Innovative Journal of Medical and Health Science

IJMHS 10 (06), 912–913 (2020) ISSN (O) 2277:4939 | (P) 2589:9341

Rituximab in MUSK-positive myasthenia: only choice without alternative?

Josef Finsterer, MD, PhD[⋆,†,1], Carla A. Scorza[2], Ana C Fiorini, MD[3], Fulvio A. Scorza, MD[4], Ritwik Ghosh, MD[5]

[1] *Krankenanstalt Rudolfstiftung, Vienna, Austria.*
[2] *Disciplina de Neurociência. Escola Paulista de Medicina/Universidade Federal de São Paulo/. (EPM/UNIFESP). São Paulo, Brasil*
[3] *Programa de Estudos Pós-Graduado em Fonoaudiologia. Pontifícia Universidade Católica de São Paulo (PUC-SP). Departamento de Fonoaudiologia. Escola Paulista de Medicina/Universidade Federal de São Paulo (EPM/UNIFESP). São Paulo, Brasil*
[4] *Disciplina de Neurociência. Escola Paulista de Medicina/Universidade Federal de São Paulo/. (EPM/UNIFESP). São Paulo, Brasil*
[5] *Department of General Medicine, Burdwan Medical College & Hospital, Burdwan, West Bengal, India.*

DOI: https://doi.org/10.15520/ijmhs.v10i03.289

Accepted 01/06/2020; Received 25/05/2020; Publish Online 06/06/2020

Reviewed By: Dr Daniel V.
Department: Medical

Key words: myasthenia–antibodies–immunosuppression–outcome–rituximab–anti—USK

1 LETTER TO THE EDITOR

With interest we read the article by Sachdeva et al. about a study of six Indian patients with anti-muscle-specific tyrosine kinase (MUSK) antibody-positive myasthenia gravis who all profited from rituximab in monotherapy over a period of 8-24 months without side effects after treatment with steroids, azathioprine, mycofenolate mofetil, cyclophosphamide, intravenous immunoglobulins or plasma exchange, failed to be effective [1]. The authors concluded that rituximab is an effective immune-modulatory therapy for MUSK antibody-positive myasthenia gravis patients who were non-responsive to standard treatment. We have the following comments and concerns.

According to table 1 in the report by Sachdeva et al., none of the six included patients, aged 32-58y, was reported to have developed side effects during a follow-up period of 8-24 months [1]. Since rituximab is well-known for various side effects in various systems (table 1), we should know if the six patients were asked for possible side effects and prospectively investigated for them. Side effects of rituximab previously reported include neuropathy, urinary or bronchial infections, headache, gastrointestinal complaints, acute thrombocytopenia, hypogammaglobulinemia, leukopenia, ototoxicity, and several others (table 1).

All patients were reported anti-MUSK antibody positive [1]. However, no anti-MUSK antibody titers were provided. It would be interesting to know these serum titers prior to starting rituximab and at the last follow-up. It would be particularly interesting to know if rituximab had a lowering effect on the anti-MUSK antibody titers or not. We also should know if clinical improvement correlated with the serum antibody levels. It should be also reported if effectiveness of rituximab could be documented by the disappearance of the initially abnormal decrement and if responsiveness of rituximab was documented by a decrease of the CD19 and CD20 cells [2].

There are several reports showing that steroids [3], azathioprine [4], or mycophenolate mofetil [3], can be effective in anti-MUSK antibody positive myasthenia. The authors should discuss why the six included patients did not respond or poorly responded to any of the standard therapies.

It is unclear why the six patients were not immediately tested for anti-MUSK antibodies after they have been shown to be negative for acetyl-choline receptor antibodies.

We should know why in patients 5 and 6 only steroids, plasma exchange, and immunoglobuline but no azatioprin, mycofenolate mofetil, or cyclosporine were tried.

Further limitations of the study are that only 6 patients were included, that the effect of rituximab in anti-MUSK antibody positive patients is already known, and that is unclear if the authors reported all their anti-MUSK antibody positive patients or only those who responded favourably to rituximab. The authors should report the total number of their anti-MUSK antibody positive patients and if they also manage anti-MUSK antibody positive patients which

⋆ Corresponding author.
† Email: fifigs1@yahoo.de.

did not respond to rituximab, as has been previously reported [5]. In this line, we should know if the authors recommend rituximab as first l ine t reatment o f anti-MUSK antibody positive patients or not.

Overall, the interesting study by Sachdeva et al. shows that rituximab may have a beneficial effect in therapy-resistant anti-MUSK antibody myasthenia but has some limitations, which need to be addressed before final conclusions can be drawn. The absence of side effects must be explained, serum titers of anti-MUSK antibodies should be provided, reasons for treatment failure with standard drugs should be put forward, the total number of their anti-MUSK antibody positive patients should be provided, and the delay of anti-MUSK antibody testing should be explained.

Organ	Side effect	Reference
Brain	Headache	[de Carmago et al. 2019]
Brain	PML	[Sachdeva et al. 2020]
Nerves	Neuropathy	[Maisons et al. 2020, Green 2019]
Ears	Hypoacusis	[Barbieri et al. 2019]
Heart	Hypotension	[D'Arena et al. 2017]
Lungs	Infection	[Lu Q et al. 2020]
Lungs	Dyspnoea, cough	[D'Arena et al. 2017]
Lungs	Bronchospasm	[D'Arena et al. 2017]
Intestines	GI complaints	[de Carmago et al. 2019]
Intestines	Bowel perforation	[Sullivan et al. 2018]
Intestines	Vomiting, nausea, diarrhoea	[D'Arena et al. 2017]
Bladder	Infection	[Lu Q et al. 2020]
Bone marrow	Thrombocytopenia	[Quereini et al. 2019]
Bone marrow	Hypogammaglobulinemia	[Albassam et asl. 2020]
Bone marrow	Leukopenia	[Albassam et al. 2020]
Muscle	Myalgia	[D'Arena et al. 2017]
Skin	Rash	[D'Arena et al. 2017]
Skin	Pruritus	[D'Arena et al. 2017]
Nonspecific	Fever	[D'Arena et al. 2017]
Nonspecific	Chills	[D'Arena et al. 2017]
Nonspecific	Rigor	[D'Arena et al. 2017]
Nonspecific	Back pain	[D'Arena et al. 2017]
Nonspecific	Arthralgia	[D'Arena et al. 2017]

PML: progressive, multifocal leukoencephalopathy

Figure 1. Side effects reported in patients under rituximab

REFERENCES

[1] Blum S, Gillis D, Brown H, Boyle R, Henderson R, Heyworth-Smith D, et al. Use and monitoring of low dose rituximab in myasthenia gravis. Journal of Neurology, Neurosurgery & Psychiatry. 2011;82(6):659–663. Available from: https://dx.doi.org/10.1136/jnnp.2010.220475.

[2] Gungor-Tuncer O, Yilmaz V, Toker A, Saruhan-Direskeneli G, Gulsen-Parman Y, Oflazer-Serdaroglu P, et al. Prompt Response to Prednisone Predicts Benign Course in MuSK-MG. European Neurology. 2017;78(3-4):137–142. Available from: https://dx.doi.org/10.1159/000479228.

[3] El-Salem K, Yassin A, Al-Hayk K, Yahya S, Al-Shorafat D, Dahbour SS. Treatment of MuSK-Associated Myasthenia Gravis. Current Treatment Options in Neurology. 2014;16(4):283–283. Available from: https://dx.doi.org/10.1007/s11940-014-0283-8.

[4] Litchman T, Roy B, Kumar A, Sharma A, Njike V, Nowak RJ. Differential response to rituximab in anti-AChR and anti-MuSK positive myasthenia gravis patients: a single-center retrospective study. Journal of the Neurological Sciences. 2020;411:116690–116690. Available from: https://dx.doi.org/10.1016/j.jns.2020.116690.

[5] Shashikala T, Sachdeva J, Mahesh K, Shree R, Jain G, Kapila A, et al. Use of rituximab in muscle-specific tyrosine kinase antibody-positive myasthenia gravis: Preliminary observations from a tertiary care center in Northern India. Indian Journal of Pharmacology. 2020;52(1):49–49. Available from: https://dx.doi.org/10.4103/ijp.ijp_333_18.

AUTHOR BIOGRAPHY

Josef Finsterer, MD, PhD Krankenanstalt Rudolfstiftung, Vienna, Austria.

Carla A. Scorza Disciplina de Neurociência. Escola Paulista de Medicina/Universidade Federal de São Paulo/. (EPM/UNIFESP). São Paulo, Brasil

Ana C Fiorini, MD Programa de Estudos Pós-Graduado em Fonoaudiologia. Pontifícia Universidade Católica de São Paulo (PUC-SP). Departamento de Fonoaudiologia. Escola Paulista de Medicina/Universidade Federal de São Paulo (EPM/UNIFESP). São Paulo, Brasil

Fulvio A. Scorza, MD Disciplina de Neurociência. Escola Paulista de Medicina/Universidade Federal de São Paulo/. (EPM/UNIFESP). São Paulo, Brasil

Ritwik Ghosh, MD Department of General Medicine, Burdwan Medical College & Hospital, Burdwan, West Bengal, India.