

Clinical Case Reports

[Open Access](#)

Antisynthetase Syndrome after chikungunya infection: a case report

Journal:	<i>Clinical Case Reports</i>
Manuscript ID	Draft
Wiley - Manuscript type:	Case Report
Date Submitted by the Author:	n/a
Complete List of Authors:	Tuño, Raiza; Hucam, Reumatologia Macabú, Mariana; Hucam, Reumatologia Athayde, Paula; Hucam, Reumatologia Moulaz, Isac; Hucam, Reumatologia Dalmaso, Bárbara; Hucam, Reumatologia Valim, Valeria; Hucam, Reumatologia Machado, Ketty Lysie; Hucam, Reumatologia
Search Terms:	Infectious diseases
Abstract:	Chikungunya is an arboviral disease caused by a virus with wide geographical distribution in endemic areas. This case report documents a patient with Antisynthetase Syndrome post-chikungunya infection. Autoimmune diseases result from breakdown of immune tolerance. Among all triggers, viruses represent the greatest environmental potential to precipitate inflammatory myopathy.

Antisynthetase Syndrome after chikungunya infection: a case report

Raiza Cansian Tuão¹, Mariana de Oliveira Macabú², Paula dos Santos Athayde², Isac Ribeiro Moulaz², Barbara Ferraço Dalmaso¹, Valéria Valim Cristo³, Ketty Lysie Libardi Lira Machado³

¹Rheumatology Resident at Cassiano Antonio Moraes University Hospital – HUCAM / UFES

²Medical Student at Cassiano Antonio Moraes University Hospital – HUCAM / UFES

³Rheumatology Attending Physician at Cassiano Antonio Moraes University Hospital – HUCAM / UFES

ABSTRACT

Chikungunya is an arboviral disease caused by a virus with wide geographical distribution in endemic areas. This case report documents a patient with Antisynthetase Syndrome post-chikungunya infection. Autoimmune diseases result from breakdown of immune tolerance. Among all triggers, viruses represent the greatest environmental potential to precipitate inflammatory myopathy.

KEYWORDS:

Case report, Chikungunya virus, Myositis, Myopathy.

INTRODUCTION

Chikungunya virus (CHIKV) is an alphavirus endemic in Africa, Asia, and South America and can be found in tropical areas with seasonal characteristics, with outbreaks reported in several countries worldwide (1,2). Chikungunya presents a broad symptom spectrum, similar to other arboviroses, including fever, rash, myalgia, arthralgia, and headache (3). When duration of symptoms persists beyond three months it reaches the chronic phase, with persistence of arthritis and joint tenosynovitis (1).

CHIKV infection can be a trigger for onset of autoimmune diseases in genetically predisposed individuals (2). In this scenario, inflammatory myopathy is an extremely rare presentation of CHIKV scarcely described in the literature. This article aims to report a rare case of an antisynthetase syndrome (ASS) post-chikungunya infection, characterized by muscle weakness, interstitial lung disease, and positive anti-Jo-1.

CASE PRESENTATION

We report a 38-year-old female patient, previously healthy, presented with high fever, adynamia, diffuse myalgia, and polyarthralgia of hands, wrists, elbows, and knees. She sought medical attention and was diagnosed with CHIKV infection, confirmed by a positive IgM Enzyme-Linked Immunosorbent Assay (ELISA) serological study in two samples. Joint pain and myalgia persisted, and after two months, she presented progressive complaints of fatigue, difficulty combing her hair, walking, and getting out of bed. She had frequent falls, dysphagia for solids, dysphonia, dyspnea on mild exertion, and was bedridden. She was then admitted to the hospital for investigation.

On physical examination, she presented decreased proximal limb muscle strength, grade 2 in lower limbs and grade 3 in upper limbs, according to Medical Research Council (MRC) scale. Pulmonary auscultation presented fine bilateral basilar crackles. Manual muscle test (MMT) of 64 out of 150 points. Locomotor examination showed arthritis in knees and ankles bilaterally.

Complementary examinations revealed elevated creatine phosphokinase (CPK: 25150 U/L [VR: 0 A 170 U/L]) and increased transaminases (TGO: 377 U/L and TGP: 264 U/L [VR: 0 A 31 U/L]). Anti-Jo-1 antibody was reagent (141 U/mL [VR: reagent > 10 U/mL]). Antinuclear antibody (ANA) with a mixed pattern of 1/80 fine dotted nuclear type and 1/160 dotted

cytoplasmic type. Electroneuromyography of four limbs confirmed a pattern of myopathy, affecting mostly proximal muscles. Magnetic resonance imaging (MRI) of thighs showed diffuse edema of muscles, without areas of liposubstitution, suggesting an acute inflammatory process (Figures 1 and 2). Chest computed tomography (CT) scan showed ground-glass opacities in bases up to the middle third of lungs, compatible with nonspecific interstitial pneumopathy (NSIP).

The diagnosis of Antisynthetase Syndrome, an immune-mediated inflammatory myopathy, post-Chikungunya infection, was then established. The patient presented with a compatible clinical, with proximal muscle weakness in all four limbs, MRI of thighs showing a muscular inflammatory process, electroneuromyography with a myopathic pattern, interstitial pneumopathy, and a positive Anti-Jo1 antibody, in addition to joint involvement.

Other etiological causes were investigated and ruled out, such as viral infections by hepatitis virus, cytomegalovirus, HIV, syphilis, and COVID-19, metabolic disorders, use of previous medications, and screening for neoplasms, confirming chikungunya as the trigger for myopathy.

Pulse therapy was started with methylprednisolone for 3 days and human immunoglobulin for 6 monthly cycles. The patient had clinical recovery and a gradual decrease in muscle enzymes, reaching 257 U/L (VR: 0 to 170 U/L) after 6 months. She was also given monthly intravenous cyclophosphamide for a period of 6 months due to pulmonary involvement. The patient maintained motor and respiratory physical therapy, evolving with grade V muscle strength in the four limbs, with no complaints of fatigue, dysphagia, or dysphonia.

Figure 1: A) Coronal T1 (hip and thigh images): absence of muscle liposubstitution. B) Coronal T2 with fat saturation (SPAIR technique): Diffuse muscular edema affecting the pelvic girdles and thighs.

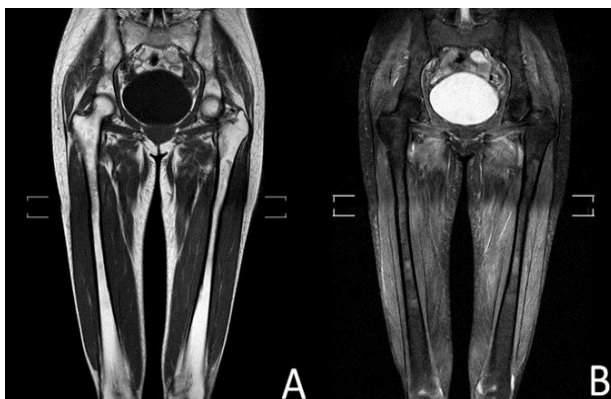
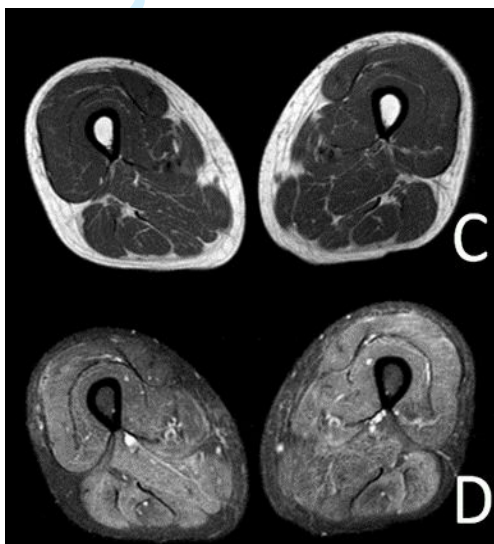


Figure 2: C) Axial T1: mild muscle volume reduction, with no evidence of liposubstitution. D) Axial T2 with fat saturation (SPAIR technique): diffuse edema of musculature of the anterior, posterior and medial compartments.



DISCUSSION

Chikungunya is an arboviral disease caused by an RNA virus with wide geographical distribution in endemic areas, and other tropical areas with seasonal characteristics that are favorable to development of disease vectors (*Aedes aegypti* and *Aedes albopictus*) (4). The chance of large outbreaks of CHIKV worldwide is high, especially in developing countries due

to abundance of vectors (5). In 2007, an infected tourist from India introduced chikungunya to northern Italy, resulting in the identification of 292 suspected cases (6).

Chikungunya is self-limited and has a broad clinical spectrum, being characterized by a characteristic triad consisting of fever, arthralgia, and rash (5). The clinical course of the disease can be divided into acute and chronic phases. In acute phase, there may be fever, symmetrical polyarthralgia, headache, nausea, vomiting, fatigue, and myalgia. Arthralgia affects large and small joints and preferentially involves more distal regions such as ankles, wrists, and phalanges (4). Joint pain may persist, characterizing onset of chronic phase, which lasts for 12 weeks to years (4). The prevalence of chronic phase is highly variable and may affect more than half of the patients (1). Complications of cardiovascular, renal, respiratory, hepatic, gastrointestinal and adrenal systems are associated with the infection and are referred to as atypical features (3).

In addition, CHIKV, like other viruses, can act as a trigger for autoimmune diseases, among them, autoimmune inflammatory myopathies, a group of diseases characterized by presence of inflammation of skeletal muscle and subdivided into Dermatomyositis (DM), Polymyositis (PM), Necrotizing Autoimmune Myopathy (MAN), Inclusion Corpuscle Myopathy (ICM) and Anti-synthetase Syndrome (SAS), according to clinical, histological, immunopathological and autoantibody characteristics (7).

Autoimmune diseases are the result of hyperstimulation of immunity, caused by breakdown of immune tolerance, which has a multifactorial etiology. Among all potential triggers for development of autoimmune diseases, viruses represent the greatest environmental potential to trigger inflammatory myopathy (IM) in genetically susceptible individuals. Inflammatory myopathy has been observed during or after viral infection, but attempts to

amplify viruses from muscles, including coxsackievirus, influenza, paramyxovirus, mumps, cytomegalovirus, and Epstein-Barr virus have failed. The best studied viral relationship so far has been with retrovirus (7). However, there are fewer case reports in the literature highlighting association of CHIKV with the development of autoimmune diseases, especially inflammatory myopathies (5,8).

Dev, et al (2019), reported a case of inflammatory myositis following Chikungunya infection in 2019 in India (8). Martins, et al (2016), reported a case of a patient presenting with myositis and encephalitis post-CHIKV infection in Brazil (5). However, this is the first case of antisynthetase syndrome post-chikungunya infection characterized in literature.

There are possible hypothesized mechanisms for development of post-infection-induced autoimmune disease. Autoreactive T cells can be activated by cross-linking with a viral antigen that bears similarity to autoantigen, and become pathogenic. Stimulation of Toll-like receptors and other pattern-recognition receptors on antigen-presenting cells leads to production of pro-inflammatory mediators, which can trigger tissue damage. Tissue destruction by T-cells and inflammatory mediators further increase release of autoantigens, potentiating the immune response (2).

Another possible mechanism is the evasion of host's innate and adaptive immune responses by the virus, as seen in mice showing a chronic inflammatory process in ankles after inoculation with CHIKV RNA and persistence of the virus in the local tissue. Furthermore, several alphaviruses, including CHIKV, have been shown to antagonize STAT activation by type I and type II interferon (9).

ASS is a rare disease with unknown incidence and a prevalence twice higher in females. It presents a broad clinical picture, with proximal muscle weakness, arthritis, arthralgia,

Raynaud's phenomenon, fever, "mechanic's hands" and interstitial lung disease. It is related to presence of anti-synthetase autoantibodies, especially anti-Jo-1, and to histological presentation of perimysial and perifascicular muscle fiber necrosis. Pulmonary involvement is related to high morbidity and mortality rates, especially interstitial lung disease (ILD), which can present with dyspnea, cough, and chest pain (7).

In this case, the patient presented with proximal muscle weakness in all four limbs, MRI of thighs showing a muscular inflammatory process, electroneuromyography with a myopathic pattern, interstitial pneumopathy, and a reagent Anti-Jo1 antibody, in addition to joint involvement. The case report presented some limitations, such as the fact that the patient did not perform a muscle biopsy, due to lack of availability of the procedure at the service. The patient also did not present mechanic's hands, a classic but not specific sign (10).

CONCLUSION

More studies are needed to highlight and detail the pathophysiology of CHIKV in development of autoimmune diseases in genetically susceptible individuals, as well as its diverse clinical presentations. It is known that viral infections can be triggers for inflammatory myopathies and therefore attention should be given to patients who persist with muscle weakness and myalgia after a Chikungunya infection.

ACKNOWLEDGMENT

No acknowledgments to be made.

CONFLICT OF INTEREST

No conflict of interest.

AUTHOR CONTRIBUTIONS

Raiza Cansian Tuão and Ketty Lysie Libardi Lira Machado: conceptualized the study, wrote, revised and edited the manuscript, analyzed and interpreted the muscle magnetic resonance images. Mariana de Oliveira Macabú, Paula dos Santos Athayde, Isac Ribeiro Moulaz and Barbara Ferraço Dalmaso: wrote, revised and edited the manuscript. Valéria Valim Cristo conceptualized and revised the manuscript. All authors were involved in editing and approving the manuscript.

ETHICAL APPROVAL

This case report was carried out following the recommendations of the ethics committee of the Cassiano Antonio Moraes University Hospital - HUCAM, Brazil.

CONSENT

Written informed consent was obtained from the patient for the publication of this case report.

DATA AVAILABILITY STATEMENT

All data included in this report are accurate to the best of our knowledge. We will make available data (images and reports) upon request.

ORCID

Raiza Cansian Tuão <https://orcid.org/0000-0003-3002-3185>

REFERENCES

- 1 – Ministério da Saúde, Brazil: Chikungunya clinical management. Brasília: 2017; 1: 1-67. https://bvsmms.saude.gov.br/bvs/publicacoes/chikungunya_manejo_clinico.pdf. Accessed October 10, 2021.
- 2 - Getts MT, Miller SD: 99th Dahlem conference on infection, inflammation and chronic inflammatory disorders: triggering of autoimmune diseases by infections. Clin. exp. immunol. 2010; 160: 15-21.

- 3- Vairo F, Haider N, Kock R, Ntoumi F, Ippolito G, Zumla A: Chikungunya: Epidemiology, Pathogenesis, Clinical Features, Management, and Prevention. *Infect Dis Clin North Am.* 2019; 33: 1003-25.
- 4- Castro APCR, Lima RAN, Santos J: Chikungunya: vision of the pain clinician. *Revista Dor (online)* 2016; 17: 299-302.
- 5- Martins HA, Bernardino SN, Santos CC, Ribas VR: Chikungunya and Myositis: A Case Report in Brazil. *J Clin Diagn Res* 2016; 10: OD05-06.
- 6- Choudhary N, Makhija P, Puri V, Khwaja GA, Duggal A: An Unusual Case of Myelitis with Myositis. *J Clin Diagn Res* 2016; 10: OD19-20.
- 7- Dalakas MC: Inflammatory myopathies: update on diagnosis, pathogenesis and therapies, and COVID-19-related implications. *Acta myol* 2020; 39: 289-301.
- 8- Dev N, Kumar R, Gogna A, Sharma S: Chikungunya-induced inflammatory myositis: a case report in India. *Trop Doct* 2019; 49: 241-3.
- 9 - Morrison TE, Oko L, Montgomery SA, et al.: A mouse model of chikungunya virus-induced musculoskeletal inflammatory disease: evidence of arthritis, tenosynovitis, myositis, and persistence. *Am J Pathol* 2011; 178: 32-40.
10. Carboni RCS, Pinto GLB, Shinjo SK. High YKL-40 serum levels and its expression in the muscle tissues of patients with antisynthetase syndrome. *Adv. Rheumatol* 2021; 61:44.