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CASE REPORT

Peripheral polyneuropathy associated with Chikungunya virus infection

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Abstract

The Chikungunya virus (CHIKV) is an arbovirus transmitted to humans through mosquito bites and can cause a series of symptoms ranging from a benign febrile illness to severe neurological conditions. We report the identification of CHIKV in a serum sample from an elderly woman with febrile illness and severe arthralgia in Brazil. The occurrence was found of peripheral polyneuropathy affecting the upper and lower limbs evidenced by electroneuromyographic findings. The patient was treated with a corticoid associated with methotrexate, suggesting that the pathophysiological basis of the case in question may be related to an immune-mediated response by T cells and inflammatory cytokines. This finding reinforces the need to be aware of the emergence of neuroinfections related to CHIKV and effective diagnoses for the early detection of neurological alterations, favoring the clinical management of these patients.

Keywords Chikungunya · Polyneuropathy · Arthralgia

The Chikungunya virus (CHIKV) is an arbovirus belonging to the genus *Alphavirus* family *Togaviridae*, which presents a single-stranded genome RNA positive sense (Hossain et al. 2018). It was first identified during a febrile polyarthralgia epidemic in Tanzania and since then has been kept in the wild by a transmission cycle involving vertebrate hosts and hematophagous mosquitoes of the genus *Aedes* (*Ae.*), especially *Ae. aegypti* and *Ae. albopictus* (Scott et al. 2017).

CHIKV causes a self-limiting disease known as Chikungunya fever, rash, myalgia, polyarthralgia, and headache. The clinical presentation disappears within a week, while joint pain may persist for months or years (Tanabe et al. 2018). However, neonates, the elderly, and patients with comorbidities are at increased risk for progression of severity, evolving with atypical and lethal manifestations, including neurological complications such as neuropathic pain, myelitis, encephalitis, polyradiculitis, or symptoms clinically associated with Guillain-Barré syndrome (Peper et al. 2016; Fred et al. 2018).

We describe herein the case of an elderly patient from a Brazilian Northeastern city who, in the course of a serious infection with the virus, presented clinical alterations due to axonal damage in the peripheral nervous system, characterized as one of the most common mechanisms in neuropathies with conduction disorders of the nervous system, congenitally acquired.

Case presentation

A 66-year-old woman was admitted to an emergency department with a complaint of fever for 4 days, severe arthralgia and myalgia, rash, ocular sensitization, nausea, abdominal pain with diarrhea, inappetence, weakness, and reduced range of motion. Patient did not refer diabetes, hypertension, rheumatoid arthritis, and autoimmune disease–associated.

CHIKV infection was diagnosed through the Reverse Transcription of the Polymerase Chain Reaction (RT-PCR), which amplifies the *E1* and *E2* gene regions of the virus. In addition, for the differential diagnosis, molecular tests were performed for the Dengue virus (DENV) and Mayaro virus

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(MAYV) and serological tests for DENV and hepatitis B and C, which presented negative results. Other complementary tests were requested according to Table 1. Along the first month after the onset of symptoms, there was exacerbation of polyarthralgia with the presence of distal edema, complaints of asthenia, and reduction of body weight. During this period, treatment with glucocorticoid was implemented. Methylprednisolone 20 mg/d was gradually reduced in the next 6 months.

In the second month of follow-up, there was persistence of arthralgia and the appearance of signs of sensorial abnormalities, such as decreased strength and sensitivity in upper and lower limbs (Fig. 2). Nerve conduction studies (NCS), which showed sensory-motor axonal pattern of peripheral polyneuropathy with decreased nerve conduction velocity and amplitude of the sensory nerve action potential in the right and left ulnar and median nerves, respectively, were requested for the right superficial fibular (Fig. 1A, B, C, D, F).

After the myography (Fig. 1G), no abnormalities were observed in the muscular points of the right and left anterior deltoid, right and left brachial biceps, right and left common hand extensor, right and left medial vast, right and left anterior tibial, and right and left medial gastrocnemius. It was observed a reduction of some potentials of motor unit action in the muscular points examined of the short abductor, right and left thumb, and first dorsal interosseous of the right and left hand. There was a moderate reduction of the motor unit action potentials in the muscular points examined of the right extensor of the right and left toes and abductor right hallux, with motor unit action potentials of increased amplitude and duration and increase of the proportion of polyphasic potentials without signs of denervation at rest.

Ultrasound of hands, wrists, feet, ankles, femoral, and shoulders and synovitis with bilateral joint effusion showed the presence of bilateral tendinopathy and periarticular edema. By following the development of neuropathy, the antimetabolite Methotrexate with dosage of 15 mg per week was associated with the treatment of symptoms, with an improvement in arthralgia and recovery of sensitivity and motor activity, resolving entirely in a period of 6 months.

Discussion

The neurological manifestations associated with the Chikungunya virus are important and less common, but they have later progression and are most serious in the elderly and newborn infants. The reported cases and the description of the clinical process suggest an increase in the neurovirulence of CHIKV (Brizzi 2017).

Mehta et al. (2018) described 865 cases of neurological disease associated with Chikungunya; one of the main indications was encephalopathy, responsible for 40.5% of the cases, and 13.4% of the patients were affected in the peripheral nervous system and 9.3% presented changes in the CNS and peripheral nervous system.

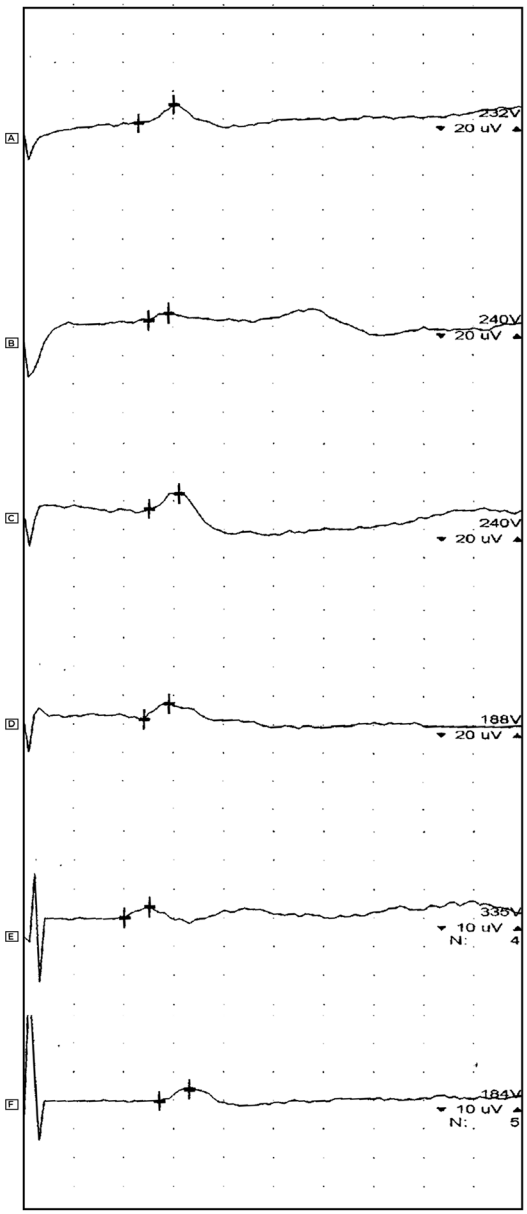
In the Americas, Bank et al. (2015) described a patient who had traveled to the Dominican Republic suffering from myeloradiculopathy after CHIKV infection. The patient fully recovered after 6 months but had persistent neuropathic pain. The authors associated this condition with a secondary immunomediated phenomenon rather than direct viral activity, proposing the use of immunotherapy to treat chronic neuropathic pain.

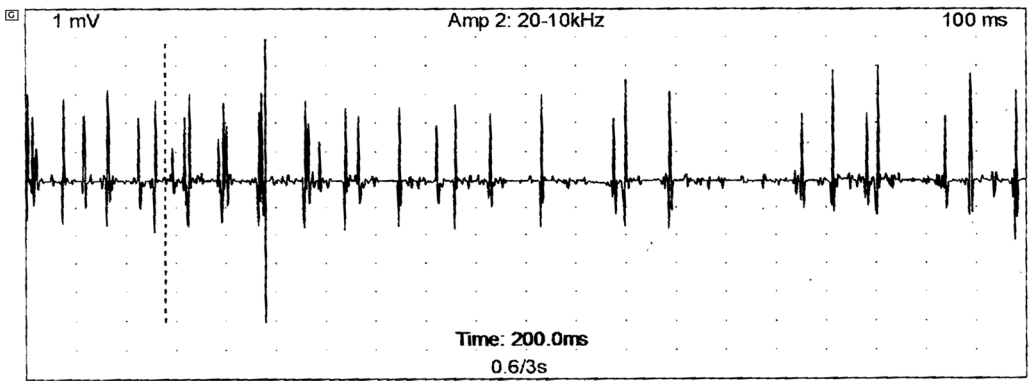
In this study, neurological complications were noted. The patient reported progressive weakness associated with loss of sensitivity in the distal limbs, besides a process of joint inflammation (Fig. 2). Peripheral axonal polyneuropathy was confirmed by means of nerve conduction studies (Fig. 1).

Table 1 Predictive laboratory results in the diagnosis of CHIKV infection

Parameter	July	August	September	December	February	March
Leucocyte (10^3 cell/mm^3)	2800	4400	7430	6954	5549	4680
Neutrophils (10^3 cell/mm^3)	1904	3344	6167	5145	3996	3323
Linphocyte (10^3 cell/mm^3)	700	924	892	1113	1110	1030
Platelet (10^3 cell/mm^3)	120,000	161,000	195,000	197,100	154,100	178,000
Creatinine (mg/dL)	Nt	0.77	0.70	0.77	0.82	0.9
Urea (mmol/L)	Nt	62	Nt	Nt	49	Nt
Creatine phosphokinase (U/L)	Nt	Nt	20	Nt	Nt	Nt
C-reactive protein mg/L	Nt	< 1.92	Nt	0.38	0.36	Nt
Oxalacetic transaminase (U/L)	Nt	19.2	Nt	Nt	18	Nt
Pyruvic transaminase (U/L)	Nt	13.3	Nt	Nt	17	Nt
Erythrocyte sedimentation rate mm/h	7.0	Nt	Nt	Nt	5.0	Nt

Nt not tested





Nerve conduction studies (motor)	
right median	
dCMAP (N > 4,0 μV)	8,7
DML (N < 4,4 ms)	3,3
NCV (elbow-wrist) (N > 49 m/s)	54,0
left ulnar nerve	
dCMAP (N > 6,0 μV)	6,6
DML (N < 3,3 ms)	2,5
NCV (elbow-wrist) (N > 49 m/s)	57,0
right superficial peroneal nerve	
dCMAP (N > 2,0 μV)	4,9
DML (N < 6,5 ms)	4,1
NCV (calf-ankle) (N > 44 m/s)	43,0
left sural nerve	
dCMAP (N > 2,0 μV)	2,3
DML (N < 6,5 ms)	4,2
NCV (calf-ankle) (N > 44 m/s)	47,0
Nerve conduction studies (sensory)	
right median	
Amplitude (N > 20,0 μV)	15,0
Latency (N < 3,5 ms)	2,3
Velocity (N > 50 m/s)	57,0
right ulnar nerve	
Amplitude (N > 17,0 μV)	5,0
Latency (N < 3,1 ms)	2,5
Velocity (N > 50 m/s)	44,0
left median nerve	
Amplitude (N > 20,0 μV)	11,0
Latency (N < 3,5 ms)	2,5
Velocity (N > 50 m/s)	52,0
left ulnar nerve	
Amplitude (N > 17,0 μV)	11,0
Latency (N < 3,1 ms)	2,4
Velocity (N > 50 m/s)	46,0
right superficial peroneal nerve	
Amplitude (N > 6,0 μV)	4,0
Latency (N < 4,4 ms)	2,0
Velocity (N > 40 m/s)	70,0
left sural nerve	
Amplitude (N > 6,0 μV)	4,0
Latency (N < 4,4 ms)	2,7
Velocity (N > 40 m/s)	52,0

Fig. 1 Representative tracing of nerve conduction studies. Reduced amplitude of sensory nerve action potential recorded from right median (A), right ulnar (B), left median (C), left ulnar (D), right superficial peroneal (E) and left sural (F) nerves, (G) volitional electromyography recorded from right extensor digitorum brevis muscle. Incomplete interference pattern with increased duration and amplitude of motor unit action potentials

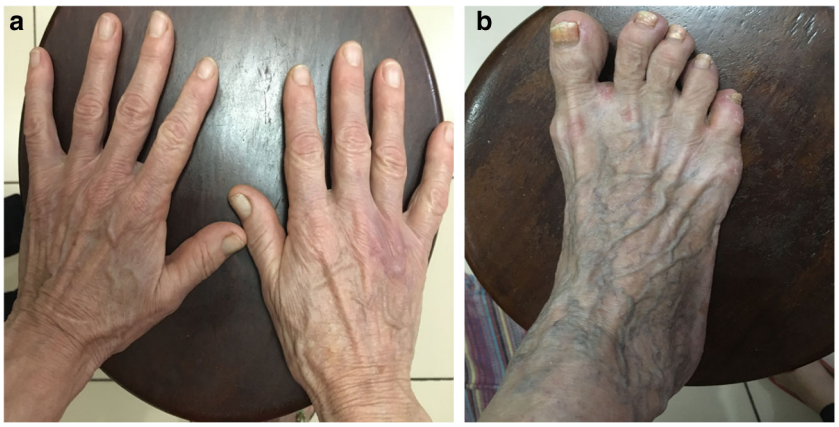


Fig. 2 Neuropathy characterized by motor alterations and muscular atrophy in symmetrical fists, hands, feet, and metacarpophalangeal joints

The autoimmune nature of some diseases observed in CHIKV infection is increasingly recognized. The virus may travel through many pathways, including retrograde axonal transport along motor neurons, and because of the molecular mimicry between pathogenic organisms and nerve cells, autoantibodies are formed, causing demyelination and deceleration of nerve conduction or action against gangliosides and Ranvier nodules, in turn, causing intermittent blocks of conduction, and as the condition progresses, persistent axonal damage (Ludlow et al. 2015; Cerny et al. 2017).

The ideal treatment is still under investigation. Various therapeutic options are being studied, such as known antimicrobial compounds, synthesis of specific compounds, nucleic acid–based antivirals, antibody therapy, and targeting host cell pathways (Powers 2017). The association of corticosteroids has benefited patients with musculoskeletal disorders associated with CHIKV, aiming to oppose the process by blocking the immune process (Chen et al. 2014).

The patient's satisfactory response to prednisolone corresponded to methotrexate, which acts by modulating the various aspects of immune and inflammatory responses, having as pathophysiological basis the situation in which it is linked to a T cell-mediated immune response and inflammatory cytokines.

We reinforce the need to investigate this emerging tendency of neuroinfections related to the CHIKV virus, through presentation of cases, randomized studies, and use of diagnostic methods that allow the early detection and prevention of neurological changes, supporting the implementation of treatment of the first chronic complications.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

Bank AM, Batra A, Colorado RA, Lyons JL (2015) Myeloradiculopathy associated with chikungunya virus infection. J Neurovirol 22(1): 125–128. https://doi.org/10.1007/s13365-015-0372-9

Brizzi K (2017) Neurologic manifestation of Chikungunya virus. Curr Infect Dis Rep 19(6). https://doi.org/10.1007/s11908-017-0561-1

Cerny T, Schwarz M, Schwarz U, Lemant J, Gérardin P, Keller E (2017) The range of neurological complications in Chikungunya fever. Neurocrit Care 27(3):447–457. https://doi.org/10.1007/s12028-017-0413-8

Chen W, Foo SS, Taylor A, Lulla A, Merits A, Hueston L, Forwood MR, Walsh NC, Sims NA, Herrero LJ, Mahalingam S (2014) Bindarit, an inhibitor of monocyte chemotactic protein synthesis, protects against bone loss induced by chikungunya virus infection. J Virol 89(1):581–593. https://doi.org/10.1128/JVI.02034-14

Fred A, Fianu A, Béral M, Guernier V, Sissoko D, Méchain M, Michault A, Boisson V, Gaüzère BA, Favier F, Malvy D, Gérardin P, SEROCHIK group (2018) Individual and contextual risk factors for chikungunya virus infection: the SEROCHIK cross-sectional population-based study. Epidemiol Infect 146(8):1056–1064. https://doi.org/10.1017/S0950268818000341

Hossain MS, Hasan MM, Islam MS, Islam S, Mozaffor M, Khan MAS, Ahmed N, Akhtar W, Chowdhury S, Arafat SMY, Khaleque MA, Khan ZJ, Dipta TF, Asna SMZH, Hossain MA, Aziz KS, Mosabbir AA, Raheem E (2018) Chikungunya outbreak (2017) in Bangladesh: clinical profile, economic impact and quality of life during the acute phase of the disease. PLoS Negl Trop Dis 12(6): e0006561. https://doi.org/10.1371/journal.pntd.0006561

Ludlow M, Kortekaas J, Herden C, Hoffmann B, Tappe D, Trebst C, Griffin DE, Brindle HE, Solomon T, Brown AS, van Riel D, Wolthers KC, Pajkrt D, Wohlsein P, Martina BEE, Baumgärtner W, Verjans GM, Osterhaus ADME (2015) Neurotropic virus infections as the cause of immediate and delayed neuropathology. Acta Neuropathol 131(2):159–184. https://doi.org/10.1007/s00401-015-1511-3

Mehta R, Gerardin P, de Brito C, Soares CN, Ferreira M, Solomon T (2018) The neurological complications of chikungunya virus: a systematic review. Rev Med Virol 28(3):e1978. https://doi.org/10.1002/rmv.1978

Peper SM, Monson BJ, Van Schooneveld T, Smith CJ (2016) That which bends up: a case report and literature review of Chikungunya virus. J Gen Intern Med 31(5):576–581. https://doi.org/10.1007/s11606-015-3459-3

Powers AM (2017) Vaccine and therapeutic options to control Chikungunya virus. Clin Microbiol Rev 31(1):e00104–e00116. https://doi.org/10.1128/CMR.00104-16

Scott SSO, Braga-Neto P, Pereira LP, Nóbrega PR, de Assis Aquino Gondim F, Dobreira-Neto MA, Schiavon CCM (2017) Immunoglobulin-responsive chikungunya encephalitis: two case reports. NeuroVirology 23(4):625–631. https://doi.org/10.1007/s13365-017-0535-y

Tanabe ISB, Tanabe ELL, Santos EC, Martins WV, Araujo IMTC, Cavalcante MCA, Lima ARV, Câmara NOS, Anderson L, Yunusov D, Bassi EJ (2018) Cellular and molecular imune respose to Chikungunya vírus infection. Front Cell Infect Microbiol 8:345. https://doi.org/10.3389/fcimb.2018.00345