Efficacy of rituximab treatment in a post-COVID-19 vaccine myositis overlapping to systemic sclerosis: a histological follow-up

Sir,

We report this first case of myositis overlapping to systemic sclerosis (SSc) after the second dose of Corminaty INN-mRNA nucleoside COVID-19 vaccine (CV), responsive to rituximab (RT) treatment.

Even if vaccination has played a crucial role in reducing the severity in COVID-19 pandemic spread (1), adverse events have raised questions in susceptible individuals (2). Recent studies have suggested an association between CV and the onset of various inflammatory myopathies, in addition to autoimmune diseases (3-7).

Less than 4 weeks later the second dose of CV (July 2021), a 22-year-old female developed symmetric hands and wrists swelling, fixed cyanosis, puffy fingers with low positive skin score and pitting scars. These symptoms progressively worsened, complaining generalised body aches and muscle soreness. She had no history of previous COVID-19 (negative polymerase chain reaction) and other infections were excluded. Initially, anti-Spike Sars, quantitative IgG S1-RBD (288 BAU WHO/mL, normal value (nv) <28) and autoantibodies ANA IFI on cells HEp-2 (1:1280 speckled), antiU1RNP (>240 U/mL, <7 normal value), antiRNP70 (74 U/mL, <7 nv) and anti-nucleosomes (>200 U/mL, <20 nv) were increased. Power Doppler ultrasound (US) revealed activity (synovitis) in right hand and (tenosynovitis) in the shoulders. Baseline capillaroscopy revealed multiple crossings and tortuous capillaries.

After the diagnosis of undifferentiated connective tissue disease in January 2022, she was initially treated with low dosage of hydroxychloroquine, prednisone and pentoxifylline.

However, in April 2022, her symptoms worsened with increased joint pain and initial ulcer of the third finger of the right hand. The treatment was adjusted with prostaglandins *i.v.* monthly infusions and amlodipine, discontinuing hydroxychloroquine (October 2022) for idiosyncratic skin reaction at increasing dose.

After an initial improvement of ulcer and puffy fingers in January 2023, Raynaud relapsed at hands and lips, as well as stiffness of the skin (hands and face) and upper and lower limbs pain with an increase of aldolase 56 U/mL (nv 0-7.6) and CK 3137 U/l (nv26-140).

An electromyography in January 2023 revealed upper and lower limbs fibrillations in proximal muscle with increase of polyphasic UM potentials of small amplitude and short duration, more accentuated in upper limbs.

In February 2023 a chest high resolution (HRCT) chest showed central bronchiectasis, and global spirometry revealed alveolocapillary diffusion reduction (DLCO 51%). The diagnosis was updated to an overlap of SSc and myositis and a treatment with oral high steroid dosage, immunoglobulin i.v. and oral mycophenolate was initiated, with an initial benefit.

Unfortunately, in September 2023, skin score and muscle markers relapsed (aldolase -260 U/mL- and CK -2320 U/l-), not responsive to prednisone and mycophenolic increased dosage.

In January 2024, a muscle biopsy showed changes in fibres size and shape, thickening of endomysia connective tissue and focal fibrosis, diffuse lymphocytic infiltrate, with scattered CD20+ cells in the interstitial compartment (Fig. 1).

In February 2024 heart MRI showed enhancement in the inferior junctional site and chest HRTC revealed an initial fibrous micronodule and a stagnation in thoracic oesophagus along its course, confirmed by oesophageal manometry that showed absence of contractility classified as Chicago Class 4.0. Thus, RT (1000 mg) was administered in March 2024, with the second dose scheduled one month later.

At histological follow up (June 2024), inflammatory infiltrates disappeared, and fibres size and shape were normalised (Fig. 2). In July 2024 the patient reported significant improvement, normal lungs and joints at US, stable after one year. Only GERD persisted, even if reduced. Prostaglandins and immunoglobulin *i.v.* were stopped on May 2025, without relapse of myositis until now; amlodipine, mycophenolate and low dosage of steroids were maintained.

In conclusion, this case highlights a rare but significant event of a post-CV overlap of myositis and SSc. The patient's condition was resistant to conventional therapies, but she responded significantly to RT. This case underscores the importance of monitoring for challenging autoimmune postvaccine myositis for its differential diagnosis (8-10)

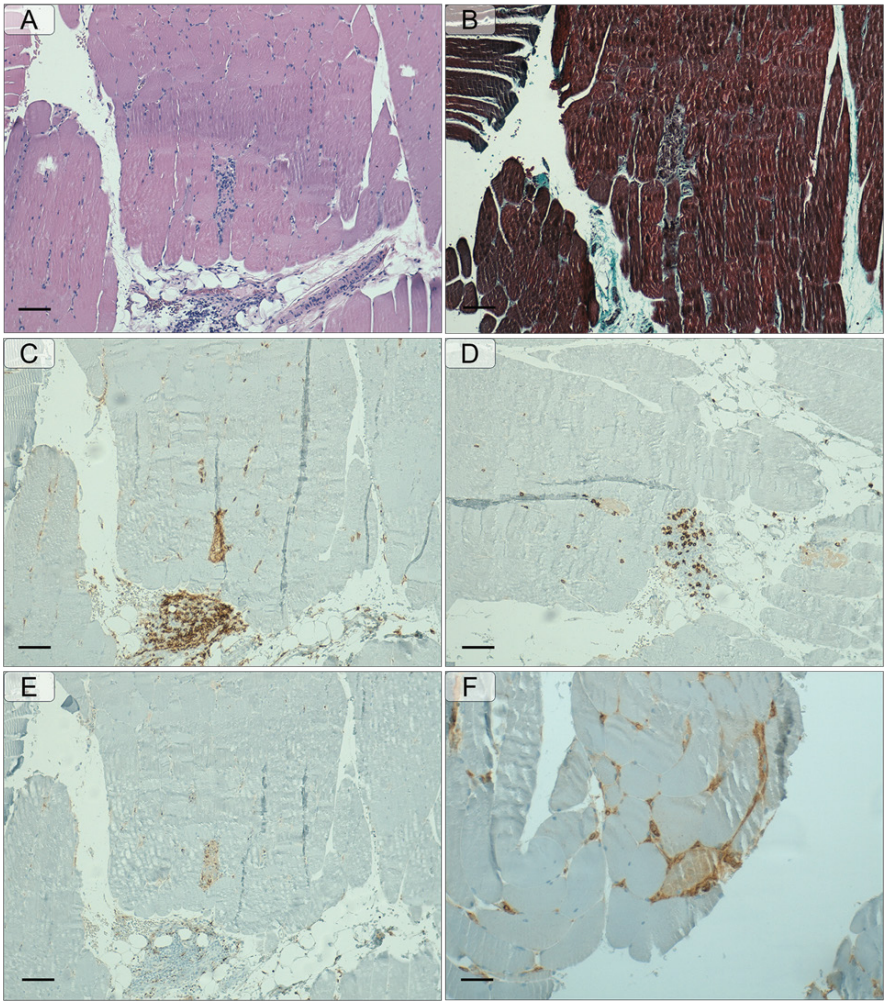

Fig. 1. Representative histopathological findings of muscle biopsy performed in January 2024. **A)** Haematoxylin and eosin stain slide shows moderate changes in fibres size and shape, along with a lymphocytic inflammatory infiltrate located at endomysia (magnification 100x, scale bar 200μm). **B)** Gomori's trichrome staining (magnification 100x, scale bar 200μm). **C)** CD4 (magnification 100x, scale bar 200μm). **D)** CD8 (magnification 100x, scale bar 200μm). **E)** CD68 (magnification 100x, scale bar 200μm). **F)** HLA-ABC (magnification 100x, scale bar 200μm).

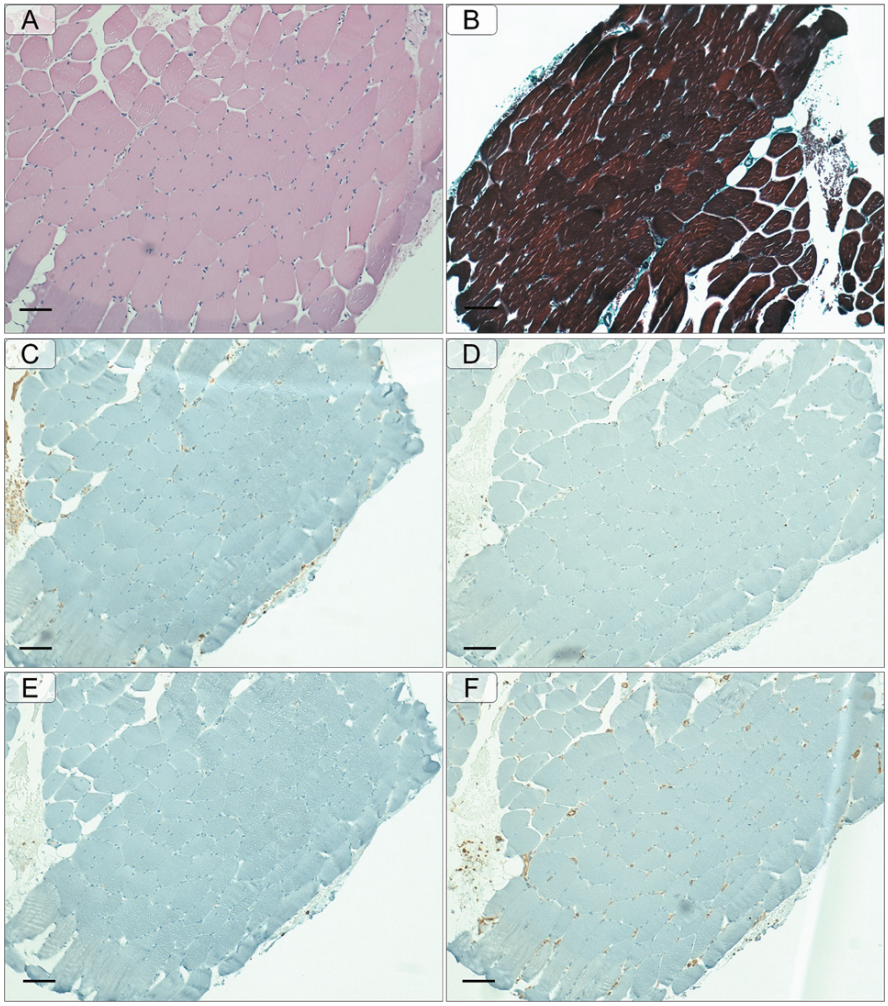

Fig. 2. Representative histopathological findings of post-treatment muscle biopsy performed in April 2024. No significant alteration was present morphologically, as well as no inflammatory infiltrates could be observed. **A**) Haematoxylin and eosin stain (magnification 100x, scale bar 200μm). **B**) Gomori's trichrome staining (magnification 100x, scale bar 200μm) **C**) CD4 (magnification 100x, scale bar 200μm) **D**) CD8 (magnification 100x, scale bar 200μm) **E**) CD68 (magnification 100x, scale bar 200μm). **F**) HLA-ABC (magnification 100x, scale bar 200μm).

and suggests that RT may be an effective treatment option in similar cases.

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