A Wandering Arthritis and Mind

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Case Presentation:

A 20-year-old university student, originally from Chicago, presented to our primary care clinic for an emergency room (ER) visit follow-up. His medical history was notable for pneumonia complicated by acute respiratory distress syndrome 3 years prior. Over the previous 6 weeks, he had multiple urgent care visits for left hip, knee, and ankle pain and swelling associated with fevers and chills. These symptoms were preceded by abdominal discomfort, nausea, vomiting, and rectal pain that he assumed was due to a hemorrhoid. Generalized arthralgias and myalgias had more recently developed in addition to his left lower extremity articular pain and swelling. Within this time period, he experienced an unintentional 40-pound weight loss.

Figure 1.

The morning of the emergency room visit he had consulted with an orthopedic surgeon who recommended an autoimmune workup. Later that day, the patient presented to the ER due to intolerable pain with his chief complaint documented as "I have an undiagnosed autoimmune disease." During the visit, he was found to have a 2.9 cm left perianal abscess on computed tomography (CT) scans of the abdomen and pelvis. The abscess was incised and drained, and he was discharged with a recommendation for sitz baths and non-steroidal anti-inflammatory drugs (NSAIDs) as needed for pain relief. He was not prescribed antibiotics. Unfortunately, wound cultures were not sent.

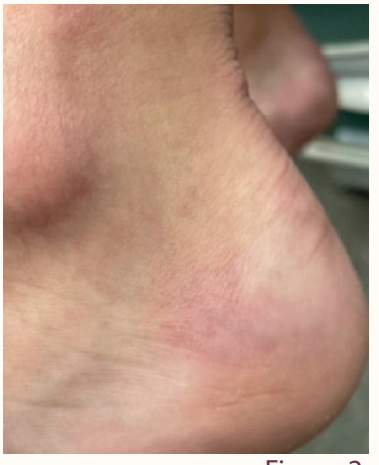

Figure 2.

At the time of presentation to our clinic, his exam was notable for tachycardia, hypotension, painful oropharyngeal ulcers, cervical lymphadenopathy, swelling along multiple nail folds, mild tenderness and swelling of the left knee and ankle, and tender nodules on both heels (Figures 1 and 2). We directly admitted him to the hospital for expedited infectious and autoimmune workup. Infectious workup, including urine and serum sexually transmitted infection studies and extensive stool studies, were all negative. Anti-nuclear antibodies (ANA) were negative, rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) undetectable, and HLA-B27 screen was negative. CT chest visualized subtle subcentimeter ground-glass opacities. Magnetic resonance imaging (MRI) of the lumbar spine and pelvis was negative for axial inflammatory changes. Inpatient endoscopy and colonoscopy did not visualize any findings to suggest inflammatory bowel disease. He was discharged with a suspected diagnosis of reactive arthritis (ReA) presumptively triggered by gastroenteritis and the perianal abscess. Fevers and migratory arthritis resolved over the following 4 weeks with daily ibuprofen.

Following this hospitalization, he developed new daily anxiety and a sense of hopelessness in the setting of a prolonged acute illness without definitive diagnosis and his complicated hospitalization. He described the multiple procedures during his hospitalization as traumatizing. He reported having difficulty sleeping with frequent awakenings from nightmares about the hospitalization and fears surrounding his illness. Mood symptoms improved in the following months with initiation of a selective serotonin reuptake inhibitor (SSRI) and consulting with a psychologist for Cognitive Behavioral Therapy.

His diffuse arthralgias recurred 1 month after resolution, with once again an elevated erythrocyte sedimentation rate (ESR) of 49, but undetectable C-reactive protein (CRP). His symptoms again improved with ibuprofen. His working diagnosis transitioned to chronic non-radiographic axial and peripheral spondyloarthritis, currently being managed with meloxicam as needed. Imaging studies continued to be negative for inflammatory changes.

Introduction

Reactive arthritis (ReA) is a subset of spondyloarthritis defined as inflammatory arthritis triggered by a gastrointestinal or genitourinary tract infection.[1,2] Due to the absence of agreed-upon clinical criteria, specific diagnostic findings, and variable disease course, ReA remains a challenging diagnosis to make, requiring a clinician well-versed in rheumatology.

Epidemiology

ReA typically affects young adults between the ages of 18 and 40 years with no difference in incidence among males and females with gastrointestinal triggers, and increased incidence in males with preceding genitourinary infection. White individuals appear to be at increased risk of developing ReA, which is attributed to the higher frequency of the HLA-B27 gene in this demographic.[3,4] Gastrointestinal infections due to Shigella, Campylobacter, and Yersinia have about a 1-1.5% incidence of leading to ReA, while genitourinary infections, such as Chlamydia trachomatis have a 4-8% incidence.[5]

Clinical Features

Rheumatic symptoms often present 1-4 weeks after the infection has resolved, which can make it challenging to identify an association.[2,4] ReA most commonly presents as an acute asymmetric oligoarthritis that can involve both small and large joints, as well as the axial skeleton. Joint involvement can exhibit an additive or migratory course. Extra-articular musculoskeletal manifestations include enthesitis, bursitis, and dactylitis.[1,2,4]

Mucosal and ocular involvement are common. Ocular symptoms typically present as uveitis or conjunctivitis. Mouth ulcers are typically painless. Rashes unique to ReA include keratoderma blennorhagicum, a pustular lesion commonly seen on the plantar surfaces, and circinate balanitis, painless psoriasiform lesions over the glans or shaft of the penis.[1,2,4] Cardiac symptoms are uncommon and include conduction abnormalities, aortic regurgitation, and pericarditis.[1]

Diagnosis

No diagnostic criteria have been established for ReA. The American College of Rheumatology last issued general guidelines in 1999, which were restricted to symptoms following an enteritis, urethritis and cervicitis with positive cultures for Chlamydia or enterobacteria, or persistent synovial infection.[2,4,6] In practice, the diagnosis is made based on the totality of the clinical picture, with increased likelihood in the setting of positive infectious work-up.[7] Given the non-specific arthritic pattern, work-up often includes investigating multiple autoimmune and infectious etiologies, with ReA ultimately being a diagnosis of exclusion.

ReA may be a self-limiting disease but it does not always fully resolve. About 65% of patients progress into the chronic arthropathy category with persistent symptoms for greater than 6 months.[2,3] Therefore, it is important to recognize the disease early and provide appropriate counselling and treatment for patients.

ReA should be suspected in individuals with sudden onset inflammatory arthropathies following a recent infection. However, a prodromal infection cannot always be identified; asymptomatic or minorly symptomatic infections can trigger ReA. A thorough history should include any preceding infections and a sexual history. There are no pathognomonic lab results or imaging findings for ReA. ESR and CRP will be elevated in the acute phase, and trend down in the chronic stage of the disease. Radiographs may visualize joint space narrowing, swelling, erosions, or bony spurs.[2,7]

Approximately 50-80% of patients with ReA also test positive for the HLA-B27 gene. The presence of HLA-B27 has been associated with an increased risk of severe symptoms and progression to chronic disease.[2-4,6] HLA-B27 genes contribute to the persistence of bacteria within the body, which is suspected to be the reason behind the high risk of developing severe ReA in these patients.[3]

Therapeutic Approach

The goals of treatment focus on decreasing pain and inflammation, minimizing disability and monitoring for relapse or progression to chronic disease.

Patients are initially managed with NSAIDs until the episode resolves. In situations where NSAIDs are contraindicated, such as renal impairment, a history of gastrointestinal disease, or significant cardiovascular disease, intra-articular glucocorticoid injections are preferred. When ReA has progressed and the disease involves multiple joints, patients may benefit from systemic glucocorticoids. In this case, it is important to provide peptic ulcer disease prophylaxis and assess risks for osteoporosis as well.[2]

Although ReA is most likely to occur following an infection, antibiotics are only indicated if evidence of missed, untreated or persistent infection is found.

When symptoms are uncontrolled despite initial therapy or if they last longer than 6 months, it is reasonable to introduce disease-modifying antirheumatic drugs (DMARDs). Sulfasalazine and methotrexate are most often the preferred agents. In severe cases of ReA where there is no improvement after 12 weeks of DMARD therapy, patients may be candidates for initiation of biologic therapy with anti-tumor necrosis factor agents.[2,5] In several studies looking at patients' responses to biologic therapy, it is important to note that patients had significant improvements in their symptoms without major side effects reported.[3]

Adjusting to Uncertainty and Chronic Illness

Fears surrounding what an autoimmune disease could mean prompted our patient's emergency room visit. Following his subsequent hospitalization, our patient struggled with disabling anxious and demoralizing thoughts following his clinical presentation, ultimately leading him to take a short-term break from university and return home. He had requested a leave of absence, which was unfortunately denied by his academic institution. Like many rheumatologic conditions, including ReA, adjustment disorders (AD) are a slippery and difficult diagnosis to make.

All individuals experience and respond to stressful events throughout their lifetimes, including issues with their health. AD refers to maladaptive emotional or behavioural responses to a stressor that lead to excessive distress and daily functional impairment. The responses are either discordant from the socially or culturally expected reactions and/or cause marked distress or impaired functioning.[5] It fills a unique space along the spectrum of psychological conditions as a transitional, subsyndromal, or subclinical disorder. Similar to ReA, either the disorder resolves or it persists and after a certain time meets criteria for a more well-defined mental health condition.[8-11]

The similarities between ReA and AD do not stop with their tempo. Both respective clinical specialties have long worked with vague and understudied understandings of these conditions. In the past decade the mental health community has increasingly acknowledged the lack of research on AD and pushed to better define the disorders. Both the Diagnostic and Statistical Manual of Mental Disorders-5th edition (DSM-5) and the International Statistical Classification of Diseases and Related Health Problems, 11th edition (ICD-11) have recently provided clearer frameworks for this historically vague condition.[8-11]

Back to the Case

Preparing this review allowed the opportunity to revisit how we might have approached this case differently if we were given another chance. Knowing what we know now, it would have been helpful to have had results from urethral and rectal swabs to assess for Chlamydia trachomatis further, and wound cultures from the perianal abscess. Results from knee or ankle arthrocentesis would have also helped solidify a diagnosis.

Like many stories of the presentation and progression of autoimmune conditions, our case does not comfortably fit within the illness script for ReA. While ReA progressing to chronic non-radiographic axial and peripheral spondylarthritis remains the working diagnosis, the patient continues to lack definitive findings. The patient was lost to follow-up for 6 months due to improvement in symptoms. He returned to university without issue. While preparing this manuscript, he reconnected with us due to recurrence of fatigue and arthralgias similar to his presentation last year, and a new erythematous rash around his neck and upper chest. He reported that, in the interim, the only symptom that did not resolve was very difficult to treat acne, primarily on his face and scalp, but also appearing along his chest, back and extremities. He reports ancestry from Italy and Ireland. He is currently undergoing workup for other uncommon autoinflammatory diseases, including Behçet Disease, Familial Mediterranean Fever, and Adult-onset Still's Disease.

Like ReA, AD requires an astute and experienced clinician within the field to make a diagnosis. However, specialized training is not required to assess and address psychological struggles within our patients. Mental health disorders are common among individuals with chronic inflammatory disease and carry significant morbidity.[12-14] Providers who care for individuals with chronic inflammatory conditions should feel comfortable screening for mood disorders, prescribing common treatments, and connecting patients with psychiatry and psychotherapy, treating disorders in tandem.

Conclusion

ReA, as well as adjustment disorders, largely remains a clinical diagnosis relying on clinical acumen. Both conditions provide poetic examples of what it means to practice medicine. To practice the art of medicine is the privilege to journey alongside a patient. We cannot always prevent, predict, or cure, but we can make the journey easier. We can acknowledge the psychological and emotional impacts on those living with the diagnoses we make, the uncertainty we navigate and the guidance we provide. In caring for this patient, we were unable to predict his disease course with certainty. However, it was critical to simultaneously acknowledge the psychological and social impact of his symptoms, along with addressing the physical distress in order to care for him appropriately.

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