**Name of Journal:** *World Journal of Clinical Cases*

**Manuscript NO:** 70711

**Manuscript Type:** LETTER TO THE EDITOR

**Rituximab as a treatment for human immunodeficiency virus-associated nemaline myopathy: What does the literature have to tell us?**

Gonçalves Júnior J *et al*. Rituximab as a treatment for HIV-NM

Jucier Gonçalves Júnior, Samuel Katsuyuki Shinjo

**Jucier Gonçalves Júnior, Samuel Katsuyuki Shinjo,** Division of Rheumatology, São Paulo University, São Paulo 01246-903, Brazil

**Author contributions:** The authors contributed equally to all aspects of this manuscript preparation and have read and approved the final manuscript; Each author meets the criteria for authorship established by the International Committee of Medical Journal Editors.

**Corresponding author: Jucier Gonçalves Júnior, MD, Academic Research,** Division of Rheumatology, São Paulo University, Av. Dr. Arnaldo 3184, 3º Andar-Sala 3131 Cerqueira César, São Paulo 01246-903, Brazil. juciergjunior@hotmail.com

**Received:** August 12, 2021

**Revised:** November 13, 2021

**Accepted: December 31, 2021**

**Published online:**

**Abstract**

We presented a letter about a case of a 37-year-old Black female with a history of human immunodeficiency virus and an undetectable viral load. She was evaluated with weakness in the scapular (grade III) and pelvic girdles (grade II), elevation of creatine phosphokinase levels and muscle biopsy compatible with nemaline myopathy. She was treated with rituximab showing improvement of the condition.

**Key Words:** Human immunodeficiency virus; Nemaline myopathy; Rituximab; Rheumatology; Therapy; Case report

Gonçalves Júnior J, Shinjo SK. Rituximab as a treatment for human immunodeficiency virus-associated nemaline myopathy: What does the literature have to tell us? *World J Clin Cases* 2022; In press

**Core Tip:** Rituximab may be a therapeutic possibility for the treatment of nemaline myopathies (*e.g.*, human immunodeficiency virus-associated and monoclonal gammopathy of undetermined significance-associated) because it is less aggressive and has fewer side effects compared to current therapies. It may be especially helpful in cases of severe visceral involvement. However, the cost and unavailability of therapy can be a limiting factor.

**TO THE EDITOR**

We read the paper of Professors Wang and Hu[1] who presented a case report about nemaline myopathy (NM) with dilated cardiomyopathy. The authors aimed to describe a rare myopathy with severe cardiovascular impairment and whose outcome was positive.

We would like to present a case of human immunodeficiency virus (HIV)-associated NM (HIV-NM), and it responded to rituximab treatment.

The case involves a 37-year-old Black female with a history of HIV and an undetectable viral load with regular use of dolutegravir, darunavir and ritonavir. Six years ago, the patient started to present objective muscle weakness in all four limbs, in addition to increased muscle enzymes and electroneuromyography with evidence of a myopathic pattern. With the initial hypothesis of polymyositis, the patient received prednisone (1 mg/kg/d) with partial improvement of clinical and laboratory status. The patient was admitted to our service for a clinical reassessment and follow-up 3 years ago. The patient had an undetectable viral load, normal protein electrophoresis and serum levels of creatine phosphokinase at 2550 U/L using methotrexate 25 mg/wk and prednisone 5 mg/d.

She had weakness in the scapular (grade III) and pelvic girdles (grade II), required a wheelchair for locomotion and showed muscle magnetic resonance with evidence of symmetrical and bilateral muscle edema in the muscular bellies of the pelvic girdle and thighs. A muscle biopsy showed a myopathic and dystrophic patterns with the presence of marginal vacuoles with nemaline rods. Regarding the possibility of HIV-NM, methylprednisolone pulse therapy 3 g was started in one dose, and immunosuppressive drugs (azathioprine 300 mg/d, methotrexate 20 mg/wk and prednisone 20 mg/d) of previous use were maintained without significant improvement. Due to refractory disease and despite off-label, the patient consented to introduce rituximab 2 g/cycle as a possible option to promote disease induction.

The patient had progressive improvement. After two rituximab cycles, there was an important improvement in muscle weakness (lower limbs grade III and upper limbs grade IV) and independence for basic activities of daily living and a drop in creatine phosphokinase (275 U/L).

According to the literature, HIV-NM usually has a good response to immunosuppressive therapy[2-4]. A case report of a 65-year-old woman with severe cardiomyopathy and NM was recently described, in which the treatment was clinical compensation for cardiomyopathy associated with autologous stem cell transplantation[4]. A German cohort demonstrated that the most effective treatment strategy in NM was autologous bone marrow transplantation, but the one performed was immunosuppression with glucocorticoids (62%)[3]. Thus, in severe cases such as the one presented by the authors[1], we ask ourselves if the use of rituximab could not be an option as a way to delay the evolution of the NM.

Among the postulated theories, two stand out: (1) HIV should result in the formation of rods and/or serve as a trigger for the immune system to destroy muscle fibers; and (2) Genetic disorders caused by HIV cause rod formation[3]. In this context, therapy with rituximab may be an interesting treatment option in NM because: (1) Recent studies have shown improvement in the weakness of rituximab with no side effects obtained; (2) Lymphocytic infiltrates in muscles of NM patients are commonly confused with polymyositis; and (3) Limited effects with treatment[5].

Another interesting point to remember is that NM is often associated with monoclonal gammopathy of undetermined significance in case series[6], retrospective studies[7] and cohorts[3], denoting exacerbated lymphocyte activity. The cause for this association, as well as for the association of NM with HIV, is still unknown. However, the good response of this pathology to immunosuppressive therapies[2-4] and bone marrow transplantation[4] denote that options, such as rituximab, with fewer side effects, better dosage comorbidity and lower risks may be a real therapeutic possibility. Even more aggressive treatment regimens such as associations with dexamethasone, thalidomide and cyclophosphamide have already been proposed[8].

Finally, we emphasize that these treatment modalities might be used as an optional treatment to the autologous stem cell transplantation or before that. However, despite the rarity of the disease, further studies with a higher number of patients and adequate follow-up are required.

**REFERENCES**

1 **Wang Q**, Hu F. Nemaline myopathy with dilated cardiomyopathy and severe heart failure: A case report. *World J Clin Cases* 2021; **9**: 2569-2575 [PMID: 33889622 DOI: 10.12998/wjcc.v9.i11.2569]

2 **Naddaf E,** Milone M, Kansagra A, Buadi F, Kourelis T. Sporadic late-onset nemaline myopathy: Clinical spectrum, survival, and treatment outcomes. *Neurology* 2019; **93:** e298-e305 [PMID: 31167932 DOI: 10.1212/WNL.0000000000007777]

3 **Schnitzler LJ**, Schreckenbach T, Nadaj-Pakleza A, Stenzel W, Rushing EJ, Van Damme P, Ferbert A, Petri S, Hartmann C, Bornemann A, Meisel A, Petersen JA, Tousseyn T, Thal DR, Reimann J, De Jonghe P, Martin JJ, Van den Bergh PY, Schulz JB, Weis J, Claeys KG. Sporadic late-onset nemaline myopathy: clinico-pathological characteristics and review of 76 cases. *Orphanet J Rare Dis* 2017; **12**: 86 [PMID: 28490364 DOI: 10.1186/s13023-017-0640-2]

4 **Turnquist C**, Grogono JC, Hofer M, Pitcher A. Sporadic late-onset nemaline myopathy: a case report of a treatable cause of cardiac failure. *Eur Heart J Case Rep* 2021; **5**: ytaa480 [PMID: 33554019 DOI: 10.1093/ehjcr/ytaa480]

5 **Lerario A**, Cogiamanian F, Marchesi C, Belicchi M, Bresolin N, Porretti L, Torrente Y. Effects of rituximab in two patients with dysferlin-deficient muscular dystrophy. *BMC Musculoskelet Disord* 2010; **11**: 157 [PMID: 20618995 DOI: 10.1186/1471-2474-11-157]

6 **Okhovat AA,** Nilipour Y, Boostani R, Vahabizad F, Najmi S, Nafissi S, Fatehi F. Sporadic late-onset nemaline myopathy with monoclonal gammopathy of undetermined significance: Report of four patients. *Neuromuscul Disord* 2021; **31:** 29-34 [PMID: 33308940 DOI: 10.1016/j.nmd.2020.11.004]

7 **Finsterer J**, Stöllberger C. Review of Cardiac Disease in Nemaline Myopathy. *Pediatr Neurol* 2015; **53**: 473-477 [PMID: 26507755 DOI: 10.1016/j.pediatrneurol.2015.08.014]

8 **Kumutpongpanich T**, Owattanapanich W, Tanboon J, Nishino I, Boonyapisit K. Sporadic late-onset nemaline myopathy with monoclonal gammopathy of undetermined significance (SLONM-MGUS): An alternative treatment using cyclophosphamide-thalidomide-dexamethasone (CTD) regimen. *Neuromuscul Disord* 2018; **28**: 610-613 [PMID: 29910095 DOI: 10.1016/j.nmd.2018.04.011]

**Footnotes**

**Conflict-of-interest statement:** The author declare they do not have conflict of interest.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

**Provenance and peer review:** Invited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review started:** August 12, 2021

**First decision:** October 20, 2021

**Article in press:**

**Specialty type:** Medicine, research and experimental

**Country/Territory of origin:** Brazil

**Peer-review report’s scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): 0

Grade C (Good): 0

Grade D (Fair): D, D

Grade E (Poor): 0

**P-Reviewer:** Liu L **S-Editor:** Fan JR **L-Editor:** Filipodia **P-Editor:** Fan JR