Sr, With the coronavirus disease 2019 (COVID-19) pandemic, we are discovering that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has properties to induce a dysregulated immune response that exceed the simple respiratory infection [1]. Several cases or case series of immune diseases have been reported concomitantly with SARS-CoV-2 infection [2, 3]. Systemic capillary leak syndrome is a rare immune disorder that evolves with repeated episodes of pseudo-shock that can occur spontaneously or can be triggered by viral infections. Here we report the case of a 38-year-old male who presented a mild COVID-19 infection concomitantly with a first flare of systemic capillary leak syndrome.

A 38-year-old man with no medical history was referred to the emergency department for diffuse abdominal pain, vomiting and malaise. He had a 1 week history of diffuse myalgia, shortness of breath, weight gain of 9 kg and bilateral leg oedema. His condition quickly progressed to shock, with blood pressure of 61/47 mmHg, respiration rate 26 per min with 4 l per min of oxygen and a body temperature of 33.4 °C. The patient was admitted to the intensive care unit.

Laboratory tests revealed lactic acidosis (pH at 7.00 and lactate at 5.7 mmol/l) and acute kidney failure (serum creatinine level 147 µmol/l). A blood count showed haemoconcentration (haemoglobin level 249 g/l and haematocrit at 70.5%). Paradoxically, biochemical assays revealed low serum proteins at 26 g/l and low serum albumin at 16 g/l. White blood cells were elevated at 34 900/mm³ with neutrophils at 32 100/mm³. Platelets were within the normal range at 403 000/mm³. There was no liver failure, no proteinuria and no albuminuria. Echocardiography showed normal myocardial function with signs of hypovolaemia. Wide-spectrum empirical antibiotic therapy was initiated as well as fluid resuscitation with 6 l of crystalloids and inotropic support (noradrenalin).

Because of neurologic deterioration, the patient was intubated. Bacterial blood cultures were negative. An abdomen and pelvis CT scan showed wall thickening of the sigmoid colon. Chest CT scan revealed a few ground glass opacities. SARS-CoV-2 infection was confirmed by RT-PCR assay by means of an oropharyngeal swab. The ferritin was elevated (1445 µg/l). At day 2 the patient was extubated. Evolution was favourable and the patient was transferred at day 6 to a standard care unit. The patient was discharged 15 days after his admission.

Diagnosis of systemic capillary leak syndrome was made by the association of hypotension, hypovolaemia, haemoconcentration and hypoalbuminemia without albuminuria. An aetiological work-up was negative: no toxic or medication ingestion; no tumour on CT scan of the thorax, abdomen and pelvis; no polycythaemia vera with the absence of mutation of V617F or exon 12 of the JAK2 gene; no immune disease (search for ANA was negative); no thyroid disorders (thyroid-stimulating hormone at 3.9 mUI/l); and no argument for anaphylaxis or angioedema (C1 inhibitor level elevated). Serological tests for human immunodeficiency virus and hepatitis C virus were negative. The patient had hepatitis B immunity post-vaccination. IgG, IgA and IgM levels were in the normal range (7 g/l, 2.2 g/l and 1.8 g/l, respectively). We detected a monoclonal IgG kappa on serum immunofixation.

Systemic capillary leak syndrome is a rare disorder that can be secondary to blood malignancies, immune disorders, toxins, medication, infections or idiopathic (Clarkson’s disease) [4]. The evolution of systemic capillary leak syndrome is marked by repeated bouts of pseudo-shock that can occur spontaneously or can be triggered by infections, especially viruses responsible for upper respiratory tract infections. Infections with influenza virus, syncytial respiratory virus or West Nile virus were identified in 52/132 (39%) patients with idiopathic capillary leak syndrome in two cohorts [4]. Pineton de Chambrun et al. [5] recently reported a case of a fatal relapse of systemic capillary leak syndrome during a SARS-CoV-2 infection but, to date, our case is the first to describe systemic capillary leak syndrome elicited by the SARS-CoV-2. Systemic capillary leak syndrome is the consequence of secretion of inflammatory mediators triggered by viruses leading to an increase in vascular permeability via disruption of adherens junctions that disjoin endothelial cells. Systemic capillary leak syndrome mechanisms could be due to massive secretion of pro-inflammatory cytokines in response to SARS-CoV-2 [6]. Direct toxicity of the virus on vascular endothelium permeability could be another explanation, which was described in viral haemorrhagic fever (Hantavirus, dengue) [7].

In conclusion, we think that it is not a coincidence that a first episode of systemic capillary leak syndrome, which is a very rare disease, occurred simultaneously with a respiratory infection caused by SARS-CoV-2. Clinicians should be aware that SARS-CoV-2 has
properties to induce an immune dysregulation and promote immune diseases.

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