Chikungunya and other Viral Arthritides

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Chikungunya fever is presently endemic in Maharashtra and adjoining regions. The virus, first isolated in Mankonde plateau along border of Tanzania and Mozambique, spreads by bite of infected mosquito *Aedes aegypti*. Various other viruses also cause arthritis lasting for variable period of time. These viral arthritides form important differential diagnosis in various rheumatic conditions. It is, therefore, necessary to know clinical patterns of viral arthritides as management in these cases is totally different than arthritis related to immunological disorders.

Viruses that cause arthritis include:

1. Hepatitis A, B, and C
2. Rubella
3. Parvovirus B19
4. Alpha viruses: Asia-Africa region- Chikungunya, Onyong-nyong, Igbo Ora Australia-America region- Ross River virus, Mayaro, Burmah Forest virus.
5. Mumpsvirus
6. Enteroviruses: Coxasakie, Echo
7. Herpetoviruses: Herpes simplex, Varicella-zoster, Epstein-Barr, Cytomegalovirus
8. Retroviruses: HIV, HTLV-1
9. Adenoviruses (few serotypes)

Chikungunya fever

The incubation period is 2-12 (2-3) days. Clinical features consist of characteristic triad of fever, rash and rheumatic manifestations.

Fever: The onset of fever is usually abrupt with intermittent shaky chills and often reaches 39-40° C (>102° F). Fever usually lasts for 2-3 days and may remit for 1-2 days to appear again in saddle-back pattern. Fever can thus last up to 2 weeks.

Rash: Rash is rare in present endemic. Some patients may present with flush over face and trunk. Rash is maculopapular but can be petechial. Pruritus and irritation may accompany. The rash commonly occurs on trunk and limbs, but other areas may be involved.

Arthritis: Crippling arthralgia is usually the initial manifestation leading to stooped posture (Mankode language, root verb "kungunyala" = that which bends up). Arthritis is quite frequent. The arthritis is polyarticular, migratory, predominantly affecting small joints of hand and feet with wrists and ankles. Swelling may occur but effusion is uncommon. Involvement of large joints is uncommon and may occur in the form of arthralgia only. Pain, but not much of stiffness, on movement in mornings is relieved by mild exercise and aggravated by strenuous exercise. Articular symptoms last for few weeks but may require months to resolve completely. About 12% patients develop chronic articular symptoms lasting up to 18 months.

Prolonged joint symptoms are particularly troublesome in elderly patients and in those with comorbid conditions such as hemiplegia or ischaemic heart disease. Previously affected joints (e.g. osteoarthritis, rheumatoid arthritis, etc) show disproportionate clinical features. Few cases of destructive joint disease reported in literature are likely to be due to another pathology.

Other features: Headache, photophobia, retroorbital pain, conjunctival injection, myalgia, back and shoulder pain, soar throat and pharyngitis can occur in some patients. Fatigue may prolong for several weeks. CHIK V infection can cause thrombocytopenia.

Children have less severe joint symptoms and disease appears to be milder. Prominent flushing and early eruptions are useful indicators. The severity of the disease appears to be increasing due to genetic changes in the virus. Although no deaths have been reported in literature, recent observations indicate that serious neurological and other complications can occur and close monitoring is, therefore, necessary in selected cases.

Investigations: Typical clinical features especially in an endemic area are sufficient for diagnosis of chikungunya arthritis. Viraemia lasts for initial 2-4 days and virus isolation is possible during this

understand how the current outbreak began and why it appears to be more virulent than those seen previously. This will also help us to understand the evolution of the virus over the course of the outbreak (6).

Six different virus samples were isolated from patients (five from Réunion and one from the Seychelles, three of which were taken early in 2005 and three from later on in 2005) and examined to determine the entire genetic sequence. The E1 gene was also sequenced from virus samples from an additional 121 patients. The results indicate that the outbreak began with a strain related to East-African strains of the virus that subsequently developed into several distinct variants. The changes found in all of the Indian Ocean sequences share certain areas where they differ from previously determined sequences and it was found that many of these changes result in modifications of the composition of the viral proteins (principle components of viruses). Many of the changes were present from the beginning of the outbreak and others appeared midway through the outbreaks and before the time when infection rates rose rapidly.

A specific example of a dramatic change is at position 226 of the E1 protein, which forms part of the viral protein coat, from the 'A version' to the 'V version'. All early viral sequences were of the A version, but after late 2005, more than 90% of the sequences were of the V version. What are the implications of such changes in the make-up of the viral genetic material? In a close relative of the chikungunya virus, a change at position 226 of E1 rendered the virus independent of the need for cholesterol (viruses normally require cholesterol to infect host cells in humans and mosquitoes). Mosquitoes do not tend to have enough cholesterol for efficient infection by viruses; however, the newer V version of the chikungunya virus may have better survival and multiplication rates in mosquitoes attributed by the independence from cholesterol. Better survival in mosquitoes could in turn have led to much more rapid spread to humans, though at this stage it all remains pure speculation. The work does begin to shed some light on the problem of chikungunya that may in fact affect a larger area than just Asia and Africa. As it is the same species of mosquitoes that spread yellow fever and dengue fever, chikungunya could potentially affect all those parts of the world already affected by these diseases (6).

Many questions, however, remain unanswered in the field of Virology such as why there is no incidence of Yellow fever in India whilst there are similar environmental conditions to the areas in Africa and exactly the same species of vector. This only goes to emphasise our lack of understanding and the need for further research into both viruses and vectors.

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period. Haemagglutination antibodies appear after viraemia and are positive by 5-7 days. IgM antibodies (ELISA) persist for more than 6 months. Rheumatoid factor may turn positive in low titres in longstanding cases. Synovial fluid is inflammatory. Arthroscopy shows atropic synovium in longstanding cases.

Pathogenesis: The virus replicates in and around synovium (synovium, periosteum and endosteum). This leads to cell death or damage. Immune response within joint tissue is another mechanism suggested. There is a possibility of immune complex deposition within the joint space although no disease correlation could be found between serum immune complexes and/or complement levels in cases of other Toga viruses studied. The virus adsorbs on platelets, causing aggregation and bleeding. Superficial capillaries in skin show erythrocyte extravasation and perivascular cuffing.

Arthritis due to other viruses

1. Arthralgias are seen in 10-14% cases of hepatitis A infection during acute phase. Arthritis due to hepatitis B is immune complex mediated. 10% patients develop symmetrical arthritis of small hand joints and knees. Arthritis can be additive or migratory and be associated with skin rashes and polyarteritis nodosa. Arthritis lasts for 1-3 weeks and resolves with onset of jaundice. Recurrent arthritis can occur in chronic active hepatitis. Hepatitis C associated arthritis is reported in isolated case reports. Other rheumatological syndromes like Sjogren's syndrome, mixed cryoglobulinaemia and fibromyalgia are closely linked with hepatitis C.

2. 60% of adults, especially females, develop severe flu like illness associated with symmetrical arthritis of small hand joints in human Parvovirus B19 infection. Trasient marrow aplasia and neuropathy may accompany. Arthritis may persist for months to years.

3. Other alpha viruses also cause disease similar to chikungunya fever. Rodents carry the Ross River virus infection found in Australia-America regions and domestic animals and rash is more prominent. Arthritis is often migratory, asymmetric and polyarticular. Only 50% can resume daily activities at the end of 4 weeks.

4. Arthritis due to mumps virus starts 1-3 weeks after clinical mumps. It is in the form of migratory polyarthritis involving large joints and lasts for about 2 weeks.

5. Rubella virus shares Togaviridae family along with alpha viruses. The virus can be found in synovium. Arthritis is more common in females and occurs after exanthem. Small hand joints, knees, ankles, elbows and wrists are generally involved. Arthritis can occur even after vaccination.

6. HIV infection is associated with protean rheumatological manifestations such as arthralgias, arthritis, spondyloarthropathies, myopathy, polymyositis and vasculitis. HTLV-1 is associated with oligoarthritis and nodular rash.

7. *Aedes aegypti* also transmits dengue and yellow fever, which have same endemic cycle. It seems possible that some cases of CHIK-V infection may be diagnosed as dengue and vice versa.

Management

Management of CHIC V infection is symptomatic and patients recover without sequelae. Patients generally recover within a week. Adequate rest and ample fluids are necessary. Paracetamol should be preferred for analgesia. Aspirin should be avoided as it can precipitate bleeding in the rash. Arthritis responds well to non-steroidal anti inflammatory drugs like ibuprofen, and naproxen. NSAID induced gastrointestinal bleeding can be troublesome in presence of chikungunya virus related thrombocytopenia. Range-of-motion exercises relieve stiffness. Chloroquin phosphate (250 mgm/day for 20 weeks) administered in 10 cases resulted in subjective improvement in 7 and improvement on Ritchie articular index in 5 cases. Local steroids can be tried in chronically affected isolated joints. There are isolated studies of ribaverin and interferon reported in literature. Chikungunya virus vaccine is still experimental. One attack of CHIK-V infection (clinical or silent) confers lifelong immunity.

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