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Case report

Rapidly progressive ischemic strokes and transient antiphospholipid syndrome during a mild SARS-CoV-2 infection

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Abstract. SARS-CoV-2 infection is associated with an increased risk of thrombotic events, especially during severe forms of disease. Here we describe the clinical history of a patient with a mild form of Covid-19 infection presenting with multiple cerebral ischemic lesions that evolved in an atypical way. (www.actabiomedica.it)

Key words: Covid-19, SARS-CoV-2, stroke, multiple, antiphospholipid, ischemic, mild

Introduction

Recent literature highlights that SARS-CoV-2 infections, especially in severe cases, are associated with an increased number of thrombotic events and thus sometimes lead to damage beyond the respiratory system (1, 2). While the reasons behind these events are not known, they are likely the result of various mechanisms (3), such as hypercoagulability states (4), hyperinflammation, endothelial damage (5), altered immune response of the host (6) and possibly dysregulation of angiotensin-converting enzyme 2 (ACE2) (7).

Multiple cases of multi-infarctual strokes in patients with a concomitant SARS-CoV-2 infection have been reported in literature (8-11). Some case-reports have also examined the occurrence of multiple strokes in patients with both a SARS-CoV-2 infection and a positivity to antiphospholipid autoantibodies (12, 13). All these reports describe patients whose condition was the result of the increased thrombotic risk linked with a severe presentation of the disease. Here, instead, we describe a patient presenting with a mild SARS-CoV-2 infection, first ever detected positivity to antiphospholipid antibodies and multiple small ischemic strokes. We also describe the atypical evolution of the ischemic lesions, which showed up with an excavated aspect after four weeks. A timeline showing a summary of the main steps in the patient's clinical history is shown in (Figure 1).

On March 18th, 2021, a 52-year-old black man attended the Emergency Room in Pordenone Hospital; he was born in Congo and had a history of arterial hypertension. The patient presented right arm weakness, confusion, speech alteration (motor aphasia), fever (38 °C) and shortness of breath. A SARS-CoV-2 infection was diagnosed on the same day, based on an RT-PCR test.

Blood pressure values were 169/110 mmHg. Hematic tests showed no sign of respiratory insufficiency (pH 7.51, pO2 77.5 mmHg, spO2 95.3% without oxygen supplementation, pCO2 35.4 mmHg, p/f 3.69

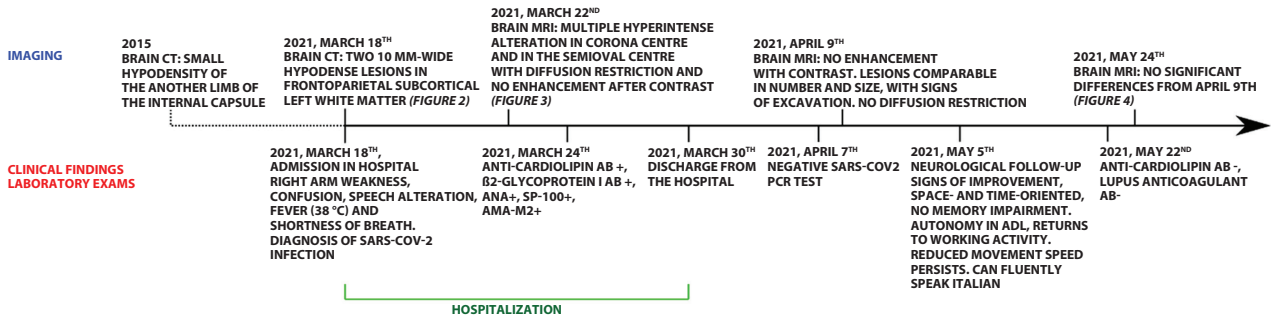

Figure 1. Clinical history timeline. Abbreviations: CT=Computed Tomography, MRI=Magnetic Resonance Imaging, Ab=Antibodies, ANA=AntiNuclear Antibodies, ADL=Activities of Daily Living.

mmHg), mild hypokalemia (3.1 mmol/L), LDH elevation (358 U/L) with an increase in inflammatory markers (CRP 3.4 mg/dL, PCT 0.05 μg/L), and normal D-dimer (363 FEU, normal value 0-500). Chest radiography showed a minimal consolidation in the lower lobe of the left lung. No visible alterations in were present in the EKG.

No ischemic lesion was present in a CT scan performed in 2015 for a persistent headache. The brain CT performed in Emergency Room revealed two 10 mm-wide hypodense lesions in frontoparietal subcortical left white matter, which were compatible with recent ischemic lesions (Figure 2).

Because of the Covid-19 infection, the patient was admitted in the Covid Medicine Department and was initially treated with acetylsalicylic acid 100 mg and low-molecular-weight heparin in deep venous thrombosis prophylactic dosage.

During hospitalization, the neurological symptoms and signs improved. The Covid-19 infection did not worsen and remained paucisymptomatic. Since there were no signs of pneumonia or acute respiratory distress, corticosteroids and oxygen supplementation were not added to therapy.

The patient underwent further exams to investigate the origin of his condition. On March 22nd, a brain MRI found multiple hyperintense alterations in the corona radiata and in the semioval centre in long-TR sequences, with diffusion restriction and no enhancement after contrast, compatible with recent ischemic lesions (Figure 3).

An echocardiography showed left ventricular hypertrophy. Electrocardiographic monitoring did not show atrial fibrillation or other alterations of the rhythm. An echo-color-Doppler of the supra-aortic arteries was normal, with no evidence of stenosis. On March 24th, hematic exams included in our vasculitis panel were positive for anti-cardiolipin IgM (mildly, 14 MPL U/mL), anti-β2-glycoprotein I IgG (67 U/mL), anti-nuclear antibodies (1:320, with a "multiple nuclear dots" pattern), and Sp100 and AMA-M2 Immunoblots. Lupus anticoagulant (LAC) antibodies were absent. Screening tests were negative for HIV, syphilis and *Borrelia*. Free S protein activity had a 60% reduction.

Radiologic signs of lung consolidation disappeared from chest radiography performed on March 29th.

Due to the laboratory findings, we requested a consultation with rheumatologists, who recommended that antiphospholipid positivity and S protein deficit be double-checked after 12 weeks from discharge. Anticoagulation therapy was not started, while anti-aggregation therapy was maintained and hydroxychloroquine administration was initiated. The patient was released from the hospital on March 30th. SARS-CoV-2 PCR test performed on oropharyngeal swab became negative on April 7th.

On April 9th, the patient underwent another MRI with contrast medium. Injection of the contrast medium did not cause enhancement of the previously described lesions, which were comparable in number and size to the findings of the March 22nd exam. However, more of them showed signs of excavation, even though diffusion restriction was no longer present.

At his first follow-up on May 5th, the neurological examination of the patient showed signs of improvement,

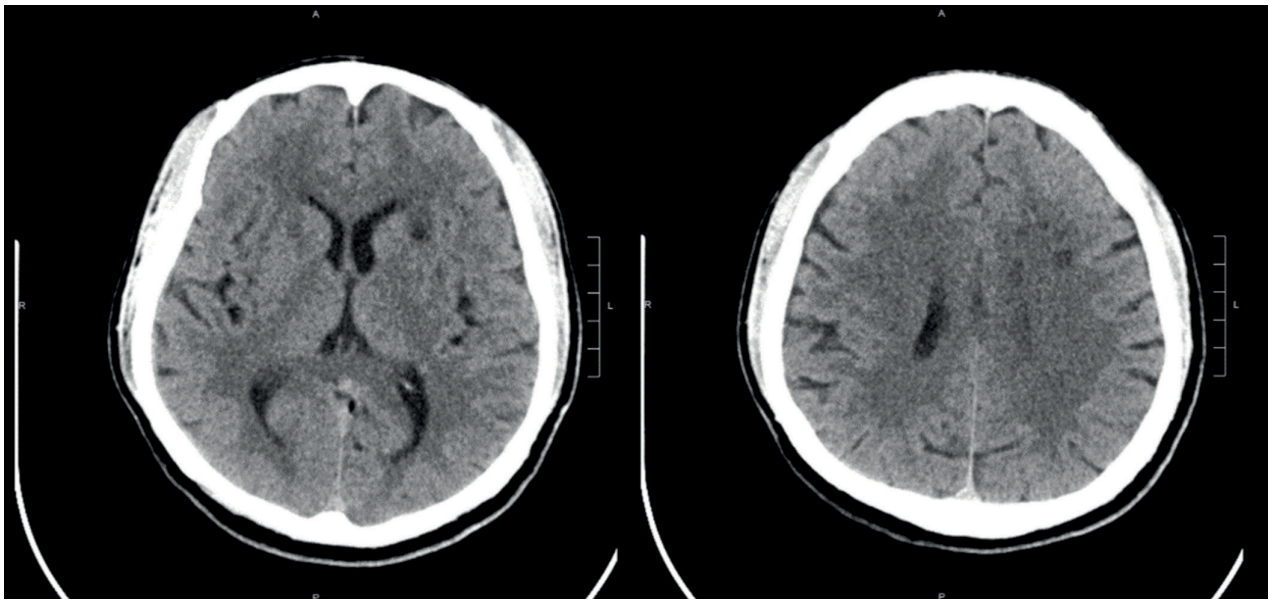

Figure 2. Brain CT scan at admission, showing two 10 mm-wide hypodense lesions in frontoparietal subcortical left white matter

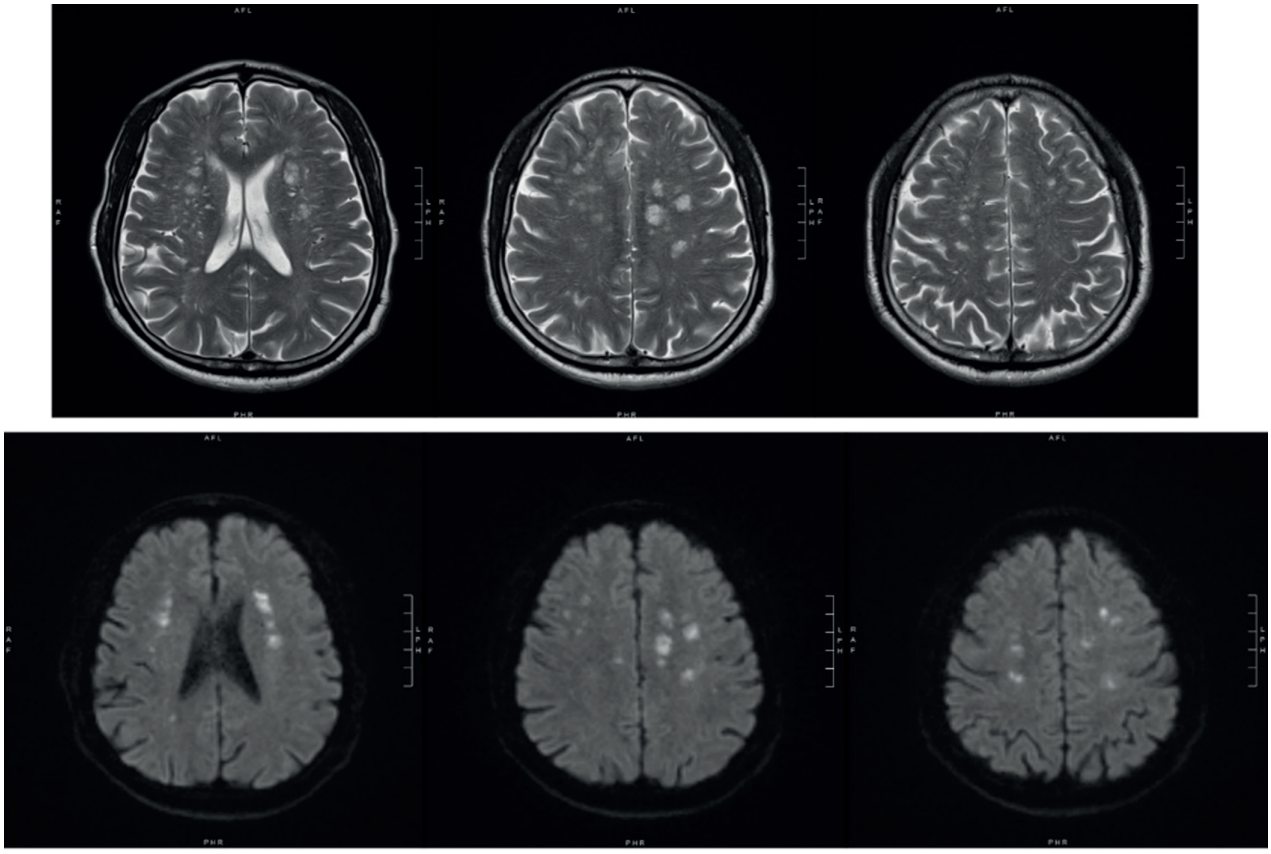

Figure 3. sections from the first MRI exam, performed on March 22nd. T2 scans are shown on the upper row, while the lower row contains DWI scans showing multiple signal alterations compatible with ischemic lesions.

as he had become well oriented in time and space and did not show any memory impairment. He regained autonomy in activities of daily living (ADL) and went back to work, though with a reduced movement speed. He was able to speak fluently in Italian.

The MRI exam was repeated on May 24th, and the findings were comparable to the previous ones (Figure 4).

When tested again on May 22nd, lupus anticoagulant (LA) antibodies levels and anti-cardiolipin antibodies (ACA) levels were negative (LA SCT Screening 0.96; DRVV Screening 0.85; ACA IgG 3.5 GPL U/mL; IgM 3.9 MPL U/mL). Free S protein activity was 69% (normal values: 50-130%).

A follow-up by an infectious disease specialist on June 1st found no alterations in the cardiopulmonary system, no palpable lymph nodes in the axillary, cervical and inguinal regions, and no skin lesions. Based on the stability of the lesions documented by the MRI exams and the improvement of his medical state, the specialist supported SARS-CoV-2 as the likely cause of the patient's disease.

Conclusions

To our knowledge, this is the first reported case of multiple cerebral ischemic lesions in a patient with a mild SARS-CoV-2 infection. We suggest that the transient anti-phospholipid syndrome presented by this patient might have been due to his Covid-19 infection. Clinicians should be aware that infarctions may occur even in mild forms of infection and could evolve in atypical patterns such as the excavations seen during our patient's follow up.

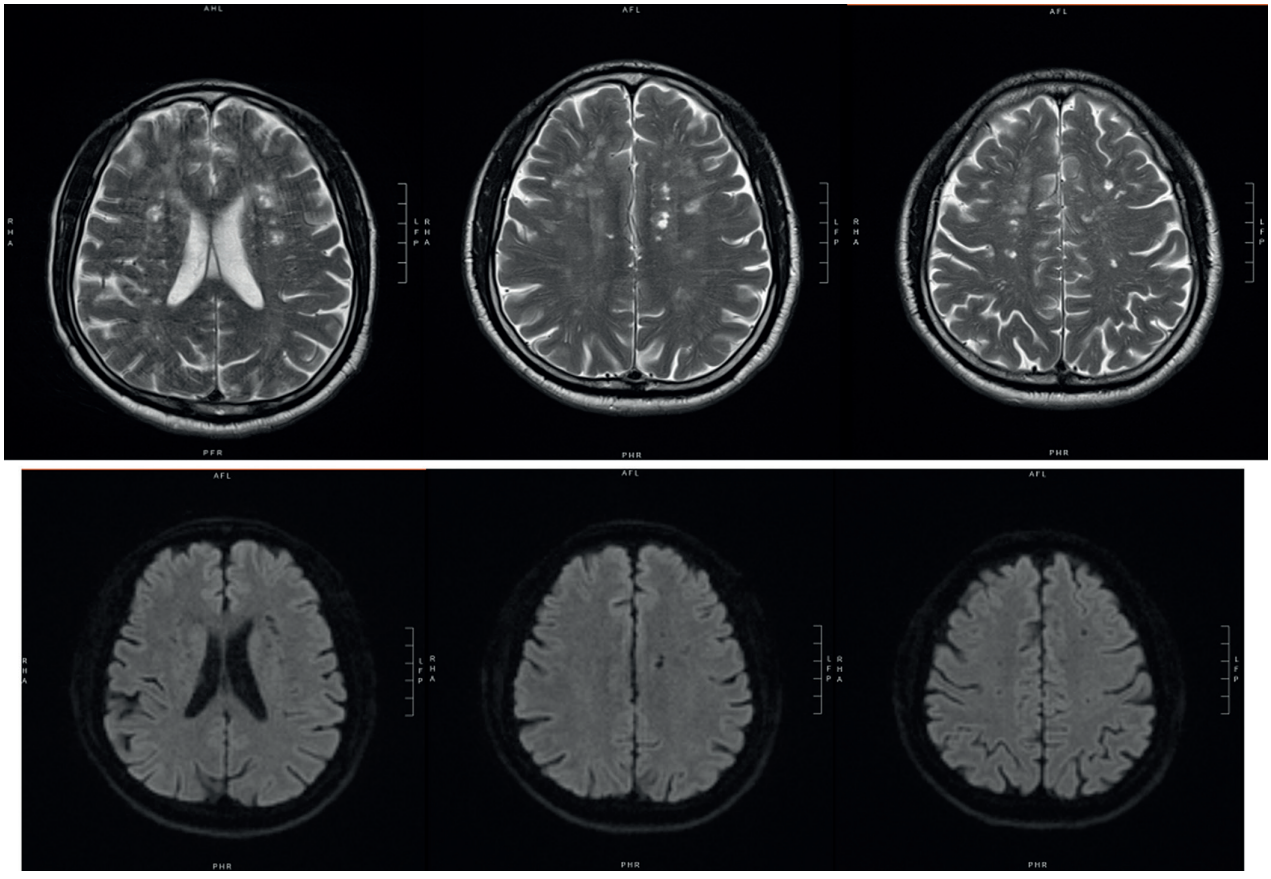

Figure 4. sections from the last MRI exam. As in the previous figure, the upper row shows T2 scans and the lower contains DWI scans. After about 2 months from the admission, the ischemic lesions showed signs of excavation.

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Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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