EDITORIAL

Mightier than the Sword – Chikungunya Arthritis

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After Dengue fever, Chikungunya (CHIKV) epidemics are occurring almost worldwide, garnering more medical attention due to the similarity in origin and initial presentation of both the diseases. They both use the same vectors and present with acute fever, myalgia, lethargy and nausea, making it important to differentiate the two upon diagnosis. CHIKV is distinguished by its added ability to cause prolonged, debilitating arthritis and by how it is self-limiting further down the disease course. It is caused by a single stranded RNA virus of the genus Alphavirus and transmitted to humans by the Aedes aegypti and Ae. albopictus. Initially, its cases were limited to tropical Africa, South Asia and Indian Ocean islands, but now due to frequent travelling, the disease has also spread to America and Europe.

The initial epidemics of fever with arthritis in the 19th century were mistaken for Dengue fever as well, but it is now felt that the presentation better fitted the Chickungunya fever (CHIKF) criterion. It has been frequently reported from Africa since 1952 and the first Asian outburst was reported from Thailand in 1958.[1,2] A major outbreak occurred in the Indian Ocean Islands in 2005[3], after which eruptions were reported from Italy in 2007 and a Caribbean Island in 2013, spreading to 14 nearby countries in a year, including the USA.[4]

A small number of individuals infected by a mosquito bite suffer from an asymptomatic infection, but the majority develops symptoms that are broadly categorized into the acute and chronic phases. The acute phase lasts 3-10 days, after approximately a 2-4 days incubation period (range 1-14 days). It is characterized by an abruptly presenting fever, myalgia, a characteristic rash and other, less common symptoms like diarrhea, vomiting, edema on limbs, bleeding, otitis, ocular disease (especially anterior uveitis) and lymphadenopathy. The rash which is mostly macular or maculopapular usually appears 3 days after the fever and mainly involves the limbs, although it can also involve the face and varies between diffuse to patchy in distribution. It is itchy and exfoliative dermatitis can frequently occur.

Polyarthralgias/Arthritis develop in most of the patients after 2-5 days of onset of fever, which marks the transition into the chronic phase of the disease. It is said to present as one of the most incapacitating manifestations in 85-100% of patients with symptomatic infection and is reportedly associated with a positive predictive value of 84.6% for the diagnosis of CHIKV infection, when presenting alongside high fever.[5] The arthralgia/arthritis is mostly symmetrical with involvement of distal small joints of wrists, hands and feet, including ankles. Involvement of the large and axial joints has been reported in 34-52% cases.[6] The arthritis is variable in severity but mostly severe and debilitating, making patients bedridden. Significant morning stiffness can also occur with joint pain and swelling- the picture can exactly simulate rheumatoid arthritis and many patients have been reported to fulfill the criteria of ACR (American College of Rheumatology) for rheumatoid arthritis. The RA factor has been reported to be negative in most of the cases, although variable results have been shown for anti-CCP positivity in different studies. Joint erosions on X-rays and MRI of affected joints have been reported in a small number of patients from India and from the Reunion Islands, with chronic arthritis.[7] Other less common symptoms of the chronic phase include neuropathy, cerebral disorder, neurosensory deficiency, burning mouth syndrome, paresthesia, cubital tunnel syndrome, gastrointestinal disorders, exanthema, bursitis, and synovitis.[8]

Severe and deadly complications have been occasionally reported in CHIKV, like myocarditis, meningoencephalitis, Guillain-Barré Syndrome, uveitis, hepatitis and craniopathies.

These are specifically seen in immunocompromised patients.

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Detection of IgM Anti-Chickungunya virus antibodies by ELISA has been a primary diagnostic test, detected in patients after 4 days of onset of fever. IgG antibodies appear usually after 2 weeks and may remain positive for years. PCR can be more useful for the diagnosis in the initial viremic phase. Viral cultures are also very effective in detecting the virus in the first 3 days of infection. The virus has not only been detected from the blood and body secretions, but also from the biopsy of synovial tissue, skin and muscles.

Large scale randomized control studies are lacking regarding the treatment of CHIKV arthritis. During the acute phase, supportive treatment in the form of IV fluids and simple analgesics like Paracetamol and NSAIDs are recommended. Animal studies have shown persistence of virus for longer periods so the role of corticosteroids in the treatment of arthritis has been debatable and there are reports of rebound arthritis after discontinuation of steroids as well.[9]

NSAIDs, analgesics and steroids are effective in relieving joint pains caused by arthritogenic viruses like Chickungunya, but the relief is often transient. Slow acting anti-rheumatoid drugs like methotrexate, sulfsalazine and chloroquine have been tried alone and in combinations with promising results, as shown in some of the studies. Chloroquine and ribavirin combination was reportedly useful in relieving the symptoms in CHIKF. Chloroquine phosphate alone was found to significantly improve Ritchie Articular Index in a small study conducted only on ten patients.[10]

Future therapies including anti-IL6 therapy, TNF antagonist, anti-RANKL therapy and those directly targeting cytokines are under trial and have been proposed as potential immunotherapies against Chickungunya arthritis. Further experimental agents including inhibitors of MCP-1, RNA interferons-mediated inhibition of CHIKV and mannose binding lectin pathway in animals have all shown some encouraging results. Overall, targeting T cell activation might come up as a potential therapy against CHIKV induced arthritis.

In conclusion, the Chikungunya virus is prevalent worldwide and is causing epidemics of chronic arthritis which can be debilitating in many patients, resembling RA. Up to date knowledge indicates that macrophages, certain antibodies, activated CD4+ T cells, cytokines and other inflammatory markers as well as the persistence of virus, all contribute to the development of arthritis and CHIKF. Disease modifying drugs like methotrexate, sulfasalazine and hydroxychloroquine have shown promising results, but there is yet a lot to be desired. Newer therapies targeting the pathogenic mechanisms are in the pipeline, showing a ray of light at the end of the tunnel.

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