Case Report

DOI: 10.7860/JCDR/2024/73566.20363

Unravelling Chikungunya's Neurological Toll: A Case Report with Insights from Magnetic Resonance Imaging of Brain

Internal Medicine Section

PONVIJAYA M YADAV[1], VIJAYASHREE GOKHALE[2], SANGRAM S MANGUDKAR[3], SINDHURI GOUD NIMMALA[4], VINEETHA NAGA LAKSHMI GIDUTURI[5]

ABSTRACT

Chikungunya, an emerging neurotropic virus, has the potential to induce various neurological abnormalities. When suspecting encephalitis, it is imperative to test for the Chikungunya virus, which requires an early diagnosis and course of treatment. This is a case report of a 54-year-old male who presented with fever, giddiness, ataxia and slurred speech. Magnetic Resonance Imaging (MRI) brain revealed typical hallmark features of chikungunya encephalitis, with an incidental right cerebellopontine angle tumour. A positive serum chikungunya antigen Polymerase Chain Reaction (PCR) validated the diagnosis. The patient was initially managed in the Intensive Care Unit (ICU), showing a dramatic response to the treatment, and then shifted to the medicine ward for further observation and management. This case underscores the importance of considering chikungunya in patients presenting with encephalitis differential diagnosis, especially in endemic regions like India. Comprehensive imaging and PCR testing were instrumental in diagnosis. Treatment included supportive care, intravenous antibiotics, antivirals and steroids, leading to significant improvement. By day 12, notable recovery was observed, and follow-up MRI brain showed no new abnormalities. This case adds to the evidence of severe neurological manifestations of Chikungunya virus, highlighting the need for early recognition and management to improve outcomes. The concurrent presentation of chikungunya encephalitis and a cerebello-pontine angle tumour emphasises the necessity for thorough neuroimaging and PCR testing in suspected cases. The patient's dramatic recovery following timely intervention demonstrates the potential for positive outcomes with appropriate management.

Keywords: Encephalitis, Encephalomyelitis, Neurotropic virus, Viral fever

CASE REPORT

A 54-year-old male employed as a chef arrived to the medicine department on a wheelchair with primary symptoms of high-grade fever, which occurred intermittently and was alleviated by antipyretic medications within 5-6 days. The fever was associated with severe arthralgia, myalgia and headache. It was associated with breathlessness during exertion; after ascending nearly two flights of stairs, the patient experienced breathlessness. Furthermore, he noted to have slurred speech for a span of 2-3 days, along with dizziness and difficulty maintaining balance while walking. The relatives also noticed a change in his level of consciousness when he was brought to the hospital immediately. The patient was non diabetic and not hypertensive and his significant previous medical history included a Coronavirus Disease-2019 (COVID-19) infection that occurred three years ago, which necessitated hospitalisation for oxygen support only. He had experienced a decline in his hearing over the last 6-8 months. For the past six years, the patient had been a chronic alcoholic and a tobacco chewer.

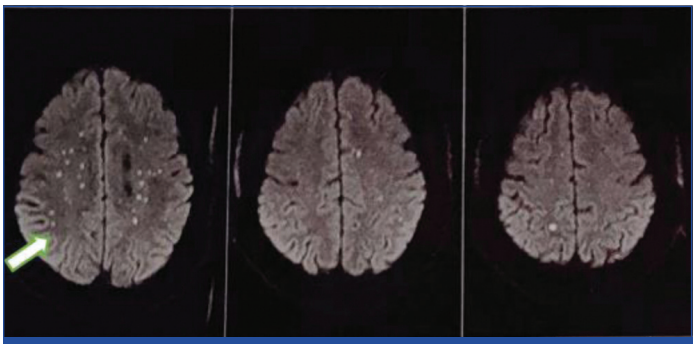
A general physical examination was normal. Upon further assessment, the patient's Body Mass Index (BMI) was 32.6 kg/m^2. He was febrile, with a temperature of 101.4° Fahrenheit. His pulse rate was 102 beats per minute, blood pressure was 130/90 mmHg and a respiratory rate was 16 breaths per minute. His oxygen saturation level was noted to be 98% on room air. He was extremely irritable and groaning. A detailed neurological examination revealed no obvious cranial nerve palsy or any neurological deficit, except for the presence of terminal neck stiffness. The tone in all four limbs was increased and the bilateral Babinski sign was positive. The knee-jerk reflex was exaggerated on both sides, whereas the rest of the superficial and deep tendon reflexes remained normal. Evaluations of the respiratory, cardiovascular and gastrointestinal systems were within normal limits.

The differential diagnosis considered included viral fever causing neurological manifestations such as dengue encephalitis, chikungunya encephalitis, herpes simplex encephalitis, Japanese encephalitis, Epstein-Barr encephalitis, bacterial meningitis and cerebrovascular accident with multiple infarcts. The laboratory investigations are mentioned in [Table/Fig-1]. Briefly, the key findings pointed towards an ongoing chikungunya virus infection, evidenced by raised total leukocyte count, thrombocytopenia, elevated D-dimer levels and chikungunya-positive serology and PCR in the Cerebrospinal Fluid (CSF). An MRI of the brain was done, which revealed multiple tiny foci of acute non haemorrhagic infarcts in the bilateral centrum semiovale, bilateral frontoparietal periventricular white matter and bilateral cerebellar hemispheres. A well-defined homogeneous enhancing extra-axial lesion was detected in the right cerebellopontine angle, possibly a vestibular schwannoma [Table/Fig-2,3]. The patient's decline in hearing was attributed to the presence of a tumour. The final diagnosis was given as acute meningoencephalomyelitis secondary to the Chikungunya virus, with an incidental right cerebellopontine angle tumour, possibly a Schwannoma.

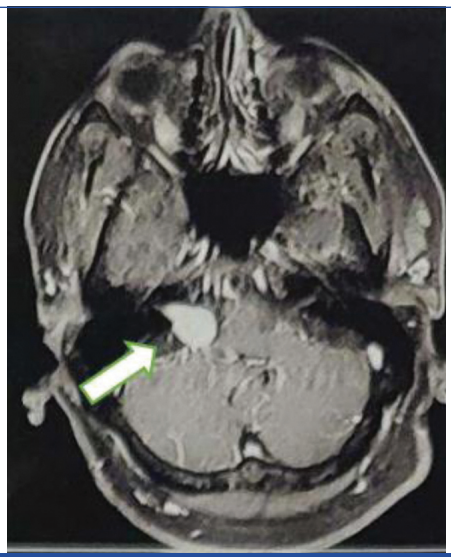
Laboratory investigations	Values	Normal range
Haemoglobin (gm/dL)	15.3	13.2-16.6
Total leukocyte count (per cubic µL)	12,400 (82% were neutrophils and 10% were lymphocytes)	4000-10000
Platelet count (/mm^3)	84,000	150000-410000
Total bilirubin (direct bilirubin, and indirect bilirubin) (mg/dL)	1.05 (0.45 and 0.6)	0.22-1.2 (direct upto 0.5 and indirect upto 1.0)
Aspartate aminotransferase Alanine aminotransferase (IU/L)	81 (mildly elevated) 30 (normal)	8-48 7-45
Creatinine/Urea (mg/dL)	1.11/33	Creatinine: 0.6-1.2 Urea: 17-49
D-dimer (ng/dL)	1064 (elevated)	0 to 500

Troponin I Creatine kinase (ng/dL)	Negative 39 (mildly elevated)	 Upto 24
ESR (mm/hr)	9	Upto 20 mm/hour Westergren method
CRP (ng/L)	200	Upto 5.0 mg/L turbidimetric method
Rapid malarial test, Serum Dengue NS1, IgM, and IgG, Weil Felix test and Leptospira IgM test	Negative	
ANA by immunofluorescence and blot	Negative	
CSF analysis: Colour CSF protein (mg/dL) CSF glucose (mg/dL) CSF total cell count (/cu.mm) CSF adenosine de-aminase (U/L)	Clear, no cobweb was noted 86 156 10 with lymphocytic predominance 0.94	 15-45 40-80 0-5 <10
CSF viral panel: Chikungunya virus Dengue virus, herpes simplex virus, Japanese encephalitis virus and Epstein-barr virus	Qualitatively positive Negative	
CSF chikungunya real-time quantitative PCR Serum chikungunya IgM Blood culture Urine culture	Positive Positive Negative Negative	

[Table/Fig-1]: Depicts the significant laboratory investigations and corresponding values.



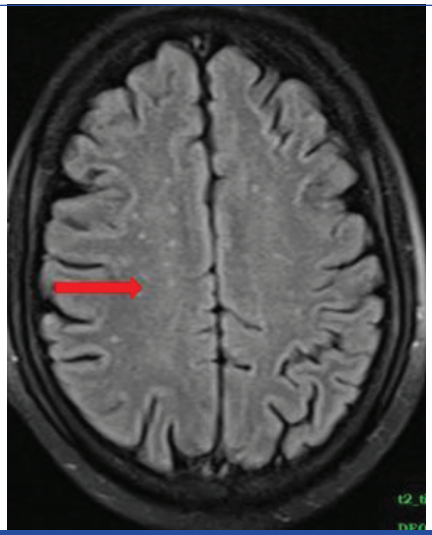
[Table/Fig-2]: MRI brain showed multiple tiny foci of acute non haemorrhagic infarct in bilateral centrum semiovale, bilateral frontoparietal periventricular white matter and bilateral cerebellar hemispheres.



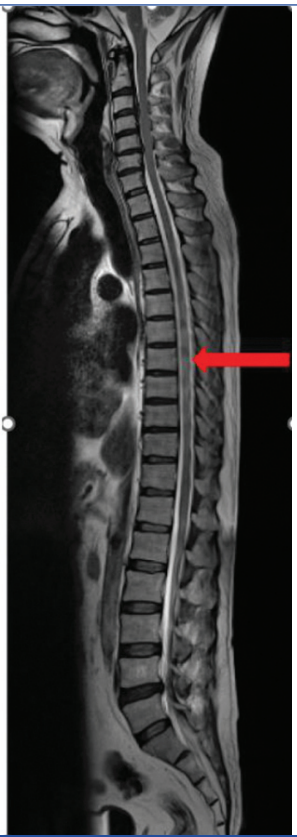
[Table/Fig-3]: Well-defined homogenous enhancing extra-axial lesion vestibular schwannoma in the right cerebellopontine angle.

The treatment given during the hospital course included an injection of ceftriaxone 2 grams i.v. twice a day, an injection of acyclovir 750 mg i.v. thrice a day, an injection of dexamethasone 4 mg i.v. thrice a day, and an injection of mannitol 100 mg i.v. thrice a day. Other supportive management, such as hydration in the form of intravenous fluids and antipyretics, was also continued. The patient showed improvement by day 12 of the ICU stay. On day 13, the patient was shifted to the medicine ward and was subsequently discharged on day 15 after observation.

The patient arrived in the Outpatient Department (OPD) with the help of a walker two weeks after discharge from the hospital. On neurological examination, the patient had a spastic gait with bilateral exaggerated knee jerks. A follow-up MRI of the brain (two weeks postdischarge) [Table/Fig-4] suggestive of multiple hyperintense foci in the bilateral centrum semiovale, corona radiata, bilateral frontoparietal periventricular white matter, and left external capsule, likely chronic sequelae of previous encephalitis. The MRI of the spine [Table/Fig-5] showed a subtle enhancement on the ventral aspect of the cord at the D8-D12 level, which was likely a sequelae of previous encephalomyelitis. The patient is still on regular follow-up visits and is given multivitamins and physiotherapy, doing satisfactorily well.



[Table/Fig-4]: Follow-up MRI Brain showing multiple hyperintense foci in bilateral centrum semiovale, corona radiata, bilateral frontoparietal periventricular white matter, left external capsule- likely chronic sequelae of previous encephalitis.



[Table/Fig-5]: MRI whole spine showed a subtle enhancement on the ventral aspect of the cord at the D8-D12 level, which was likely a sequelae of previous encephalomyelitis.

DISCUSSION

Chikungunya, an alphavirus from the *Togaviridae* family, is transmitted by the bite of the *Aedes aegypti* mosquito. Chikungunya fever may present typically with high-grade fever, arthralgia, headache and rash. Severe arthralgia is the hallmark feature of chikungunya fever, often causing bent posture in the patients. The incidence of severe complications of chikungunya fever, including neurological issues, has been increasing. Chikungunya accounts for approximately 3-16% of acute encephalitis syndrome cases in India and this trend is on the rise [1].

The virus impacts the central nervous system through two different methods. The virus can cause injury directly on the axons or indirectly through immune-mediated mechanisms [1]. Autoimmune-mediated injury leads to demyelination as a result of attack on the myelin sheath of Schwann cells [2]. Neurological complications of chikungunya arise a result of neurotropism demonstrated by the virus. Currently, the analysis of CSF is the preferred method of investigation. The *Aedes aegypti* mosquito belongs to the *Togaviridae* family. Chikungunya infection results from enhanced vector competence.

This virus was first isolated in Calcutta, India, and several outbreaks have been reported since then. In both adults and children, the transmission of the virus occurs directly via mosquito bites, while neonates can have vertical transmission. It usually has a bimodal distribution, with the mean age of around 49 years and a second peak occurring during infancy [3].

The fever-arthralgia-rash spectrum, along with encephalomyelitis, can have variety of differential diagnosis that need to be ruled out. The differential diagnosis could be viral fevers causing neurological manifestations such as dengue encephalomyelitis, chikungunya encephalomyelitis, herpes simplex encephalomyelitis, Japanese encephalomyelitis, Epstein-Barr encephalomyelitis, bacterial meningitis and cerebrovascular accidents with multiple infarcts. Hence, differentiating these viruses is important, particularly in tropical regions like India, where outbreaks have been reported.

Neurological complications of chikungunya infection are infrequent, uncommon and variable. Manifestations are because of the neurotropism demonstrated by the virus. Various manifestations majorly include meningoencephalitis, encephalomyeloradiculitis, Guillain-Barré syndrome, cranial nerve palsies, neuropathy and ocular complications like conjunctivitis, uveitis, retinitis, retinal detachment, retinal haemorrhage and optic neuritis [3,4]. Less frequently described syndromes include behavioural changes, sensorineural hearing loss, stroke, meningism and encephaloneuropathy [5].

Currently, there are no specific antiviral agents or vaccines for the chikungunya virus, but research is ongoing. Two of the few agents that have been clinically tested are chloroquine and ribavirin, both known to have a safety profile for postviral arthritis. A recent study that tested an insect-specific alphavirus as the vaccine platform found that it elicited immunogenicity in mice and macaques after a single dose. Supportive care and symptomatic management, including adequate hydration with intravenous fluids and antipyretics for fever, remain the mainstay of treatment. Ophthalmological and neurological complications can be treated with steroids, but recovery is variable. A vaccine may be available in the near future and is currently under research. Until then, maintaining a high degree of suspicion for neurological manifestations, along with early diagnosis and treatment, will definitely reduce the mortality rate of chikungunya encephalitis [5].

This patient developed acute encephalitis due to chikungunya fever, followed by myelitis and ultimately recovered. Diverse neurological complications develop secondary to the chikungunya infection, including myelitis and encephalitis, both of which were seen in present patient. The others include encephalopathy, Guillain-Barré syndrome, acute disseminated encephalomyelitis and branch retinal artery occlusion [3]. Patients are usually viremic for the first 48 hours [4].

Chandak NH et al., reported neurological complications in patients during the Nagpur, India outbreak of chikungunya between June and December 2006 [6]. They labeled chikungunya as a neurotropic virus, indicating that encephalitis being common, but the outcomes were generally good. Cerny T et al., studied and classified the neurological complications of chikungunya fever [2]. According to their findings, neurological complications fall into the categories of atypical and severe complications, with 65% of these patients showing positive serum IgM and blood RT-PCR results, and 62% showing positive CSF IgM and RT-PCR results. However, it is crucial to conduct all these tests within one week of the onset of the illness. In present case, patient had IgM antibodies and was RT-PCR positive in both the blood as well as in the CSF.

Ellul M and Solomon T studied acute encephalitis and gave an algorithm for diagnosis and management [7]. A similar pattern with was followed in present study case. Khatri H et al., reported a case of chikungunya virus-associated encephalitis and encephalopathy, with CSF pleocytosis, brain imaging and EEG all contributing to the diagnosis [8]. The MRI brain picture was almost diagnostic of chikungunya encephalitis, findings similar to those of index patient. There were bilateral, multiple, tiny, punctuate white matter lesions with increased signals on diffusion-weighted images. Therefore, MRI imaging can be useful as an exclusive tool for diagnosis.

Anand KS et al., reported on an outbreak of chikungunya in Delhi around 2018-19 [9]. Of the 42 patients with neurological complications, 12 had encephalitis, and four patients succumbed to the illness. The patients who died were elderly and had co-morbidities. In present case, patient recovered, although myelitis still persists. Júnior JG et al., reviewed chikungunya encephalitis and explained two mechanisms of CNS injury caused by the virus [10].

A direct injury to the oligodendrocytes, astrocytes, choroid plexus and meninges causes encephalitis and encephalopathy. This patient is likely to have suffered a direct injury. The other mechanism is autoimmune injury, which targets the myelin sheath of Schwann cells, causing axonal neuropathy. Until then, maintaining a high degree of suspicion for neurological manifestations, along with early diagnosis and treatment, will definitely reduce the mortality rate of chikungunya encephalitis.

CONCLUSION(S)

When diagnosing any viral encephalitis, it is important to consider chikungunya encephalitis. In addition to blood and CSF IgM and RT-PCR, it is important to conduct imaging studies such as MRIs of the brain and the spinal cord, as they can aid in diagnosis. Although no specific antiviral treatment is available, supportive measures do help patients navigate the crisis period. Some residual CNS damage, as seen in present patient, may take longer to recover.

Acknowledgement

Authors would like to thank Department of Neurology, Dr. D. Y. Patil Medical College and Hospital, Pimpri, Pune, Maharashtra, India.

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PARTICULARS OF CONTRIBUTORS:
1. Senior Resident, Department of Internal Medicine, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India.
2. Professor, Department of Internal Medicine, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India.
3. Professor, Department of Internal Medicine, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India.
4. Junior Resident, Department of Internal Medicine, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India.
5. Junior Resident, Department of Internal Medicine, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Dr. D. Y. Patil Vidyapeeth, Pune, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Sindhuri Goud Nimmala,
B 61, Old Girls Hostel, Dr. D. Y. Patil Medical College and Hospital,
Pune-411018, Maharashtra, India.
E-mail: sindhurigoudnimmala@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jun 18, 2024
- Manual Googling: Jul 27, 2024
- iThenticate Software: Oct 22, 2024 (8%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Jun 14, 2024**
Date of Peer Review: **Jul 05, 2024**
Date of Acceptance: **Oct 26, 2024**
Date of Publishing: **Dec 01, 2024**