

## CASE REPORT

# SARS-Cov-2 Infection and severe proximal myopathy secondary to dermatomyositis and overlap systemic sclerosis: A Case Report from Zambia

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## ABSTRACT

**Background:** Myositis has been reported to be associated or triggered by viruses. Genetic and environmental factors are documented risk for myopathies. Viruses have also been shown to modify the clinical course of auto-immune diseases. We therefore report a case of SARS-Cov-2 infection in a 26-year-old female black Zambian patient with proximal myopathy.

**Case presentation:** We present the case of a 26-year-old chemical factory worker with severe acute respiratory distress syndrome corona virus 2 (SARS-cov-2) infection and proximal myopathy. She presented to a local private hospital with fever, weakness and flu-like symptoms after being exposed to a colleague diagnosed with SARS-cov-2

infection at the time Zambia declared the July 2021 third wave of SARS-cov-2 pandemic. She also reported difficulties in climbing stairs, had Raynaud's phenomenon, proximal myopathy, classic dermatomyositis features, symptoms of systemic sclerosis, raised creatine phosphokinase (CPK), and a positive nasopharyngeal PCR test for SARS-Cov-2 infection.

**Conclusions:** We presented, for the first time in Zambia, the case of a patient with SARS-Cov-2 infection and severe proximal myopathy secondary to newly diagnosed dermatomyositis and overlap systemic sclerosis. The myopathy appeared to have been worsened by SARS-Cov-2 viral infection.

## INTRODUCTION

Coronavirus disease 2019 (COVID-19) was declared a pandemic in March 2020 by the World Health Organization<sup>1,2</sup>. Myositis have been reported to be associated or triggered by viruses<sup>3</sup> such as

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SARS-Cov-2. Viruses have also been shown to modify the clinical course of auto-immune diseases such as dermatomyositis, type 1 diabetes and systemic lupus erythematosus (SLE)<sup>4,5</sup>. The pandemic of SARS-Cov-2 infection, which was in its third wave in Zambia at the time of diagnosis, posed diagnostic and therapeutic challenges for patients with suspected systemic inflammatory autoimmune diseases. These included lack of access to specialized rheumatologist, expensive laboratory and imaging tests as well as high cost of medication. A surge in the incidence of systemic inflammatory autoimmune diseases such as dermatomyositis was noted during 2020 and 2021, the period coinciding with the occurrence of corona virus pandemic<sup>6,7</sup>. In Zambia, there has been no published work yet on SARS-Cov-2 infection and myopathies. We therefore report a case of SARS-Cov-2 infection in a patient with proximal myopathy in a newly diagnosed 26-year-old black Zambian woman with dermatomyositis and overlap systemic sclerosis.

### CASE PRESENTATION

A case is presented of a 26-year-old black Zambian woman (works as a logistic and procurement officer in a local chemical factory) who presented with 3 days' history of cough, fever, myalgia, and flulike symptoms on 30<sup>th</sup> July 2021 to a local private hospital. She reported complaints of feeling abnormally cold with chills and joints pains for two weeks prior to her hospital visit. She had presented earlier on to a local clinic with complaints of slowly progressive skin rash on the hands, arms, shoulders and chest, body weakness, difficulties in swallowing and backache for two months. She had a past medical history of Raynaud's phenomenon for a few months. She had been increasingly finding it difficult to stand from squatting position. She reported no history of smoking nor drinking alcohol. But she reported history of fever and flulike symptoms in her workmate who later tested positive for SARS-Cov-2 PCR a week prior to her hospital visit. She reported a positive family history of rheumatic symptoms in her mother.

On examination, her vital signs revealed a pulse of 105 beats per minute, she had blood pressure of 135/85 mmHg and was tachypnoeic with respiratory rate of 24 breaths/minute. Her temperature was 36.7 °C. Her oxygen saturation was in conclusive using the pulse oximeter (no other non-invasive modality was available at the time of examination) due to Raynaud changes in her peripheries. Her jugular venous pressure (JVP) was raised. She had cold peripheries, peripheral cyanosis and fingertip ulceration, findings compatible with Raynaud's phenomenon. She had microstomia, periorbital hyperpigmentation [Picture 1] and V sign on the chest [picture 1]. Tightening fibrosis of skin was observed on the inner side of both elbows and Gottron's rash [Picture 2] was seen over bony prominences, mostly of the proximal interphalangeal joints (PIPs) and metacarpophalangeal joints (MCPs) on both hands. Shawl and holstersigns were positive too. She had non-pitting edema of both lower extremities with calcinosis [Picture 3]. She had proximal muscle weakness which was more pronounced in her lower extremities as evidenced by her failure to stand from squatting position. A working diagnosis of dermatomyositis and overlap systemic sclerosis with SARS-Cov-2 infection was made based on the clinical features she presented with. Diagnosis of dermatomyositis was supported by the presence of proximal myopathy, Gottron papules, classic skin rash with V sign [ See picture 2], Shawl sign and Holster sign and elevated muscle enzymes. Features suggestive of systemic sclerosis included Raynaud's phenomenon [picture 2], sclerodactyly, dysphagia, thickened fibrotic skin and microstomia.

Blood samples were collected from the internal jugular vein for initial laboratory screening owing to fibrotic skin changes in both upper limbs and other parts of the body making it difficult to access peripheral veins. Her complete blood count showed hemoglobin of 12.6 g/dl, white blood cell count (WBC) of  $9.0 \times 10^3$  /uL with moderate lymphocytosis of 47.5 % compared to 37.0 % neutrophils and mixed cell count of 15.5 % and normal platelets. Her urea (2.93 mmol/L)

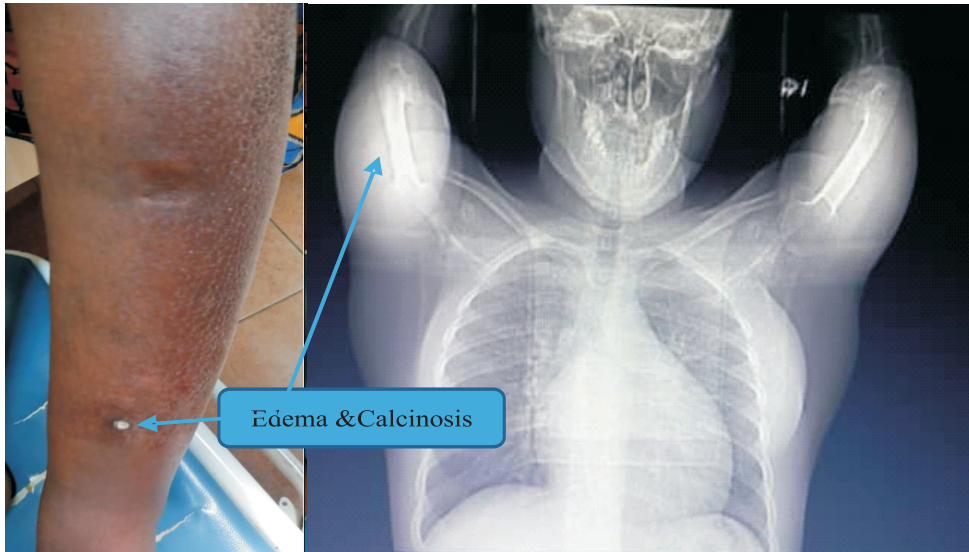


**Picture 1: Skin changes before & after treatment**  
heliotrope rash, thickened hyper pigmented skin seen and calcinosis.

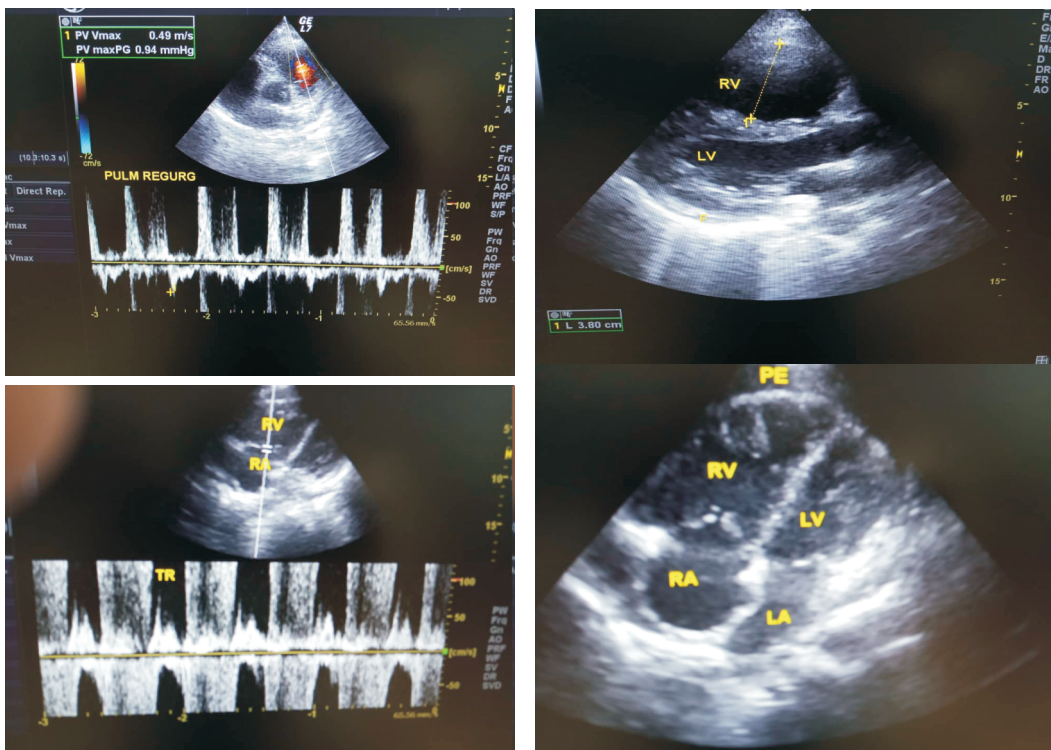


**Picture 2 Hands changes** showing Gottron rash, peripheral cyanosis with ischemic fingertip ulcers consistent with Raynaud Phenomenon





**Picture 3**  
Lower Limb and CT Scan image showing muscle edema and calcinosis



**Picture 4: ECHO.** Apical two chambers, parasternal long and short axis views showing pulmonary valve regurgitation, dilated right ventricle and tricuspid regurgitation secondary to cor pulmonale.



andcreatinine (55.8 umol/L) were normal. Her D-dimer was slightly elevated (0.80 mg/L, lab reference < 0.50). The complement reactive protein (CRP) was elevated (110 mg/dl) and SARS-cov-2 PCR test was positive.

Further tests showed elevated creatine phosphokinase (CPK) of 190 U/L (normal range 29-166 U/L) and lactate dehydrogenase (LDH) of 425 U/L (normal range 0-250). Anti-CCP antibodies for rheumatoid arthritis (RA) were negative. Autoantibodies targeting the proliferating cell nuclear antigen (Anti-PCNA) for SLE were positive though anti-double stranded DNA (ds DNA)antibody test was negative. Antinuclear antibody test (ANA) was very strongly positive (estimated titre 1: 3200 of nucleolar pattern).Anti-centromere antibody (ACA), anti-topoisomerase I antibody (Scl 70 IgG), anti PM-Scl 100 and anti-U1-RNP antibodies were negative. Anti-Jo-1 antibody, centromere B antibody, and anti-Mi-2 antibody were equally negative. Anti-Ro, antiphospholipid antibodies, C3, C4, anti-Smith, aldolase, anti-fibrillar antibodies and nail fold videocapillaroscopy and electromyography (EMG) were not done due to high costs involved [See **Table 1**].

Chest X-ray showed cardiomegaly. Computed Tomography (CT) Scan [see picture 3]of chest and upper limbs showed radio-opacity of the biceps and triceps due to muscles edema and calcinosis. It also showed reticular opacities predominantly in the lower lung zones. MRI of the muscles (proximal upper and lower limbs) showed muscle edema [Picture 3]. Muscle biopsy was performed under local anaesthesia results of which showed no features of inflammatory changes or infiltration of muscle by mononuclear cells though this was performed after starting medication.

SARS-Cov-2 infection was diagnosed based on her symptoms and the positive SARS-Cov-2 PCR test. Dermatomyositis and overlap systemic sclerosis was diagnosed in this patient based on her symptoms and positive laboratory investigations

(ANA, CPK). She had difficulties in climbing stairs prior to COVID 19 infection but muscle weakness appeared to have worsened during the infection. Hence, she was admitted to the hospital for close monitoring and further work up.

Due to the positive SARS-cov-2PCR test, the patient was referred to a tertiary care government hospital which was specifically designated by the ministry of health as a referral center for SARS-cov-2 cases. The treatment protocol included oral/intravenous dexamethasone 6 mg“*omnie die*” (OD)<sup>7</sup>, intravenous Remdesivir 200 mg loading dose then 100 mg OD, antibiotics agents such as Azithromycin 500 mg OD, or Amoxycyclav 625 mg “*ter die sumendum*” (TDS), therapeutic (1 mg/kg) or prophylactic (0.5 mg/kg) low molecular weight heparin, prophylactic anticoagulants such as Dabigatran 150 mg or 300 mg “*bis in die*” (BD) depending on severity and D-dimers levels, supplements of vitamin C500mg BD and zinc supplement<sup>7,8</sup> and anti-inflammatory agents such as Colchicine 0.5 mg OD. Dabigatran was considered as a first-line choice for oral anticoagulation at discharge because no INR monitoring was required. This choice was also explained by the availability of a specific reversal agent (Idarucizumab,a specific non-vitamin K antagonist oral anticoagulant reversal agent that will only reverse the anticoagulant effects of dabigatran)<sup>9,10</sup>.

Her symptoms eventually improved after the treatment and she was subsequently discharged from the Covid19 center after two weeks of treatment. On her review, she complained of dyspnea, easy fatigability and the lower limbs edemahad worsened. Further investigations were conducted to evaluate her symptoms. Echocardiography [see figure 4]showed a preserved systolic function but her right sided cavities (right atrium and right ventricle) were dilated with tricuspid and pulmonary regurgitations. She was re-admitted for treatment of cor pulmonale. Herthyroid stimulating hormone (TSH) was 12.98 milli-international units per liter) (range from 0.27 to 4.2) and free T4 was in normal range (1.46 ng/dl, lab

Table 1: Investigations

LABORATORY TESTS	Results
Hemoglobin	12.6 gr/dl
White Blood Cell Count	9.0x10 <sup>3</sup> /µl
Platelets	251x10 <sup>3</sup> /µl.
HIV-1 and -2 antigen/antibody	Negative
D-dimer	0.80 (< 0.50) mg/L
High-sensitivity C-reactive protein	110 (1-4) (mg/L)
Thyroid-stimulating hormone (TSH)	12.98 mIU/L (0.27-4.20)
Free T4	1.46 ng/dL (0.8-1.8)
TSH Receptor Antibody	0.971 IU/L (<1.75)
Microsomal (TPO) Antibody Titre, Serum	1.26 IU/MI (<= 5.61)
Creatine Phospho Kinase (CPK)	190 U/L (29-168)
LDH-Lactate Dehydrogenase	425 U/L (0-250)
Aldolase	Not done
Antinuclear antibody (FANA) titer	1:3200 (<1/80) (NUCLEOLAR pattern)
Anti-double-stranded DNA antibody	Negative (IU/mL)
Anti-Cyclic Citrulinated peptide (CCP) antibody	Negative (< 5.0 U/ml)
Rheumatic factor	Negative
Urea	2.93 mmol/L
Creatinine	55.8 µmol/L
Urinalysis	PRO negative, GLU negative
CXR	Cardiomegaly, reticular opacities
CT Scan Muscles	Radiopaque proximal muscles
MRI muscles	Muscle inflammation
CT Scan Chest	Reticular opacities
ECHO	TR, PR, RV & RA enlargement
Kidneys Ultrasound	Rt (8.0 cmx5.20cmx5.08 cm), Lt (9.06cmx5.33cmx5.0cm)
Anti-centromere antibody (ACA)	Negative
Anti-Proliferating Cell Nuclear Antigen (PCNA)	Intensity 11 (Positive)
Anti-Topoisomerase I Antibody (Scl-70 IgG)	< 20 RU/mL
Anti-U1-RNP Antibodies (Anti-U1RNP IgG)	< 5 U/mL
Anti-Jo-1 Antibody	Intensity 1 (Negative)
Anti PM-Scl 100	Intensity 2 (Negative)
Centromere B Antibody	Intensity 0
Anti-Mi-2 Antibody	Intensity 1 (Negative)
Muscle biopsy	Negative for inflammation and malignancy



reference of 0.8-1.8). In addition to the overlap syndrome (Dermatomyositis and Systemic Sclerosis), she was also diagnosed with possible subclinical hypothyroidism though TPO (Thyroid Peroxidase) and anti-TSH receptors antibodies were negative.

On subsequent review, she was initiated on immunosuppressive agents for dermatomyositis treatment using high dose prednisolone (1 mg/kg/day) and Azathioprine (2mg/Kg/day). A proton pump inhibitor was prescribed for gastro protection. She was advised to avoid exposure to cold temperature and wearing layers of warm, loose-fitting clothing, including socks and gloves to help improve Raynaud's symptoms. Angiotensin converting enzyme (ACE) treatment was postponed due to her normal kidney function and blood pressure. The patient has responded well to treatment and has shown progressive resolution of her symptoms including the skin lesions with her muscle enzymes now within normal ranges [See figure 1]. Prednisolone dose has been tapered down to below 0.5mg/kg/day to minimize side effects.

## DISCUSSION

We reported, for the first time in Zambia, the case of a 26-year-old black Zambian woman with SARS-Cov-2 infection who presented with worsening proximal myopathy. She presented with worsening features of dermatomyositis and systemic sclerosis. She had a positive autoantibody test to nuclear antigens (ANA), however she did not fulfil the criteria for SLE according to the 2019 EULAR/ACR classification for SLE<sup>11</sup>. Mixed connective-tissue disease (MCTD) was ruled out after obtaining a negative anti-U1-ribonucleoprotein (RNP) antibody and the absence of SLE.

Hence the diagnosis of an overlap syndrome with dermatomyositis and systemic sclerosis was made as the patient had classic features of two different rheumatic diseases with presence of specific autoantibodies.

Monti et al<sup>7</sup> described the clinical course of SARS-

Cov-2 infection in patients with chronic rheumatoid disorders. There are reports of symptoms mimicking connective tissue disease occurring at the early phase of SARS-cov-2 infection. Beydon et al<sup>12</sup> documented a case of MRI diagnosed myositis secondary to SARS-cov-2 infection. The association of muscle inflammation with interstitial pneumonia has been reported either with SARS-cov-2 infection or autoimmune myositis<sup>13</sup>.

Our patient reported history of proximal myopathy, Raynaud's phenomenon and skin diseases several months prior to the diagnosis of SARS-cov-2 infection, though weakness symptoms worsened during the time she had SARS-Cov-2 infection. It was therefore observed that the myopathy in the patient was not due to the SARS-cov-2 infection, however, it may have worsened it. She however presented with clinical and radiological features of heart failure secondary to cor pulmonale, which was attributed to possible pulmonary hypertension. Pulmonary arterial hypertension (PAH) is a major cause of morbidity and mortality in patients with connective tissue disorders. Histological findings include intimal proliferation and medial hypertrophy of pulmonary arterioles<sup>14</sup>.

Exposure to certain viruses or chemicals such as polyvinyl chloride and silica are other possible causes of myositis<sup>15</sup>. Our patient worked for a local large chemical company supplying products to the mining, agriculture, public health and other sectors. It is not clear if chemicals played a major role in the patient's symptoms, however the exposure was quite substantive as she was involved in acquisition and sale of all products at the company.

## CONCLUSIONS

In conclusion, inflammatory myopathy or worsening pre-existing myopathy should be considered as a cause for persistent respiratory failure and muscle weakness in patients with SARS-cov-2 infection. However, further studies are needed to elucidate the mechanisms, appropriate treatment, and long-term outcomes of muscular manifestations

associated with SARS-Cov-2 infection.

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## Author contribution statement

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## Competing interest statement

The authors declare no conflict of interest

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