SARS-CoV-2–associated myopathy with positive anti–Mi-2 antibodies: a case report

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This article was published on 17 Mar 2023 at www.hkmj.org.

This version may differ from the print version.

Hong Kong Med J 2023;29:Epub
https://doi.org/10.12809/hkmj219938

Case report

A 36-year-old female presented to the Emergency Department of the University Clinical Centre of Serbia in August 2020 with bilateral weakness and aches in the proximal muscles of the upper and lower extremities, limited limb movement, and poor tolerance of physical exertion. Symptoms had developed 4 weeks after hospitalisation for coronavirus disease 2019 (COVID-19) pneumonia and progressed rapidly over the next weeks (Fig). During her hospitalisation for COVID-19, she was treated with the corticosteroid (CS) methylprednisolone 0.5 mg/kg for 10 days, and prophylactic low-molecular-weight heparin, azithromycin (500 mg/day for 3 days), and antipyretics. Physical examination revealed weakness of the proximal muscles (grade 3/5) but no other abnormalities. Nasal swab screening for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by polymerase chain reaction test was negative. Blood work-up showed elevated levels of creatine kinase (CK) [28 731 U/L], myoglobin, and troponin (Table). Renal function tests were normal (blood urea nitrogen: 8.0 mmol/L, serum creatinine: 45 μmol/L, estimated glomerular filtration rate: >60 mL/min). Immunoserological analysis was positive for assessment of antinuclear antibodies (1:640) and myositis profile (Mi-2++ and Ro-52++). The patient was then referred to the Clinic of Allergy and Immunology of the same centre for further evaluation. Electromyoneurography of the upper and lower extremities revealed moderate-to-severe myopathic lesions in the proximal muscles with a pattern characteristic of inflammatory myopathies. Testing of respiratory muscle strength revealed decreased maximal inspiratory pressure of 62%. Lung computed tomography scan and echocardiography were normal. Muscle biopsy and magnetic resonance imaging were not performed due to temporary restrictions during the pandemic.

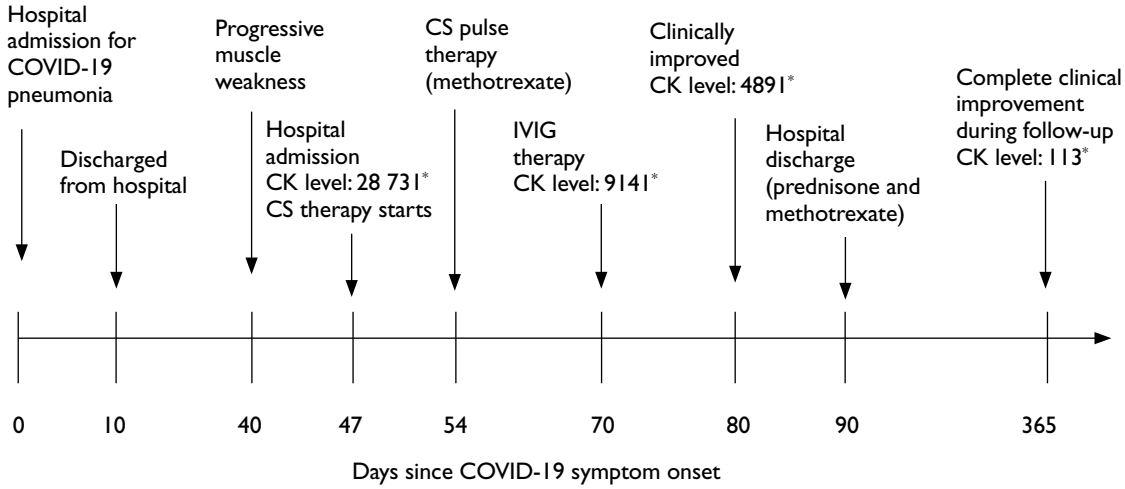

FIG. Timeline of the case
Abbreviations: CK = creatine kinase; COVID-19 = coronavirus disease 2019; CS = corticosteroids; IVIG = intravenous immunoglobulin
* Unit: U/L

TABLE. Selected laboratory analysis of the patient during the disease course

Parameter (reference range)	COVID-19 diagnosis	Autoimmune myopathy diagnosis	Discharge from hospital	One-year follow-up
AST, U/L (0-31)	181	834	245	16
ALT, U/L (0-34)	345	345	373	36
CK, U/L (0-145)	2876	28 731	4851	113
LDH, U/L (0-247)	675	2882	1095	181
Myoglobin, ug/L (<36.4)	*	>1000	*	*
hs-troponin T, ng/L (<14)	*	855	130	65

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; CK = creatine kinase; COVID-19 = coronavirus disease 2019; hs-troponin T = high-sensitivity troponin T; LDH = lactate dehydrogenase

* Not done

The remainder of a thorough work-up was normal. Autoimmune myopathy associated with COVID-19 was suspected and the patient was prescribed high-dose CS (1 mg/kg/day) followed by pulse therapy of 500 mg/day methylprednisolone for 3 consecutive days. Methotrexate (22.5 mg/week) was introduced. No clinical or laboratory improvement was evident after 2 weeks, hence intravenous immunoglobulins (0.4 g/kg/day) were given for 5 days. This therapy led to significant clinical improvement and a gradual decline in muscle enzymes. During follow-up, a trial of CS withdrawal and methotrexate dose reduction resulted in worsening of proximal muscle weakness and rise in serum CK. After 1 year of follow-up, the patient remained on methotrexate 20 mg/week and prednisone 5 mg/day. Repeated immunoserological analysis was still positive for antinuclear antibodies (1:640) and anti–Mi-2 antibodies.

Discussion

Myalgias, muscle weakness, and elevation of muscle enzymes are commonly seen in COVID-19 patients, but are typically resolved within a few weeks with conservative treatment. Direct viral invasion of muscles, toxic effects of cytokines and dysregulated immune stimulation have been proposed as possible mechanisms. There are several reports of COVID-19–related myositis/rhabdomyolysis with serum CK level as high as 427 656 U/L.[1,2] Most patients recover with conservative treatment. In our patient, a mild increase in muscle enzymes was noticed during COVID-19 infection. Nonetheless early signs of myopathy may have been masked by the CS therapy prescribed for COVID-19 pneumonia. Due to the presence of anti–Mi-2 and anti–Ro-52 antibodies, which are characteristic of dermatomyositis, we carefully examined the skin and nailfolds, but there were no suggestive findings at first presentation or subsequent follow-up. A limitation of our work was the lack of muscle histopathology or magnetic resonance imaging. Nonetheless the clinical picture, 1-year disease course, electromyographic pattern typical of inflammatory myopathies, and persistent positivity for anti–Mi-2 antibodies suggest that SARS-CoV-2 infection may have triggered the development of autoimmune myopathy in our patient.

A case of COVID-19–associated inflammatory myopathy with severe facial, bulbar, proximal limb weakness, and elevated CK level, suggestive muscle biopsy and positive anti-SSA, anti–SAE-1, and anti-Ku antibodies, has been reported. The patient was successfully treated with a 5-day course of 1000 mg methylprednisolone.[3] Nonetheless there are no data on the subsequent clinical course.

Recently, a COVID-19–associated myopathy caused by type I interferonopathy has been described.[4] The patient presented with general weakness, myalgias, fever, bibasilar lung infiltrates, and significantly elevated serum CK and troponin levels. Immunohistochemical analysis of deltoid muscle biopsy specimen revealed abnormal expression of major histocompatibility complex class I antigen on sarcolemma and sarcoplasm, and presence of myxovirus resistance protein A on muscle fibres and capillaries. The authors speculated that increased expression of type I interferon was responsible for SARS-CoV-2 myopathy in their patient through up-regulation of proteins that are toxic to muscle cells.[4] Nonetheless deposition of myxovirus resistance protein A in muscle fibres and capillaries is also an early feature of dermatomyositis. Given the lack of data on immunoserological analysis and follow-up of the patient, an early phase of dermatomyositis cannot be excluded.

The number of reports of autoimmune disease developing in patients with COVID-19 is increasing. Molecular mimicry has been proposed as a potential mechanism.[5] A recent study identified three immunogenic linear epitopes with high sequence identity to SARS-CoV-2 proteins in patients with dermatomyositis, implying a possible contribution of SARS-CoV-2 to the development of autoimmune inflammatory myopathies.[6] Additional mechanisms may also be involved, highlighting an urgent need to better understand the immune processes that underlie viral-induced autoimmunity in COVID-19.

Physicians should carefully evaluate patients who present with progressive elevation of muscle enzymes and be alert to the possible occurrence of autoimmune myopathy triggered by COVID-19. Early diagnosis facilitates timely initiation of adequate treatment, preventing long-term consequences and complications.

Author contributions

Concept or design: A Plavsic, S Arandjelovic, A Peric Popadic, S Raskovic, R Miskovic.

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Analysis or interpretation of data: A Plavsic, A Peric Popadic, S Raskovic, J Bolpacic, R Miskovic.
Drafting of the manuscript: A Plavsic, S Arandjelovic, J Bolpacic, R Miskovic.
Critical revision of the manuscript for important intellectual content: All authors.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have disclosed no conflicts of interest.

Funding/support

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethics approval

Ethics approval was not required as per guidelines for publishing case reports of Ethics Committee of the University Clinical Centre of Serbia. Patient consent has been obtained concerning treatment and procedures, and the patient has given written informed consent to the publication.

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