > 50% of IBD patients.[4] They include both axial and peripheral involvement with articular joint issues in 30% of IBD patients. Other rheumatologic complications include osteoporosis, aseptic necrosis, polymyositis, and soft tissue infections.[3]

Inflammatory arthritis is defined by pain, increase in warmth and joint swelling with or without effusion, leading to decrease joint mobility. Associated periarticular features include surrounding tendonitis, clubbing, periostitis and granulomatous lesions of the joint and bone. Inflammatory arthritis often presents with morning stiffness that improves with movement and ambulation.[4]

The arthritic EIM can occur before, during, or following the diagnosis of IBD. The arthritis may be related to the underlying IBD activity. It occurs equally between males and females, and is more common in patients with extensive colonic disease e.g. UC with pancolitis rather than isolated left sided disease.[4] Subclinical bowel inflammation has been found in 2/3 of patients with spondyloarthropathy and likely plays a role in the recurrent joint inflammation.[5]

The arthritic manifestations can be categorized into axial or peripheral arthropathy. Axial arthropathy includes ankylosing spondylitis (AS) and isolated sacroiliitis. AS can occur up to 26% IBD patients, with male preponderance. Patients typically present with back or buttock pain worse in the morning with improvement with activity. Thirty to fifty percent have associated peripheral arthritis and strong association with the HLA–B27 gene. Over time, patients will develop spinal flexion impairment. Axial involvement is independent of the gut activity.[4] On the other hand, the peripheral arthropathy has different characteristics. The peripheral arthropathy is further sub divided into Type 1 and Type 2. Type 1 peripheral arthritis is pauciarticular, involving fewer than 5 joints. Involved joints are typically large weight bearing like knees, ankles, hips, elbows and shoulders. Arthritic episodes are typically self-limited and parallel IBD disease activity. It has been reported in 3.6 % of UC and 6 % of CD patients. Each flare up can last between 5-10 weeks.[4,6] Type 2 peripheral arthritis is poly-articular, involving more than 5 joints that are generally symmetric, most commonly the metacarpophalangeal joints or other smaller joints. Unlike Type 1, flares are not associated with IBD activities and can last months to years. Both forms of arthritis are not erosive or deforming.[3] Because most peripheral arthropathy is pauciarticular and self-limiting in nature, xray are usually normal. Some common radiographic findings include dactylitis, enthesitis and periarticular osteopenia.[3] In association with arthritis, enthesitis has been found in up to 50% of IBD patients.[7] Enthesitis occurs as focal inflammation of tendon, ligament or joint capsule at a bone attachment site. Common locations are the Achilles tendon, plantar fascia insertion on the calcaneus, and patellar tendon insertion on the tibial tubercle. For axial arthropathy EIM, the most common site is the interosseous ligament of the sacroiliac joints.[3]

Treatments

Treatment for peripheral arthritis EIM is aimed at treating underlying IBD and acute symptom relief. Modalities includes oral analgesics, local intra articular steroid injections, IBD treatment and physical therapy.

First line analgesics for IBD include acetaminophen or tramadol. Use of NSAIDs and selective cyclooxygenase-2 inhibitors has been limited due to concern of worsening IBD symptoms. NSAIDs should be used only if bowel disease is not active. This is not likely as the type 1 peripheral arthropathy EIM is related to underlying IBD. There are few studies regarding Cox 2 inhibitor treatment for IBD. A retrospective chart review of 27 patients with CD or UC receiving celecoxib or rofecoxib reported 22 patients with no change in IBD activity and 14 patients with improvement in their arthritic symptoms.[8] Another open label trial of rofecoxib showed no worsening IBD symptoms in 32 patients and 60% reporting improvement in arthralgias.[9] Other IBD drug options such as sulfasalazine have been used in ankylosing spondylitis doses at 500mg bid to 1500mg tid showed better results than placebo at reducing morning stiffness and improving quality of life.[10] Mesalamine has unclear effects. For patients that do not respond to above modalities, a short course of steroids can be beneficial for symptom treatment in UC patients, while tumor necrosis factor-alpha inhibitor trials can be used for both CD and UC patient.[4] Currently infliximab has been used to treat of IBD related disease.

An open label trial of infliximab in patients with active CD and axial symptoms showed improvement in arthritis or arthralgia in 61% with 46% free of symptoms.[11] Partial or total proctocolectomy can induce remission of peripheral arthritis in UC patients but has no effect on axial involvement, while the colonic resection in CD does not appear to affect the arthritis.[4] Both type of arthritis can benefit from physical therapy especially back exercises for the axial arthropathy to prevent back and neck deformities.

Our patient most likely had peripheral arthropathy type 1 with arthritis of her ankle and enthesitis of the surrounding tendons. Her UC condition was sub optimally controlled despite being on mesalamine. Her prior episode of cellulitis with slow recovery despite hospitalization could be due to the nature of EIM of IBD. Her elevated WBC, CRP and SED rate were reflection of the active underlying UC rather than signs of joint infections. The iron deficiency anemia also reflected GI blood loss from the active UC. This was supported by her response to steroid therapy rather than acetaminophen or antibiotics. Once her IBD was controlled with more intensive infliximab therapy, her EIM symptoms resolved along with improvement of her IBD symptom.

Conclusion

IBD is associated with multitude of EIM, which can parallel the underlying GI disease activity and can predict IBD development or control. It is important for physicians to consider EIM of IBD as possible a etiology of non intestinal problems in patients with UC or CD. Often, treatment of underlying IBD along with EIM symptomatic management can provide relief and improve quality of life especially with arthropathy. Monitoring for EIM and prompt intervention can help preserve functions and quality of life in IBD.

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