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Parkinsonian syndrome after chikungunya: A case study

Adalgiza Mafra Moreno, Jacqueline Fernandes Nascimento, Luciana Armada, Marco Orsini, Marília Salete Tavares, Antonio Marcos da Silva Catharino

ABSTRACT

Introduction: Although fever and malaise are the most common symptoms, the chikungunya virus can cause long-term chronic complications. Among the serious conditions arising from the pathology, certain patients have been observed to have neurological symptomatology, including parkinsonian. The onset of Parkinson's disease is marked by a progressive degeneration of the neurons that produce the neurotransmitter dopamine, which are related to the mastery over body movements.

Case Report: A 46-year-old woman with a previous history of chikungunya virus infection, sought neurological care complaining of a "problem at her arm." Neurological examination revealed a rigid-akinetic component that has improved with the use of Levodopa.

Conclusion: It was observed with this case study that neurological manifestations of post-chikungunya virus are presented in the clinical case, including worsening of parkinsonian symptoms. The use of the Levodopa over a period of six months was effective in reducing the symptoms reported by the patient.

Keywords: Chikungunya, Levodopa, Parkinson's disease, Parkinsonian syndrome

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INTRODUCTION

Chikungunya is an arbovirus transmitted by bites from the *Aedes aegypti* mosquito or ticks that result in deforming sequelae. Fever and malaise are the most common symptoms, however, the chikungunya virus can cause chronic complications such as arthralgia. However, this is not the only possibility of sequelae. Among the severe conditions arising from the condition, certain patients have been observed to have neurological symptoms, including parkinsonian symptoms [1].

Parkinson's disease has a globally estimated prevalence of about 1–3% of the population over 60 years of age, and is prevalent in males. It is marked by the progressive degeneration of the neurons that produce the neurotransmitter dopamine, closely related to the control of body movements [2, 3].

Contrary to popular belief, parkinsonian syndrome and Parkinson's disease (PD) are two distinct conditions. Research indicates that there are two types of Parkinson's, body-first and brain-first, respectively, since PD begins with the loss of the ability to produce dopamine in the brain. This substance is related to different functions and its deficiency translates into symptoms, such as: involuntary tremor at rest, rigidity, postural instability, and bradykinesia [3, 4].

The parkinsonian syndrome or parkinsonism is a term used to classify a large number of diseases of different causes, which encompass common symptoms

of parkinsonism, such as tremor, bradykinesia, and rigidity. Parkinson's disease is one of the most frequent manifestations of the parkinsonian syndrome with 75% incidence among all forms of parkinsonism. Overall, consideration of the clinical signs, monitoring from the onset of the disease, and the nature of the progression are important for an accurate diagnosis [3].

Parkinsonian syndromes can occur as a side effect of medications that block dopamine activity in the brain, such as antipsychotics, by poisoning by heavy metals and degenerative and viral diseases [5–7], which justifies the reason for this study. Thus, the objective of this paper is to describe the clinical case of a patient diagnosed with parkinsonian syndrome after infection by chikungunya.

CASE REPORT

A 46-year-old woman sought neurological care in August 2020, presenting as main complaint: "arm with problem." She reported having chikungunya two years ago. She also reported that since then she has had hemiparesis in the right side, with progressive worsening since February 2020. The clinical examination revealed a hemiparetic gait on the left with spasticity, asymmetrical reflexes, more noticeable on the right, with a rigid-akinetic component and asymmetrical bilateral palmomental reflex.

An electroencephalogram was performed, which presented nonspecific results. Densitometry and thyroid examination were normal. Skull magnetic resonance imaging (MRI) performed by the patient in November 2019, showed foci of microangiopathy, without other changes, cervical MRI with small disc protrusion C5–C6 and C6–C7 and normal spinal cord. Thoracic MRI was without hernias.

Skull scintigraphy using TRODAT showed marked nigrostriatal dopaminergic dysfunction (Figure 1).

The cerebrospinal fluid (CSF) examination revealed: blood-brain barrier dysfunction; presence of type 2 oligoclonal bands with intrathecal IgG synthesis; protein-cytological dissociation with intrathecal IgG immunoliberation profile.

Serologic tests: Herpes IgG 23.4—reference <0.9; and IgM 1.38—reference <0.9; HIV: negative; human T-lymphotropic virus (HTLV): negative; Syphilis: negative.

Genetic evaluation identified in DNAJC6 a variant of uncertain significance. The DNAJC gene is associated with autosomal recessive juvenile onset PD (PARK19) (MedGen UID: 316141). In LRRK2, a variant of uncertain significance had also been identified. The LRRK2 gene is associated with autosomal dominant PD 3 (PARK3) (MedGen UiD: 339628). A variant of uncertain significance was identified in SLC6A3. The SLC6A3 gene is associated with autosomal recessive childhood parkinsonism and dystonia 1 (PKDYS1) (MedGen UID: 1648442) (Figure 2).

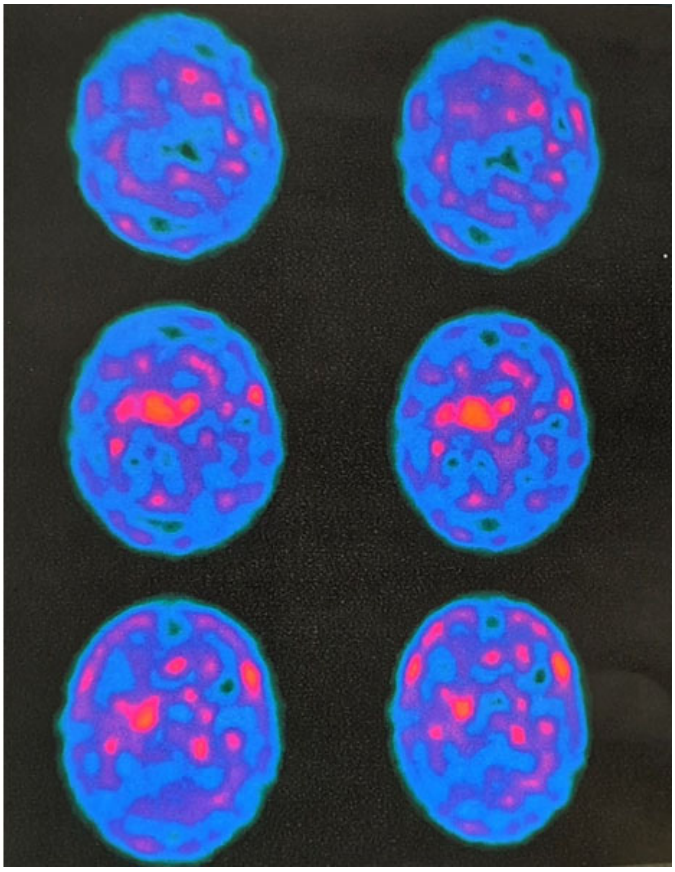

Figure 1: Skull scintigraphy with marked nigrostriatal dopaminergic dysfunction.

Variant(s) of Uncertain Significance identified.

GENE	VARIANT	ZYGOSITY	VARIANT CLASSIFICATION
DNAJC6	c.1113G>A (Silent)	heterozygous	Uncertain Significance
LRRK2	c.3823G>A (p.Val1275Ile)	heterozygous	Uncertain Significance
SETX	c.2471A>G (p.Tyr824Cys)	heterozygous	Uncertain Significance
SLC6A3	c.1676C>T (p.Ala559Val)	heterozygous	Uncertain Significance

About this test

This diagnostic test evaluates 66 gene(s) for variants (genetic changes) that are associated with genetic disorders. Diagnostic genetic testing, when combined with family history and other medical results, may provide information to clarify individual risk, support a clinical diagnosis, and assist with the development of a personalized treatment and management strategy.

Figure 2: Genetic test.

Treatment was proposed with the use of Levodopa/benserazide 100/25 mg twice a day. A month after starting treatment the patient reported improved gait patterns with the use of Levodopa, while maintaining a component of stiffness. The dose of Levodopa was increased to 4 times a day. In February 2021, the patient reported an improvement with dopamine replacement through the administration of Levodopa, with an improvement in hemiparetic gait, no spasticity, symmetrical reflexes, improvement of the rigid-kinetic component, no longer being observed stiffness, bilateral palmomentonian, and slight tremor in the right hand.

At the present date, the patient continues to use Levodopa. In May 2021, she remained stable with mild stiffness on the right side, and was advised to reduce the use of Levodopa for evaluation. In June 2021, the

patient presented joint pain after reducing the use of Levodopa, which persisted for two weeks. She returned to medication with partial improvement and slight dyskinetic movements in the right upper limb and jaw. In September 2021, the use of Levodopa was reduced to 3 times a day without worsening of the condition.

After six months of treatment, the drug therapy used proved to be efficient in reducing the symptoms. The patient continues to present slight rigidity and bradykinesia in the right upper limb, and no longer presents pyramidal signs. Treatment with Pramipexol 0.375 mg once a day was initiated.

DISCUSSION

Dopaminergic neuronal loss in PD is accompanied by inflammatory processes and changes in microglia, astrocytes, innate immune cells, and infiltrating peripheral immune cells [8].

Several studies state that the development of PD can be caused directly by the invasion of the central nervous system by specific viral pathogens or indirectly through the host response to infection [9–11].

In 1991, Giraldi et al. [9] reported the case of a 60-year-old woman who developed a complete and unaltered parkinsonian syndrome four months after the onset of a viral meningoencephalitis. Viral surveys performed on the patient showed an increase in anticytomegalovirus (anti-CMV) antibodies, mainly in the cerebrospinal fluid.

In a recent paper, Schultz et al. (2021) [12] presented a detailed study that evaluated brain organoids from a non-Parkinson's and Parkinson's patient infected with the chikungunya virus. Both were observed for two weeks. The Parkinson's organoids lost mass and exhibited a different antiviral response than the non-Parkinson's organoids. Neurotransmission data from infected Parkinson's and non-Parkinson's organoids showed downregulation of IL-1, IL-10, and IL-6 and were associated with mood and contributed to the depression seen in patients after chikungunya infection. Both organoid types had increased expression of CXCL10, which is linked to demyelination.

The available results are insufficient to determine the role of the identified variants in the presented disease, because not all variants present in a gene cause disease. However, the mutations presented are of genes linked to parkinsonism.

CONCLUSION

Neuroinflammation plays an important role in the cause and effect relationship in the dopaminergic neuronal loss of Parkinson's disease. In this sense, this neuroinflammation can be triggered directly by the invasion of the central nervous system by viral pathogens as in the reported case, an infection caused by the chikungunya virus.

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Author Contributions

Adalgiza Mafra Moreno – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Jacqueline Fernandes Nascimento – Analysis of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Luciana Armada – Acquisition of data, Analysis of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Marco Orsini – Acquisition of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Antonio Marcos da Silva Catharino – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission
The corresponding author is the guarantor of submission.

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Conflict of Interest
Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.