CLINICAL VIGNETTE

A Case of Chikungunya Arthritis

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Case Presentation

A 45-year-old man without significant past medical history presented to rheumatology for two months history of migratory joints pain. Two months prior to the visit, he visited India and Singapore on a family vacation for total of ten days. On the day of his return to the United States, he started having low grade fevers, chills, and watery diarrhea. His primary care physician started ciprofloxin 500 mg twice a day for total of one week and the diarrhea resolved.

As soon as the diarrhea improved, he noticed severe dull pain of his neck pain and stiffness that was constant, without radiation. The pain wakes him at night, and he was unable to turn his neck because of the pain. He started ibuprofen 400 mg twice a day and the neck pain resolved within one week. As soon as the neck pain resolved, he noted onset of bilateral foot pain that was similar in nature with swelling and inability to walk. This also resolved after one week. When the foot pain resolved, patient noted bilateral knee pain with swelling and was referred to rheumatology.

On the day of the visit, patient stated that the knee pain resolved but he noted onset of bilateral hand pain and swelling and unable to make a fist. Musculoskeletal ultrasound showed inflammation of the extensor tendons of his right index finger. Initial serology workup was negative for antinuclear antibody (ANA), rheumatoid factor (RF), anti-cyclic citrullinated peptide (CCP), human leukocyte antigen (HLA) B-27, and inflammatory markers were normal (sedimentation rate and c-reactive protein). Infectious testing was negative for hepatitis B, hepatitis C, QuantiFERON-TB Gold, human immunodeficiency virus (HIV), Zika Virus antibody, and Dengue Fever Virus antibody. Chikungunya antibody IgM was marked elevated at 4.46 IV [Reference Interval: < 0.79 IV or less: negative, 1.10 IV or greater, positive] and Chikungunya antibody IgG was also elevated at 3.24 IV [Reference Interval: < 0.79 IV or less: negative, 1.10 IV or greater, positive]. He was diagnosed with Chikungunya arthritis and started on naproxen 500 mg twice a day. His joint pain resolved after three months of naprosyn therapy.

Discussion

Chikungunya fever (CHIKF) is caused by Chikungunya virus (CHIKV), a single-stranded RNA virus that belongs to the *Togaviridae* family.[1] The global spread of the disease attributed to two mosquito vectors, *Aedes aegypti* and *Aedes albopictus*, that carried CHIKV from Africa and Asia throughout Africa, Asia, Oceania, Europe, and America with millions of reported cases across 45 countries and 46 of the 50 states in the United States.[2] The virus's name is from the local dialect of the Makonda area in Tanzania and translated as "to become contorted", which describe the stooped pasture of many patients affected with Chikungunya when experiencing severe joint pain.[1]

Chikungunya infections can be divided into three phases: incubation phase, acute phase, and chronic phase.[3] The incubation phase varies between one to twelve days after the mosquito bite. During the initial two to six days of infection, the chance of virial transmission from human host to susceptible vector is the greatest. It has also been reported that 3% to 28% of the individuals infected with CHIKV remain asymptomatic.[3]

After the incubation phase, CHIKF enters the acute phase with high fever, headache, polyarthralgia/arthritis, lymphadenopathy, and anorexia.[1-3] The arthralgias symptoms are often distal and symmetrical affecting the hands, wrists, shoulders, knees, ankles and feet. Atypical joint involvement includes the spine, sternoclavicular joints, or temporomandibular joints. Some patients present with maculopapular rash, and nodular, vesicular, bullous, and desquamative skin lesion have also been reported.[2] More severe extra-articular manifestation like encephalitis, optic neuritis, uveitis, facial paralysis, sensorineural deafness, myocarditis, and cardiac arrhythmias has been reported, primarily in new borns and the elderly.[1,2] Dengue virus and Zika virus infection can present similarly and may be presented as co-infection with Chikungunya virus.[3] It is important to screen for all three viruses during the initial evaluation.

Treatment for acute CHIKF is generally supportive care. Analgesic, anti-pyretic, and non-steroidal anti-inflammatory drugs (NSIADs) are often used for symptom relief.[3,4] Some expert caution against the use of NSAIDs during acute phase for fear of Dengue virus infection mimic CHIKF and later develop hemorrhagic complication.[2] A randomized control trial has examined the use of chloroquine for acute CHIKF but concluded there is no benefit during acute stage of the illness.[5]

After a transient resolution of symptoms, Chikungunya infections enter the chronic phase which is characterized as persistent arthritis.[1-3] Some patients have continuing symptoms

between the acute and chronic phases, but most experience a "biphasic illness" with a temporary resolution of all symptoms.[2] Symptoms during chronic phase includes symmetric, migratory, oligoarticular or polyarticular arthritis with morning stiffness and joint edema.[1-3] Twenty-five to 82% of patients with CHIKF will progress to chronic joint symptoms.[2] One systematic review estimated 52% of American CHIKF patients progress to chronic phase with various joint complaints.[6] Extra-articular manifestations have been described including new-onset Raynaud's phenomenon, neuropathic pain syndrome, sensorineural impairment, paranesthesia, and digestive disorders. Both articular and extra-articular manifestations often last from months to years.[2,3]

Treatment for Chikungunya arthritis has been a topic of great debate. NSAIDs are often the first therapy without consensus on dose, frequencies, and period of administration.[3,4] One study reported improvement of symptoms in 89% of the patients with Naproxen 550 mg twice daily, celecoxib 400 mg daily, or etoricoxib 90 mg daily.[7] One case report used colchicine at 0.6 mg daily for patient who failed initial NSAIDs treatment with resolution of all joint symptoms within one week.[8] Conventional disease-modifying antirheumatic drugs (DMARDs) have also been reported in various cohort studies and demonstrated efficacy in managing Chikungunya arthritis.[2-4] A cohort of 139 patients compares hydroxychloroquine 400 mg daily vs combination therapy (MTX weekly, sulfasalazine 1 g daily, and hydroxychloroquine 400 mg daily) showed significant improvement in combination therapy group in Disease Activity Score of 28 joints.[9] Biologics including anti-tumor necrosis factor (TNF) and abatacept has been reported in case reports of patients who did not respond to conventional DMARDs.[2-4] The latest drug gaining recognition is ribavirin, a synthetic nucleoside analog that inhibits RNA and DNA viruses. It has been studied at 200 mg twice daily for seven days and also demonstrates improvement of patients' joints symptoms, in a small study.[10] More controlled studies are needed to develop treatment guidelines for Chikungunya arthritis.

Conclusion

Chikungunya has emerged as a global disease affecting millions of people with significant musculoskeletal morbidity. Any patient has traveled to endemic areas including Africa, Asia, and Oceania with fever and joint pain should be screened for Chikungunya virus, Dengue virus, and Zika virus. More research is needed to clarify management of Chikungunya arthritis.

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