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Case Report



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Chikungunya encephalitis: A case report

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ABSTRACT

Rationale: Transmitted to humans *via* the *Aedes* mosquito, Chikungunya virus (CHIKV) is associated with multi-system complications, sometimes collectively referred to as “atypical features.” However, a disorder of the nervous system appears to be the most common severe complication of CHIKV infection.

Patient’s Concern: A seventy-five-year-old patient from India presented to the hospital with fever, chills, rigors, and multiple joint pains for which he was worked up.

Diagnosis: CHIKV encephalitis.

Interventions: The patient was treated initially on supportive therapy with antipyretics, intravenous fluids; however, during his hospital stay, the patient had altered sensorium during which he was managed in the intensive care unit; required mechanical ventilation.

Outcomes: The patient succumbed to his illness.

Lessons: Treating clinicians should keep CHIKV disease in the differential diagnosis in cases of febrile exanthems associated with disabling arthritis, especially in a CHIKV-endemic country like India.

KEYWORDS: Chikungunya; Rash; CHIKV encephalitis; Polyarthrititis

from African and Asian countries in the 1960s and 1970s. Since 2005 CHIKV has become a reemergent disease with epidemics on the Comoros Islands of the Indian ocean followed by outbreaks in Mauritius and the French island of La Reunion[3]. In India, the disease has relapsed in the form of multiple outbreaks in its various spreading to about 30 states and Union territories till the year 2019[4]. It is typically characterized by triad of acute febrile illness, maculopapular rash, and arthritis. Saddleback pattern high-grade fever and myalgia occur after an incubation period of three to seven days and lasts for three to five days. Bilateral symmetrical polyarthrititis is explosive in onset and involves distal joints more commonly than proximal joints including distal interphalangeal joints[5]. Pruritic maculopapular rash, often involving the extremities, generally appears three days after the onset of fever and resolves over the next three to seven days[6]. In most individuals, CHIKV infection is generally a self-limiting, mild to moderate infection without severe hemorrhagic manifestations, unlike Dengue fever. However, severe CHIKV disease involving almost every organ system has been reported in the form of neurological involvement, respiratory failure, myocarditis, acute hepatitis, and renal failure[7]. In this case report we present a unique case of neurological manifestations of CHIKV disease in an elderly patient who presented with features of acute febrile illness followed by the development of altered mental sensorium.

1. Introduction

Chikungunya fever is a reemerging infection affecting tropical, sub-tropical, and even temperate regions[1]. It is an arboviral disease caused by the Chikungunya virus (CHIKV) of the genus Alphavirus and Togaviridae family transmitted by mosquito bites of mainly *Aedes aegypti* and *Aedes albopictus*, the species also responsible for transmission of dengue virus and Zika virus. CHIKV was first discovered after a 1952-1953 epidemic in the eastern African subcontinent[2]. Since then multiple outbreaks have been reported

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2. Case report

A seventy-five-year-old male patient presented to a tertiary care center with chief complaints of high-grade fever for the last eight days which was associated with chills, rigors, and myalgias. He also developed a red-colored rash 6 days back which first appeared on his right foot followed by his left foot over two days. This rash was associated with a history of pain in multiple joints of feet including bilateral ankle, tarsometatarsal, proximal interphalangeal, and distal interphalangeal. The pain was also concomitantly present in the wrist, carpometacarpal, proximal interphalangeal and distal interphalangeal joints of bilateral hands. The joint pains were associated with morning stiffness. There was no history of retro-orbital pain and bleeding from any orifices. The patient had no history of any comorbidity or an immunocompromised state.

On examination, he was conscious, oriented to time, place, and person, and had a pulse rate of 106 beats/ minute with other vital parameters like blood pressure, blood sugar, respiratory rate, and

pulse oximetry within normal limits. A general physical examination revealed reddish purple maculopapular, non-blanchable, non-tender rash present over bilateral feet up to ankles. Systemic examination was unremarkable. He was admitted in the hospital and was worked up on the lines of acute febrile illness with polyarticular arthritis and rash.

His hemoglobin was 12.5 g/L, platelet count was $151 \times 10^9/L$ and total leucocyte count was $11 \times 10^9/L$ with normal differential count. Serum electrolytes, renal function tests, and urine examination were all normal. Liver function test showed elevated values of transaminases - AST: 144 IU/L and ALT: 81 IU/L. On further evaluation for etiology, the patient tested positive for Chikungunya IgM antibodies by enzyme-linked immunosorbent assay technique (ELISA). He tested negative for dengue NS1 antigen, dengue IgM, scrub typhus IgM, anti hepatitis C, hepatitis A IgM, hepatitis E IgM, and HIV serologies (all tested by ELISA). Blood culture and urine culture were also sterile. Ultrasound whole abdomen and chest X-ray were normal. Peripheral arterial

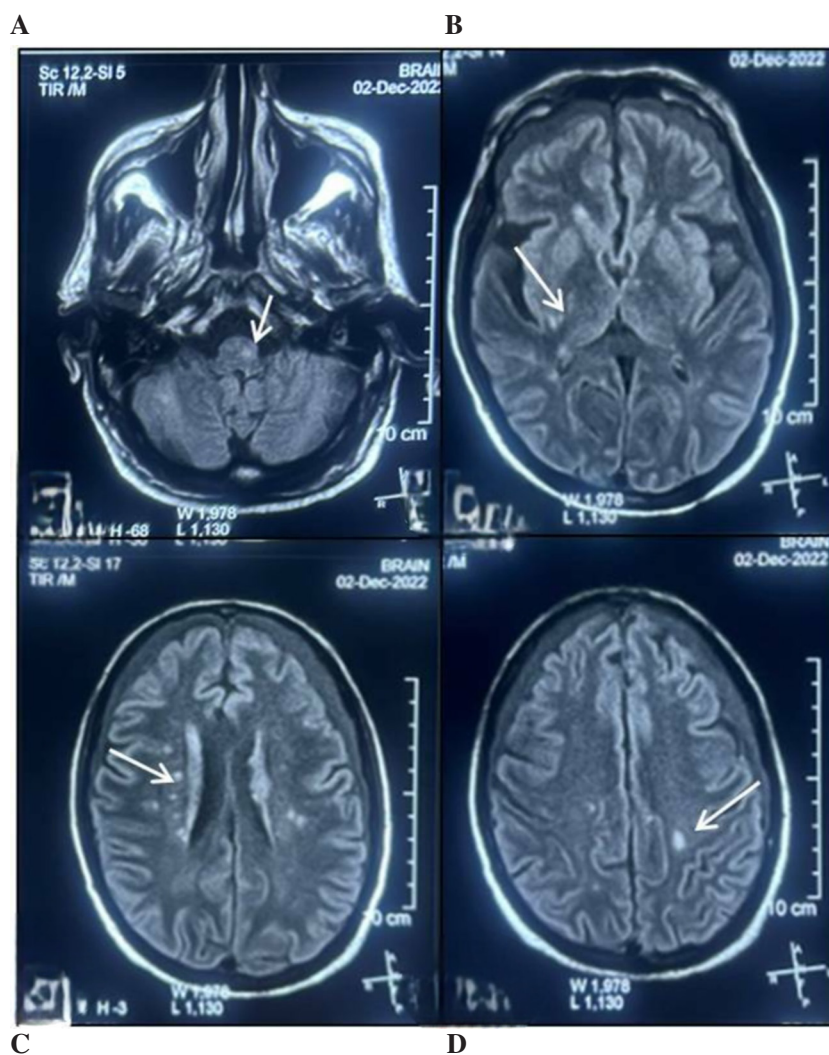


Figure 1. Axial fluid-attenuated inversion recovery (FLAIR) MRI brain images showing multifocal small lesions (arrows) involving the medulla (A), basal ganglia (B), and cerebral white matter (C & D), more in the periventricular region. No diffusion restriction or susceptibility changes seen in the lesions.

disease and lower limbs venous thrombosis were ruled out by arterial doppler and venous compression doppler of bilateral lower limbs. In the setting of acute febrile illness with polyarthritides and maculopapular rash, along with positive Chikungunya IgM serology, the diagnosis of Chikungunya fever was kept. Patient was managed with acetaminophen, intravenous fluids, and supportive therapy. He became afebrile on the tenth day of his illness. However, the patient developed altered mental sensorium on the third day of hospital admission *i.e.*, on the eleventh day of his febrile illness, which was insidious in onset and was gradually progressive. Initially, he was drowsy but was able to follow commands. His sensorium worsened over five days so much so that he was unable to follow any verbal commands and was not able to identify his relatives by the fifth day. He was intubated for airway protection and was put on mechanical ventilation. On examination, bilateral plantar reflexes were extensor. There were no signs of meningeal irritation. Fundus examination was normal. Non-contrast computed tomography (NCCT) head was done and was found to be normal. Diagnostic lumbar puncture was done on the same day of development of altered mental sensorium and cerebrospinal fluid (CSF) workup was suggestive of 5 cells/ μ L with lymphocytic predominance, protein 83 mg/dL, glucose-47 mg/dL (concomitant blood glucose: 148 mg/dL) with sterile CSF culture. CSF was positive for Chikungunya IgM antibody by ELISA. CSF polymerase chain reaction (PCR) assay was negative for herpes simplex virus (HSV) DNA and CBNAAT. Contrast-enhanced magnetic resonance imaging brain was done and showed bilateral hyperintensities in the medial temporal and frontal lobes on T2 weighted and Fluid attenuated inversion recovery sequences (Figure 1).

In a patient with CHIKV fever who developed altered mental sensorium and had CSF and MRI findings as above, the diagnosis of CHIKV encephalitis was kept. On the sixth day of mechanical ventilation, the patient developed shock and metabolic acidosis. Initially, renal function tests were normal but later he developed acute kidney injury and oliguria. He succumbed to his illness even after the best possible efforts.

A written informed consent was duly signed by the patient. The consent was obtained after explaining to the patient that no identity will be revealed and the case information, including pictures will be used for education purpose only. The patient gave positive consent for publication and authors certify that written patient consent is present, procured for publication.

3. Discussion

CHIKV disease has become rampant in India and all over the world over the last two decades. It presents as an acute febrile illness with joint and skin manifestations and usually has a self-

remitting course over 2 weeks. However, chronic sequela in the form of post Chikungunya chronic arthralgia/arthritis has been well documented[8]. Rarely CHIKV fever can have severe systemic manifestations leading to poor clinical outcomes. They have been mostly reported during massive outbreaks seen post-rainy season[9]. Severe systemic manifestations are observed more commonly in people with advanced age (age > 65 years), in neonatal infection, and in persons with underlying chronic medical comorbidities (diabetes mellitus, cardiovascular disease)[10,11]. Although not a neurotropic virus-like HSV and Japanese encephalitis virus (JE), CHIKV has long been associated, in literature, with a myriad of rare neurological manifestations in the form of meningoencephalitis, seizures, acute flaccid paralysis, Guillain-Barré syndrome, cranial nerve palsies, and myelitis. Among these, meningoencephalitis is the most frequent neurological manifestation[12]. It is unknown why only some patients develop Chikungunya encephalitis after having Chikungunya febrile illness; genetic and immunologic factors probably play an important role.

CHIKV encephalitis occurs during the acute phase of illness and may be associated with neurological sequelae like epilepsy, postinfectious dementia, and cognitive disorder and with mortality. Neurological complications in the neonatal period have been associated with delayed neuro-developmental outcomes. A cohort study done by Gérardin et al. found that 16.6% of cases of CHIKV-associated encephalitis resulted in death, while 30% to 45% of children were discharged with persistent disabilities[13]. Like other arboviral encephalitis, CSF pleocytosis is not always a feature of CHIKV encephalitis. CHIKV encephalitis does not have a characteristic diagnostic pattern on neuroradiology imaging unlike encephalitis caused by other viral pathogens like HSV, which have distinct imaging findings. Moreover, at times no imaging abnormalities have been detected[12]. As the three arboviruses: CHIKV, dengue virus, and Zika virus are transmitted by the same mosquito species and the latter two viruses have known neurological manifestations, in the case of acute febrile illness with rash it is imperative to test for these viruses together according to appropriate epidemiological setting, to rule out co-circulation and co-infection as it is associated with more dismal outcome[14]. Subtle clinical pointers for CHIKV disease are the presence of maculopapular rash, severe bilateral distal polyarthritides, and absence of severe hemorrhagic complications, unlike dengue fever. The possibility of CHIKV encephalitis should always be kept in high-risk patients who develop clinical features of encephalitis, like altered mental sensorium, seizures, *etc.* As there is no approved antiviral therapy for the disease, only supportive management remains the cornerstone of the treatment[15]. In the absence of an effective vaccine, efficient vector control measures remain the best strategy for disease prevention.

In conclusion, since Chikungunya fever is a reemerging infection,

not only in tropical regions but also subtropics and temperate regions. CHIKV encephalitis should always be kept as an important differential in patients presenting with acute febrile exanthem, polyarthritides, and altered mental sensorium. Extremes of age, mainly the elderly, cardiovascular, neurological, or respiratory dysfunctions, and decompensated comorbidities need special consideration. Currently, supportive treatment and vector control measures are the only available ways to tackle this menace.

Conflict of interest statement

The authors report no conflict of interest.

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Authors' contributions

VK & JK: Case presentation, data collection, investigations and writing of original draft. PS: Literature review, writing of original draft including conclusion, references. NB: Intellectual content, literature search, manuscript final editing and review.

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