Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Contribution of authors

AB wrote the article and administered bacteriophages to the patient. EH and EC managed the patient in the infectious diseases department and reviewed the article. CP tested and prepared bacteriophages and reviewed the article. JR characterised the *S. aureus* strain, provided it to CP, wrote and reviewed the article. LL performed the last free flap surgery and reviewed the article. MP was the neurosurgeon in charge of the patient and reviewed the article.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments.

Disclosure of interest

C.F. is employed by the commercial company Pherecydes.

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COVID-19 as a cause of immune thrombocytopenia

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Immune thrombocytopenia (ITP) is a rare autoimmune disease characterized by isolated thrombocytopenia below 100,000/μL and no other cause of thrombocytopenia [1]. Clinical presentation is heterogeneous from absence of symptoms to mild mucocutaneous bleeding or even life-threatening hemorrhage. ITP can be a primary condition or secondary to other diseases especially viral infections. ITP has been described during the course of several viral infections: HIV, EBV, CMV, HCV but only once during severe acute respiratory distress coronavirus 2 (SARS-CoV-2) [2].

On April 2020, an 84-year-old man was admitted to hospital for a 10-day history of cough and progressively worsening dyspnea. He had medical history of polymyalgia rheumatica and essential tremor. His medications were prednisone 5 mg/day and propranolol. On arrival, the patient required oxygenation therapy with a flow rate of 4 L/min. Physical examination showed bilateral crackles on auscultation. Platelet count was 330,000/μL. CT scan showed diffuse ground-glass opacities and condensations involving more than 50% of pulmonary parenchyma highly suggestive of SARS-CoV-2 infection and sub-segmental pulmonary embolism. SARS-CoV-2 diagnosis was confirmed using RT-PCR on nasopharyngeal swabs. The patient received an antibiotic therapy with ceftriaxone, therapeutic anticoagulation with rivaroxaban, and prednisone was replaced by hydrocortisone. The patient remained febrile, with oxygenation therapy dependence during the first five days. On day 6, sudden onset of spontaneous macroscopic hematuria and bilateral epistaxis was observed. Platelet count was then at 4000/μL with no schistocytes on blood smear, hemoglobin level

was at 12.7 g/dL, WBC at 9200/μL, lymphocyte counts at 330/μL. Fibrinogen was at 7.3 g/L and INR was at 1.52. Vitamin B9 and B12 were normal. Autoimmune workup did not reveal any ENA, ANCA, and platelet antibodies. The search for antiphospholipid antibodies showed a lupus anticoagulant antibody.

As immune thrombocytopenia was the most relevant diagnosis and due to severe bleeding, we started prednisone (1 mg/kg/day) and one course of intravenous immunoglobulins 1 g/kg. The day after, platelet count was at 57,000/μL, and at one week it was at 155,000/μL. Due to the patient's altered condition and the rapid rise in platelet count, we did not perform bone marrow aspiration.

Acute ITP can be triggered by many viruses. An ITP flare has recently been described during Zika virus infection [3]; and once during non-symptomatic infection with SARS-CoV-1 [4]. We describe here the second case of SARS-CoV-2-induced ITP.

COVID-19 is an emerging pandemic that appeared in December 2019. COVID-19 is caused by SARS-CoV-2, responsible for severe pneumonia in less than 20% of cases. Thrombocytopenia is considered a poor prognostic factor during SARS-CoV-2 infection [5]. However, even if platelet counts are significantly lower in severe patients, it rarely decreases below 100,000/μL.

COVID-19 thrombocytopenia could be secondary to direct platelet-virus interaction via pathogen recognition receptors (PRR). This interaction leads to platelet activation and subsequent clearance by the reticuloendothelial system [6]. It could also be secondary to sepsis.

In our case, thrombocytopenia is lower than what is usually observed during COVID-19 and may be secondary to an immune-related mechanism. Indeed, an autoimmune process can be induced by many viruses by several mechanisms. The most relevant mechanism is molecular mimicry between the virus component and platelet glycoproteins [7]. Interestingly, Zhang et al. demonstrated that several HCV core-envelope peptides shared molecular mimicry with glycoprotein IIIa, a part of an integrin complex found on platelets. Those peptides could induce the production of antibodies which acquire the ability for platelet fragmentation [8]. To date, no sequence homology between SARS-CoV-2 and platelet components has been described. Moreover, the recognition of SARS-CoV-2 by PRR (mostly TLR7) could stimulate autoreactive B cells and then induce the production of autoantibody directly against platelet glycoprotein. Median time for seroconversion after onset of SARS-CoV-2 infection is approximately 12 days; then RNA detectability decreases from the second week of the infection [9].

In our case, ITP occurred on day 16 after the first symptom of COVID-19. The suddenness and severity of thrombocytopenia could be explained by the patient's advanced age as coronavirus induced higher antibodies production in older people [10]. Polymyalgia rheumatica is usually not associated with ITP and as cases of drug-induced ITP, i.e. rivaroxaban and ceftriaxone, have very rarely been reported, the best explanation for thrombocytopenia was virus-induced ITP. The clinical and biological remission with steroids and intravenous immunoglobulins confirmed this hypothesis.

SARS-CoV-2 is an infectious agent to be listed as an ITP-inducing virus. Urgent treatment of ITP, including corticosteroid therapy, should not be delayed.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments.

Contribution

SH designed the study. SH collected the data and wrote the initial draft.

All authors provided clinical data of patients, contributed to editing the article, and approved the final version of the article.

Disclosure of interest

The authors declare that they have no competing interest.

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