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COVID-19 Case Report

Treatment-Resistant Acute Upper Limb Ischemia in a Patient With Systemic Lupus Erythematous and Concomitant SARS-CoV-2 Infection: A Case Report

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To describe the case of a young female patient, affected by Systemic Lupus Erythematous, hospitalized for severe SARS-CoV-2 infection pneumonia and presenting a treatment-resistant acute upper limb ischemia.

Two days after hospital admission, the patient suffered sudden right upper limb pain associated with mild functional impairment. At physical examination, radial and ulnar pulses were absent, and no flow signal was detected at duplex ultrasound scan. Therefore, an acute limb ischemia diagnoses was posed. Despite several surgical and endovascular revascularization attempts, the patient underwent an above the elbow amputation in 10th postoperative day from first surgical embolectomy, and she died for respiratory failure 25 days after hospitalization.

Our case of acute upper limb ischemia seems to confirm that clinical manifestation and fate of thrombotic disorder in COVID-19 patients could be precipitated by concomitant autoimmune diseases.

Infection sustained by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), also known as coronavirus disease 2019 (COVID-19), could presents with few or no symptoms. Nevertheless, in some cases, COVID-19 could develop a severe life-threatening disease characterized by systemic inflammation, microvascular damage and coagulopathy.[1]

Inflammation, thrombosis and microvascular obstruction may lead to multi-organ dysfunction, including myocardial injury, regardless the presence of atherosclerotic coronary disease.[2] Several cardiovascular manifestations, including thrombosis, arrhythmias, heart failure and shock[3,4] are observed during COVID-19 infection. Thrombosis is often clinically evident as venous thrombosis or pulmonary embolism, but, in about 4% of cases, thromboembolic complications determine arterial thrombosis.[5]

Male sex, older age, obesity, arterial hypertension, and atherosclerotic disease, well-known conditions predisposing to endothelial dysfunction, are significantly related to cardiac and vascular complication during COVID-19 disease.[3,6] Furthermore, COVID-19 infection likely induces or exacerbates autoimmune disease in predisposed patients, although in absence of definitive data.[7-13]

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The aim of this report is to describe the case of a young female patient, affected by Systemic Lupus Erythematous (SLE), observed in our Hospital for severe pneumonia related to SARS-CoV-2 infection, presenting a treatment-resistant acute upper limb ischemia.

CASE REPORT

A 47-year-old female patient came to our Hospital Emergency Department for sudden onset of cough, dyspnea, and fever. The patient was affected by SLE under treatment with low-dose oral corticosteroids. At arrival, arterial blood pressure was 110 of 60 mm Hg, heart rate 100 beats/min, and oxygen saturation 86%. Blood test revealed leukocytosis 25.700/uL associated with high systemic inflammatory marker value (C-reactive protein, 31.17mg/dL), and presence of lupus anticoagulant (LA). Urgent computed tomography showed the presence of a bilateral interstitial pneumonia. Oropharyngeal molecular swab test for SARS-CoV-2 infection was positive, and the patient was admitted in intensive care unit, under non-invasive mechanical ventilation. Prophylactic therapy with low molecular weight heparin was immediately started (6.000UI/die), and corticosteroid oral therapy was not discontinued.

Two days after hospital admission, patient suffered of acute right upper limb ischemia, associated with mild functional impairment. At physical examination, radial and ulnar pulses were absent, and no flow signal was detected at duplex ultrasound scan (DUS). An urgent surgical embolectomy was performed with optimal immediate technical results, and immediate radial and ulnar pulses reappearance. After surgery, unfractionated heparin was administered as a continuous intravenous infusion, aiming at an aPTT ratio of 2–2.5.

In second postoperative day, the patient suffered from a recurrent upper right limb ALI, and a further surgical embolectomy, plus brachial artery angioplasty with autologous venous patch, was performed. Even at that time, technical and clinical success were immediately achieved.

Nevertheless, in less than 24 hours, clinical condition of the upper limb worsened again, and at DUS examination no peripheral pulses were present. Therefore, a selective right brachial artery angiography, via percutaneous common femoral artery access, was performed, revealing acute occlusion of brachial, radial, and ulnar arteries, and no flow to the palmar arch. Endovascular mechanical thrombectomy (Cat-6, and Cat-3 Indigo System Catheters; Penumbra Inc, Alameda, CA) was attempted with suboptimal technical result, and partial flow restoration. Local fibrinolytic therapy (Urokinase 75.000UI/hour) was administrated for the subsequent 48 hours, without heparin discontinuation.

After 48 hours, angiography showed no flow restoration, but contrast medium extravasation form brachial artery patch (Fig.1). In order to continue local fibrinolytic therapy, an endoconduit across brachial and radial arteries via covered stentgrafts implantations (3 × 16,3 × 24, and 5 × 40mm BeGraft; Bentley Innomed GmbH, Hechingen – Germany) completely excluded patch extravasation.

Though, in 10th postoperative day from first embolectomy, due to the absence of flow restoration and the loss of upper limb viability (complete functional impairment, anesthesia, and persistent cyanosis), an above-the-elbow amputation was performed.

Finally, 5 days after demolitive intervention, patient's general and respiratory conditions worsened till requiring invasive mechanical ventilation, and exitus occurred in 25th day after hospitalization, due to COVID-19 diffused pneumonia.

DISCUSSION

The present experience reports the inauspicious outcome of SARS-CoV-2 infection, complicated by treatment-resistant upper ALI in a young female patient affected by SLE.

COVID-19 disease is a severe acute respiratory syndrome, characterized by symptoms involving the upper and lower airways, fever, cough, and dyspnea, which can evolve to acute respiratory distress syndrome, shock, and multiple organ failure. Moreover, the disease is associated with a state of hypercoagulability, increasing the incidence of venous and, less often, arterial thrombo-embolic events and cardiovascular complication.[2,14]

Recently, a potential link between COVID-19 and autoimmune disorders has been postulated, even if not clearly demonstrated. Interestingly, both COVID-19 and SLE are prone to present multi-organ involvement, pulmonary complications, myocarditis, cytopenia, and coagulation disorders. Moreover, the treatment of SLE includes immunosuppressants and corticosteroids that could increase patients' vulnerability to infections. On the other hand, recent studies have shown that immunosuppressive therapies seem to reduce systemic inflammation and the risk of developing

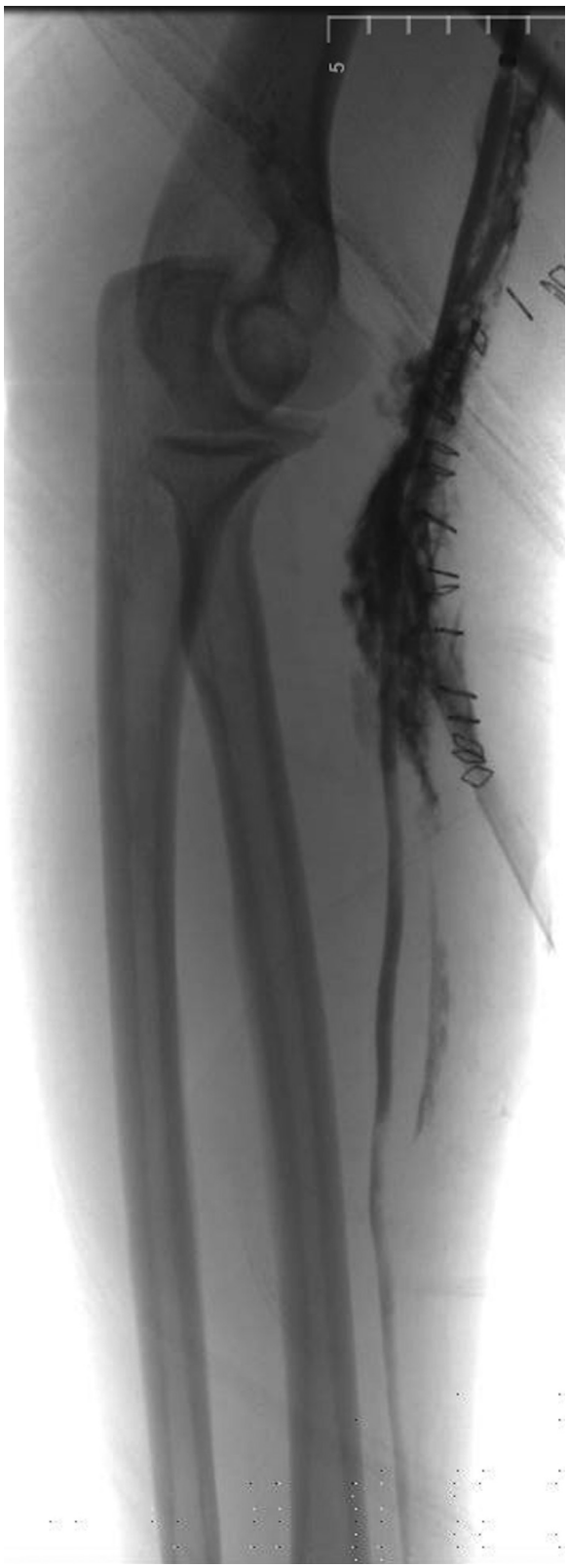

Fig. 1. Digital subtraction angiography showing contrast medium extravasation from brachial artery patch.

respiratory distress syndrome in COVID-19 patients.[7-14]

Despite current studies failed to achieve any statistically significant difference in outcomes between COVID-19 patients with and without rheumatic disease, a potentially interesting correlation was detected regarding value of activated partial-thromboplastin time (aPTT) and its related thrombotic risk.

Indeed, prolonged aPTT has been observed in COVID-19 patients at higher rates than other patients, suggesting that COVID-19 may cause or exacerbate blood clotting abnormalities. LA, a type of autoantibody which can cause hypercoagulability, was identified as the primary cause of prolonged aPTT in 91% of patients with aberrant results. These findings were replicated in a report that found 45% of severe COVID-19 patients and 87.7% of ICU patients with an abnormal aPTT also had positive LA results. While LA is not diagnostic of SLE, antiphospholipid antibodies, including LA, are found in approximately 50% of SLE patients and SLE is considered a risk factor for both venous and arterial thrombosis. Although an elevated risk of thrombosis among the subset of COVID-19 patients with SLE has not yet confirmed, abnormal clotting observed in both COVID-19 and SLE suggests that patients affected by both risk factors may require additional monitoring for thrombosis.[7,12]

All those are really consistent with the here presented case: our patient had high LA level and this, associated to SARS-CoV-2 infection thrombotic disorders, could potentially explain the dramatic outcome observed after acute upper limb ischemia, despite several revascularization attempts performed via pharmacological, surgical and endovascular techniques.

Lastly, about the use of a pharmacological adjuvant therapy (thrombolysis) to achieve revascularization, it should be underlined that urokinase administration is a well-known risk factor for potentially life-threatening hemorrhagic complications especially recently surgically treated patients under anticoagulant therapy.[15] Nevertheless, in present study an outside instruction for use indication to fibrinolytic therapy was given aiming to obtain limb salvage in a such compromised patient.

CONCLUSIONS

Our case of acute upper limb ischemia confirms that clinical manifestation and fate of thrombotic disorder in COVID-19 patients could be precipitated

by concomitant autoimmune diseases and high LA plasmatic level.

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