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Case report of COVID-19 in an elderly patient: could SARS-CoV2 trigger myositis?

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Abstract. – Though the exact etiology of autoimmune diseases still remains not completely known, there are various factors which are known to contribute to be trigger of autoimmune diseases. Viral infection is known to be among the other. It is known as the infection from severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) can be an autoimmune trigger, so, we suppose that SARS-Coronavirus (SARS-CoV-2) could be as well.

Several authors have highlighted the temporal consequence between SARS-CoV-2 and autoimmune diseases.

In this case report we described a patient admitted for COVID-19 pneumonia with completely negative autoimmunity at admission who developed major pulmonary interstitial disease. During the hospitalization the weaning difficulties from oxygen led us to the repetition of autoimmunity pattern which became positive (both during hospitalization then after two months from dismission) with marked positivity for specific antibodies for myositis even after the patient's infectious healing. In the follow-up, the patient continued to have asthenia and muscle weakness despite steroid therapy. She is still in follow-up and will be further evaluated over time.

Can we therefore think that in this case the development of autoimmunity can persist beyond the infectious phase and determine over time the development of a real autoimmune myositis?

Key Words:
COVID-19, Autoimmunity, Myositis, Antibody, Interstitiopathy.

Introduction

As known, though the exact etiology of autoimmune diseases still remains not completely known, there are various factors which are believed to contribute to the emergence of an autoimmune disease. They included genetic predisposition and the environmental triggers, such as bacterial, viral, fungal and parasitic infections, environmental agents, hormonal factors[1-5].

Several viruses have been identified as possible trigger of autoimmune disease, such as Parvovirus B19, Ebstein Barr, Cytomegalovirus, Herpes virus 6, Hepatitis A and C, Rubella virus[6-12].

In December 2019, a new type of Coronavirus infection emerged in Wuhan that determined in the subsequent months a still ongoing pandemic.

It is now well established that COVID-19 infection is composed of a primary phase that will be considered "viral" and a secondary phase that will be considered "autoimmune".

In literature, it is reported that autoimmune phenomena exist in subjects with SARS. Therefore, taking into account the high genetic similarity between SARS-CoV-2 and SARS, it is likely that an autoantibody mechanism might be present during SARS-CoV-2 infection too[13].

Verdoni et al[14] published the association between COVID-19 and Kawasaki syndrome (KS) in pediatric patients in which the majority of patients had positive SARS-CoV-2 IgG but negative IgM and swabs. The delay between the pandemic peak of COVID-19 and the occurrence of hyper-inflammatory syndrome in children does not point to a direct effect of the infections, but rather towards an immune-mediated disease.

In Vojdani's letter[15] to Clinical Immunology, a more frequent antibody elevation, in particular of Antinuclear Antibodies (ANA), Extractable Nuclear Antigen Antibodies (ENA) and anti-actin and anti-mitochondrial antibodies, was highlighted following the acute infection.

Other works have highlighted the similarities between COVID-19 pneumonia and anti-MDA-5-positive dermatomyositis associat-

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ed to a rapid interstitial lung disease. Wang et al[16] pointed out that the interstitial picture of COVID-19 pneumonia with severe lung involvement is very similar to the interstitial diseases found in dermatomyositis for clinical, imaging, cytokines and pharmacological treatment, however placing them in differential diagnosis.

Several recent reports[17-18] have suggested that SARS-CoV-2 infection could lead to various autoimmune and auto-inflammatory disease in both children and adults.

Myositis are systemic rheumatological diseases of unknown etiology that affect skeletal muscle tissue. Usually they are manifested by worsening muscle weakness in the limbs and increased serum levels of muscle enzymes accompanied by characteristic histopathological electromyographic manifestations.

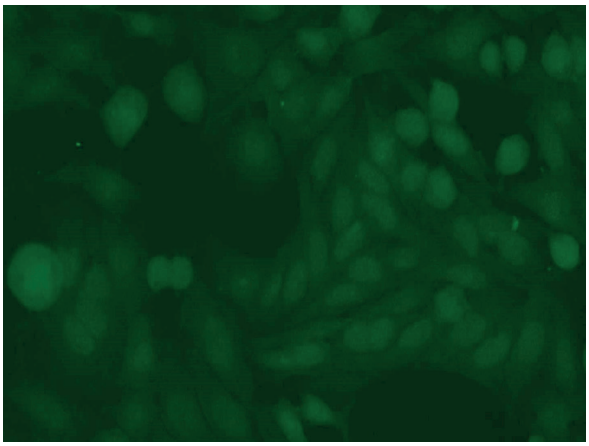

Figure 1. Fluorescent microscope image in 20× magnification. Fluoroscopic pattern at admission. Hep-2 cells show no specific fluorescence at admission.

Case Presentation

A 77 years old woman was admitted to the Emergency Unit for chills and fever from one week. In medical history was reported obesity, monoclonal gammopathy, diabetes, chronic obstructive pulmonary disease, atrial fibrillation, chronic renal failure, previous heart failure.

On admission chest x-ray showed nuanced parenchymal thickening in the middle-upper right and middle-basal left fields. On blood chemistry we observed leukopenia, increase in C-reactive protein (5.94 mg/dL, normal value n.v. 0-0.8), elevation of lactic dehydrogenase (LDH 535 U/L, n.v. 230-500) and mild renal insufficiency (creatinine 1.44 mg/dL, n.v. 0.4-1.0).

The patient performed COVID-19 swab, by Real Time Reverse Transcription-Polymerase Chain Reaction (rRT-PCR), that resulted positive.

On arterial gas analysis we observed severe respiratory failure; oxygen supplementation was started initially with nasal cannula, therefore with continue positive air pressure (C-PAP).

Therapy with lopinavir/ritonavir and hydroxychloroquine was started associated to antibiotics therapy (doxycycline and ceftriaxone) and anticoagulant.

He was, therefore, hospitalized in Semi-Intensive Department for Care. The autoimmunity was performed: ANA, ENA and anti-neutrophil cytoplasmic antibodies (ANCA), and resulted negative with normal range of complement at admission (Figure 1).

After fifteen days from hospitalization, despite the improvement in blood chemistry and persistent apyrexia, the patient could not be weaned from the C-PAP helmet. Hematochemicals and autoimmunity were repeated and showed ANA positive with cytoplasmic pattern (1:320) granular type, Anti-Ku and anti-MI 2b positivity (Figure 2). COVID-19 swab was repeated and resulted negative.

Steroid therapy was then started at a dosage of 1 mg/kg. In the next days we assisted to a progressive improvement in respiratory exchanges and weaning from CPAP first, and then, from oxygen.

The patient was then discharged with steroid therapy in decalage and re-evaluated on an outpatient basis after 2 months.

A persistent alteration of the auto-antibodies was confirmed with a further increase in title

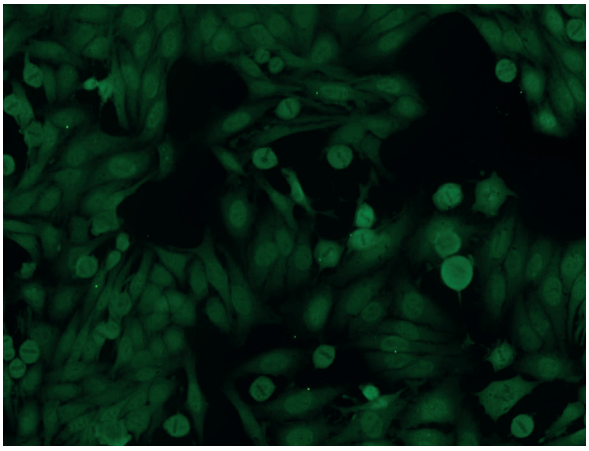

Figure 2. Fluorescent microscope image in 20× magnification. Fluoroscopic pattern after fifteen days and two months after dismission. In the indirect immunofluorescence test with Hep-2 cells, antibodies against Ku and Mi-2β exhibits a fine speckled fluorescence of the cell nuclei while the nucleoli are positive in parts.

with cytoplasmic pattern (1:160), centriole pattern (1:320), granular pattern (1:160) and myositis blot (used after specific pattern are detected on immunofluorescence) resulted positive with elevation of the title (Anti-Ku and anti-MI-2β) (Figure 3). Clinically the patient was stable, complaining only significant weight decrease and diffuse weakness.

Methods

ANCA and ANA were detected by indirect immunofluorescence (IIF) using EUROIMMUN test kits. The confirmatory tests were performed by line-blot technology following the manufacturer's instructions (EUROIMMUN). The tests are specific for the following antigens. EUROLINE Myositis: antibodies anti: Mi-2 alpha, Mi-2 beta, TIF1g, MDA5, NXP2, SAE1, Ku, PM-Scl100, PM-Scl75, Jo-1, SRP, PL-7, PL-2, EJ, OJ, Ro-52. EUROLINE Scleroderma: antibodies anti: Scl-70, CENP A, CENP B, RP11, Rp155, fibrillarin, NOR90, Th/To, PM-Scl100, PM-Scl75, Ku, PDGFR, Ro-52.

Discussion

The observation of this case led us to analyze the correlation between the strong incidence of pulmonary interstitial disease, with onset even after the beginning of the infection, and the interstitial disease evidenced in dermatomyositis/myositis.

The question arises spontaneously; patients with even severe interstitial disease with antibodies positivity, could be considered affected by a secondary autoimmune pathology that determined the development of an interstitial disease secondary to the viral pathology? More specifically, could the presence of anti-Ku and anti-MI 2β antibodies, known to be associated with myositis and implicated in pulmonary interstitial disease, be the cause of the development of an interstitial disease?

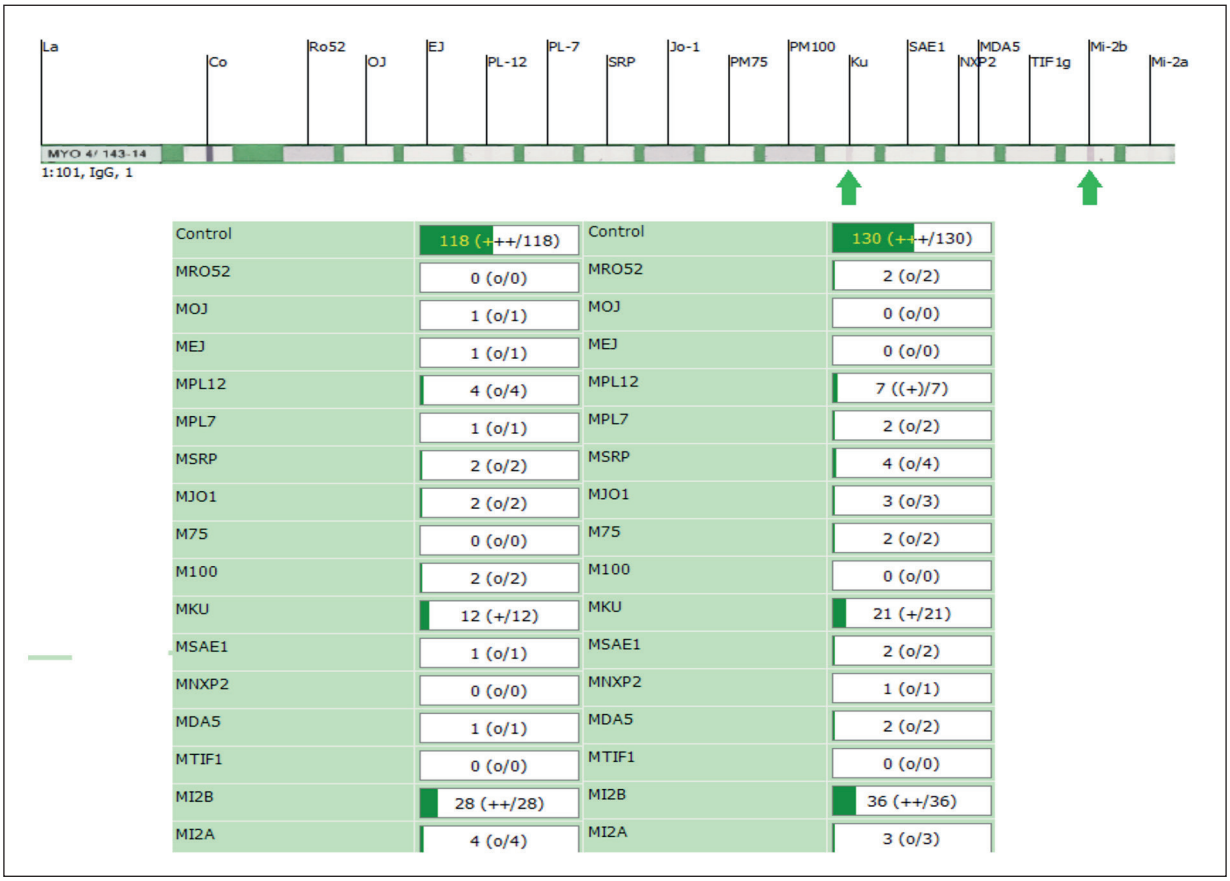

Figure 3. Myositis Profile blot at fifteen days and two months after dimission. The immuno blot detects IgG antibodies to Mi-2β and Ku.

It is not surprising at this point to think that these patients, as already highlighted by Wang et al[16], have several similarities with patients affected by dermatomyositis and respond clinically to the administration of steroid therapy.

This is why we decided to follow our patient also in further evaluation.

Why does the elevation of auto-antibodies persist in this patient even after the infectious event?

Is that occurrence a consequence of inflammatory response to SARS-CoV-2 or is the origin of an autoimmune myositis?

Conclusions

The possible role of SARS-CoV-2 is not yet completely clear but the already documented association of COVID-19 with the beginning of other autoimmune disease may make us think that also myositis could be triggered by COVID-19 infection. Of course the condition needs additional experiences and studies.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Statement of Human and Animal Rights

All procedures performed in the study were in accordance with the Ethical Standards of the Institutional and/or National Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable Ethical Standards.

Informed Consent

The patient was informed of the scientific and clinical interest in her disease as well as of this anonymous publication. She gave an informed verbal consent to the anonymous publication.

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