LETTER TO THE EDITOR

Free flap reconstruction of distal extremity necrosis after COVID-19-related multisystem inflammatory syndrome in a pediatric patient

Dear Editor,

Multisystem inflammatory syndrome in children (MIS-C) is a recently recognized spectrum of disease symptoms and signs associated with COVID-19 infection. As defined by the Centers for Disease Control and Prevention (CDC), MIS-C is diagnosed in individuals aged <21 years presenting with fever; laboratory evidence of inflammation; clinically severe illness requiring hospitalization; multisystem (≥2) organ involvement (dermatologic, cardiac, renal, respiratory, hematologic, gastrointestinal, or neurological); a positive test for current or recent SARS-CoV-2 infection, and no plausible alternative diagnoses. (Centers for Disease Control and Prevention (CDC), 2019) Among the clinical scenarios of multisystem compromise, vascular manifestations at the foot level (including edema, exanthems, chilblains, ischemia, and distal necrosis) are occasional signs that have been described in various reports. (Jimenez-Cebrian et al., 2021)

We present a 7-year-old female patient with COVID-19 disease and acral necrotic lesions of the lower limbs that underwent microvascular tissue transfer. The patient was admitted with a diagnosis of COVID-19 pneumonia (SARS-CoV-2 detected at RT-PCR testing). Twelve days later, ischemic/livedoid lesions associated with severe pain, rapidly progressing to necrosis, appeared in the patient’s feet. The patient’s initial investigations revealed hemoglobin (Hb) of

![Preoperative view of patient's distal lower extremities.](image1)

![Immediate postoperative view.](image2)

![Postoperative CT-angiography showing adequate perfusion through the dorsalis pedis artery.](image3)

![A well-perfused flap, adequately healed surgical wounds, and normal ambulation with satisfactory restoration of the right foot contour was noted 10 weeks after surgery.](image4)

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12.9 g/dl, a white blood cell count (WBC) of 8280/μl (with 73% of neutrophils), and a platelet count of 454,000/mm³. Other abnormal laboratory results exhibited elevated C-reactive protein (CRP, 57.9 mg/dl) and mild elevation of activated partial thromboplastin time (aPTT, 46.2 s). Autoimmunity serological analysis showed negative values for antinuclear antibodies (ANA), anti-neutrophil cytoplasmic antibodies (ANCA), and anti-cardiolipin antibodies (IgM: 0.7 MPL; IgG: 1.2 GPL). The D-dimer value (0.28 mcg/ml) and prothrombin time (PT, 13.5 s) levels appeared to be within the normal range. The patient also presented normal liver enzymes, serum electrolytes, and renal functions. During the hospital stay, the patient did not require administration of vasopressors/inotropes. Several weeks after the onset of symptoms, once necrosis delimited as proximal as the distal metatarsal region bilaterally (Figure 1a) and the patient had recovered from the respiratory disease, surgical debridement was carried out, which left the 1st, 2nd, and 3rd metatarsal bones on the right foot (dorsal and plantar surfaces) and the distal end of the 1st metatarsal bone on the left foot (dorsal surface) exposed. In a second stage, microsurgical reconstruction of the right foot with coverage of the exposed bony surface was performed using a free myocutaneous latissimus dorsi flap (Figure 1b). The dorsalis pedis were used as recipient vessels, and anastomoses were performed in an end-to-end fashion (Figure 1c). Preoperatively, a computed tomographic angiography had shown normal patency of the popliteal, peroneal, tibialis posterior, tibialis anterior, and dorsalis pedis arteries. In the same stage, a V–Y advancement flap was used to cover the defect on the 1st metatarsal distal region on the left foot. The postoperative course was uneventful, with no evidence of vascular-related complications. Abnormal postoperative laboratory tests included a Hb of 9.7 g/dl, platelet count of 404,000/mm³, CRP of 33.7 mg/dl, and aPTT of 44.2 s. All other postoperative laboratory investigations were within normal limits. Enoxaparin was administered postoperatively at a dose of 1 mg/kg/dose subcutaneously every 12 hours for 4 days. Ten weeks after surgery, the patient exhibited a well perfused flap, all the surgical wounds adequately healed, and normal ambulation with satisfactory restoration of the right foot contour (Figure 1d).

Hypercoagulability is one of the most challenging scenarios for microsurgeons. As recently described, COVID-19 is a systemic disease with a potential serious hematological derangement that can include elevated D-dimer levels and platelet count, PT and aPTT prolongation, increased fibrin degradation products, and, less frequently, disseminated intravascular coagulation (DIC), possibly representing a hypercoagulable state. (Kanatas et al., 2020; Mangialardi et al., 2021) Moreover, current literature suggests that prolonged aPTT in patients with severe COVID-19 can be related to the presence of lupus anticoagulant (LAC), which can, in turn, be associated with a hypercoagulable tendency promoting the onset of microthrombosis. (Bowles et al., 2020) Recent reports on MIS-C after SARS-CoV-2 infection have also shown a frequent overlap of its clinical features with Kawasaki disease and other viral-associated hyperinflammatory syndromes, making an accurate diagnosis challenging. (Yilmaz Çiftdogan et al., 2022) Pathogenesis of Kawasaki-like MIS-C is thought to be immune complex-mediated, which derives in activation of inflammatory cells (including monocytes and neutrophils) and recruitment of platelets, resulting in thrombocytosis (commonly seen in Kawasaki disease and presented in our patient). (Lo & Newburger, 2018) Although there are several studies aiming to describe the pathophysiolog and clinical characteristics of this condition, reports including specific recommendations for patients with MIS-C who also have surgical indications are mainly null. With a non-surgical focus, it has been suggested that, due to the presumable hypercoagulable state induced by this condition, patients with MIS-C should be treated with therapeutic doses of low-molecular weight heparin and, even so, be followed closely in terms of thromboembolism risk. (Keskin et al., 2022) On the other hand, patients with indications for microvascular surgery in which formal risk assessment and/or medical history indicates high perioperative thrombotic risk are also generally recommended to have a preoperative consultation with hematology. (Pannucci et al., 2015)

While robust data with which to make strong recommendations is still scarce, in light of our results and limited current evidence, (Morales-Perez et al., 2021) we suggest that free flaps should still be considered in patients with COVID-related MIS-C that had undergone previous hematological investigations, that are being strictly monitored for the risk of thromboembolic events, and that are under adequate antithrombotic therapy using therapeutic doses of low-molecular weight heparin, especially in those in which reconstruction cannot be differed.

**DATA AVAILABILITY STATEMENT**

The data that support the findings of this study are available from the corresponding author upon reasonable request.

**ETHICS STATEMENT**

This study protocol was approved by the institutional ethics committee for research and all procedures performed involving humans were performed in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from the participants of the study for authorized use of their pictures for teaching and medical purposes.

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