Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/mjafi

Correspondence/Letter to the Editor

Muscle MRI is not sufficient to diagnose SARS-CoV-2 associated myositis

Dear Editor,

With interest, we read the article titled 'Myositis in a patient with coronavirus disease 2019: A rare presentation' by Gupta et al. published in Med J Armed Forces India. 2021 Jul; 77 (suppl 2): S486-S489[1] about a 49- year old SARS-CoV-2 asymptomatic but positive female with painful, lower-limb and proximal-dominant quadriparesis since 14 days prior to admission, mild creatinekinase (CK) elevation, and mildly elevated blood sedimentation rate being diagnosed as myositis upon muscle MRI findings.[1] A causal link between the myositis and the SARS-CoV-2 infection was suspected. She was treated with intravenous immunoglobulins (IVIG) and recovered with regard to muscle weakness within two weeks.[1] The study is appealing but has several limitations, which raise concerns and comments.

We do not agree with the diagnosis SARS-CoV-2 associated with myositis.[1] Though clinical presentation and muscle MRI findings, elevated CK, elevated blood sedimentation rate, and recovery upon administration of IVIG are compatible with myositis, there are several arguments against myositis. The C-reactive protein and the leukocyte counts were normal, the myositis panel was negative, and the antinuclear antibodies (ANA) and antineutrophil cytoplasmic antibodies (ANCA) were negative. Muscle MRI was carried out without the application of a contrast medium, which is crucial for documenting an inflammatory reaction. Furthermore, T2-hyperintensities on muscle MRI could also represent fibrosis or fatty degeneration. This is why it is crucial that needle electromyography (EMG) and muscle biopsy had to be performed. Diagnosing myositis without EMG and muscle biopsy is not acceptable and can result in misleading results and wrong diagnoses. Muscle biopsy is essential for assessing if myositis was infectious or immunogenic and if there was muscle cell necrosis.

Missing is the exclusion of a hereditary neuromuscular disorder and the family history. It has to be known if any of her first-degree relatives suffered from a muscle disease or ever experienced rhabdomyolysis or complications during general anesthesia.

Missing is the exclusion of mild rhabdomyolysis. Although normal renal function and only mildly elevated CK argue against rhabdomyolysis, MRI findings and myalgia are compatible with acute muscle cell necrosis. Thus, it is conceivable that the patient had, in fact, mild rhabdomyolysis and it has to be known if the urine was ever cola-colored or myoglobin was ever elevated.

The patient was vegetarian, and there was obviously malnutrition resulting in protein deficiency, vitamin-B12 deficiency, and vitamin-D deficiency. Unfortunately, the erythrocyte count and the serum iron levels were not provided. Iron deficiency should be excluded at it has been reported to cause myopathy.[2] Celiac disease can also go along with painful proximal muscle weakness.[3]

Missing is a follow-up muscle magnetic resonance imaging (MRI) to document if the T2-hyperintensities truly disappeared with clinical improvement. The patient was investigated at the 14-day follow-up only by a clinical exam. A follow-up investigation of CK and blood sedimentation rate were not provided.

Missing is the documentation of a positive SARS-CoV-2 PCR in the case description.[1] Only the abstract mentions that the index patient was SARS-CoV-2 positive, but in the main text, it is only mentioned that the PCR was negative "after 10 days".[1] It has to be known from which compartment the specimen was taken that resulted in a positive PCR. Missing are the reference limits of various parameters.

Overall, the elegant study has several limitations that challenge the results and their interpretation. SARS-CoV-2 associated myositis needs to be confirmed by muscle biopsy. All possible differentials of myalgia with muscle MRI T2-hyperintensities need to be thoroughly excluded.

REFERENCES

1. Gupta S, Dixit PK, Prasad AS. Myositis in a patient with coronavirus disease 2019: a rare presentation. *Med J Armed Forces India*. 2021 Jul;77(suppl 2):S486–S489. https://doi.org/10.1016/j.mjafi.2020.10.015.
2. Dziegala M, Josiak K, Kasztura M, et al. Iron deficiency as energetic insult to skeletal muscle in chronic diseases. *J*

Cachexia Sarcopenia Muscle. 2018 Oct;9(5):802–815. https://doi.org/10.1002/jcsm.12314.
3. Hadjivassiliou M, Chattopadhyay AK, Davies-Jones GA, Gibson A, Grünewald RA, Lobo AJ. Neuromuscular disorder as a presenting feature of coeliac disease. *J Neurol Neurosurg Psychiatry*. 1997 Dec;63(6):770–775. https://doi.org/10.1136/jnnp.63.6.770.

Josef Finsterer
Klinik Landstrasse, Messerli Institute, Vienna, Austria
E-mail address: fifigs1@yahoo.de

Reply to 'Muscle MRI is not sufficient to diagnose SARS-CoV-2 associated myositis'

Dear Editor,

We are thankful to the reader for showing interest in our article, its critical appraisal, and raising certain queries.[1] However, we beg to disagree with all points raised. The point wise reply to these queries are as follows:

(i) *Diagnosis of myositis*: Contrary to popular belief a diagnosis of muscle involvement requires only a good clinical history and examination. Investigations only confirm the suspicion. With a clinical profile of rapidly progressive proximal weakness with preserved reflexes and sensations the localization in the muscle. This was further confirmed once MRI showed extensive muscle involvement. An electro-physiology may not have further helped.

(ii) *MRI suggesting fibrosis or fatty infiltration*: The old adage "we treat the patient not the image" is applicable here too. If the person had a long duration of symptoms (years) the differential diagnosis of a similar MRI picture could have been fibrosis or fatty infiltration. In a person with no past history these differential diagnosis cannot be applied.

(iii) *Muscle biopsy essential to make a diagnosis of infections vs immunogenic*: Inflammatory muscle disease (polymyositis or dermatomyositis) will present a less rapid course (days to weeks) with skin changes (in case of dermatomyositis). Response to IVIg is also less dramatic with majority taking a few days to weeks to improve. Muscle biopsy in inflammatory disease with immunohistochemistry is definitely helpful, but chiefly in distinguishing between the different types (polymyostis vs dermatomyositis vs inclusion body myositis).

(iv) *Hereditary muscle disease:* History (duration of symptoms and no family history) is good enough to safely exclude that diagnosis.

(v) *Rhabdomyolysis*: Clinical profile is different (usually toxic patient).

(vi) The iron deficiency was excluded as peripheral blood smear showed no microcytic hypochromic red blood cells (RBC) and normal ferritin. Her erythrocyte count was 2.61 million/μL (3.7-5.6) and serum iron was not done because of very low suspicion of iron deficiency anemia along with finding of low serum vitamin B12 with macrocytic RBC with hypersegmented neutrophils explaining vitamin B12 deficiency as the cause of anemia.

(vii) Celiac disease is known to cause various neurological manifestations in 6-10% of patients.[2,3] Most frequent manifestations are ataxia and peripheral neuropathies.[4] However, a diagnosis of celiac disease was not perused because of different clinical profiles, absence of iron deficiency anemia, intestinal symptoms or any other clue.

(viii) The initial test was done at the time of evaluation, which showed positive reverse transcriptase-polymerase chain reaction (RT-PCR) from the nasopharyngeal and oropharyngeal swab. The test done after 10 days showed negative RT-PCR for SARS-CoV-2 from the nasopharyngeal/oropharyngeal swab.

Viral myositis is a well known entity. One of the major symptoms of COVID-19 infection is myalgia telling us that this virus does involve the muscles in some patients. However, presenting predominantly with significant muscle involvement causing weakness is unique.

REFERENCES

1. Gupta S, Dixit PK, Prasad AS. Myositis in a patient with coronavirus disease 2019: a rare presentation. *Med J Armed Forces India*. 2021 Jul;77(suppl 2):S486–S489. https://doi.org/10.1016/j.mjafi.2020.10.015.
2. Ibiapina J, Neto S, Carolina A, Vieira L, Magalhães FG, Silva GS. Neurological manifestations of celiac disease. *Arq Neuropsiquiatr*. 2004;62(4):969–972.
3. Hadjivassiliou M, Chattopadhyay AK, Gibson A, Grünewald RA. Neuromuscular disorder as a presenting feature of celiac disease. *J Neurol Neurosurg Psychiatry*. 1997;63:770–775.
4. Mearns ES, Taylor A, Thomas Craig KJ, Puglielli S, Cichewicz AB, Leffler DA, et al. Neurological manifestations of neuropathy and ataxia in celiac disease: a systematic review. *Nutrients*. 2019 Feb;11:380.

Prashant Kumar Dixit
Graded Specialist (Medicine), Command Hospital (Air Force), Bengaluru, India
E-mail address: dixitafmc@gmail.com

3 September 2021
Available online 10 December 2021

0377-1237/$ – see front matter

https://doi.org/10.1016/j.mjafi.2021.11.002