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COVID-19-induced thrombocytopenia

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Introduction

The most common symptoms seen in patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are fever, cough, asthenia, or dyspnea [1]. Thrombocytopenia and lymphopenia are the most frequent hematological abnormalities observed in patients with SARS-CoV-2 infection [2, 3]. The mechanisms by which thrombocytopenia occurs are not yet known. However, it was suggested that it could be related to the direct effect of the virus on hematopoiesis, cytokine storm, an increase of autoantibodies and immune complexes, and increased consumption by platelet activation, aggregation, and microthrombi formation [4]. We present three cases of thrombocytopenia after a acute, highly lethal pneumonia coronavirus disease 2019 (COVID-19).

Case 1

A 76-year-old male presented to the emergency room with epistaxis and petechiae in the lower limbs 15 days after discharge of COVID-19. The patient had several pathologies: hypertension, dyslipidemia, ex-smoker with chronic obstructive pulmonary disease (COPD), and carrier of an aortic prosthetic tube since 2008 anticoagulated with rivaroxaban, he was under treatment with methotrexate due to rheumatoid arthritis. In 2018, a nephroureterectomy was done due to a urothelial carcinoma and in complete remission since then. The patient was previously admitted for 8 days due to bilateral pneumonia with a positive nasopharyngeal swab for SARS-CoV-2 RNA detected by quantitative reverse transcription polymerase chain reaction (*q*RT-PCR). He was treated with hydroxychloroquine, azithromycin, lopinavir/ritonavir, ceftriaxone, and corticosteroids. Anticoagulated with low-molecular-weight heparin (LMWH) during admission. The patient always maintained a platelet count (PLT) of over 150,000/mm^3.

When the patient presented with epistaxis and petechiae was admitted to the emergency room he had a blood pressure (BP) of 122/54 mmHg, heart rate of 89 bpm, and oxygen saturation of 95% while he was breathing ambient air. Urgent laboratory tests revealed a PLT of 16,000/mm^3, hemoglobin (Hb) – 15.6 g/dL, white blood cells (WBC) – 5.8 x 10^3/mm^3, lymphocytes – 0.93 x 10^3/mm^3. Prothrombin time (PT) – 13.4 s, activated partial thromboplastin time (aPTT) – 34.1 s, D dimer – 0.52 mg/ml. At that time, he continued with positive PCR for SARS-CoV-2 in the nasopharyngeal swab. Peripheral blood smear showed isolated thrombocytopenia without morphological alterations. Direct and indirect Coombs tests conducted were negative. Anti-PF4-heparin antibodies test proved negative. Autoimmune workup revealed positive antinuclear antibodies (ANA) and negative DNA. Bone marrow aspiration didn´t show morphological cellular disorders, compatible with peripheral thrombocytopenia. Viral serology studies for human immunodeficiency virus (HIV) and hepatitis C virus (HCV) were negative. He had hepatitis B virus (HBV) passed (HBsAg negative, positive Ac. HBs, and Ac. HBc) with negative PCR for DNA-HBV. Suspecting that SARS-CoV-2 was a causal factor in immune thrombocytopenia, we suspended rivaroxaban and then gave treatment with immunoglobulins (IVIG) at a dose of 0.4 mg/kg/day for 5 days and corticosteroids at 1 mg/kg/day was started. PLT after the second dose of IVIG reached to 30,000/mm^3. At this point, anticoagulation with enoxaparin 20 mg/day was reinitiated, which was gradually increased by adjusting the dose to platelet count. Four days after treatment, after reaching PLT – 68,000 mm^3, anticoagulation was administrated at therapeutic doses. The patient showed good evolution, without bleeding, and four days after admission, he was discharged home with a plan to be followed up in 1 week for repeat laboratory tests. One week later he had PLT – 134,000/mm^3 with a descending corticosteroids treatment.

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Case 2

A 30-year-old male presented an episode of spontaneous epistaxis with a PLT of 50,000/mm^3 on the second day of admission due to COVID-19. The patient had a previous history of a cortico dependent chronic ITP since childhood. In July 2018, he began treatment with Eltrombopag without response. In January 2019, a splenectomy was made with a complete response since then. In his last analytical control, he had PLT – 299,000/mm^3. He went to the emergency room on March 17, 2020, with fever and cough of four days of evolution. Upon arrival, he presented a BP – 141/85 mmHg, heart rate – 126 bpm, temperature – 38°C, and 98% saturation on room air. Laboratory test revealed Hb – 17 g/dL, PLT – 60,000/mm^3, WBC – 12.77 x 10^3/mm^3, lymphocytes – 1.24 x 10^3/mm^3, coagulation: INR – 1.21, prothrombin activity – 74%, aPTT – 31.1 s, D dimer – 0.1 g/dL. The physical examination revealed no petechiae or bruising. An emergency chest radiograph showed bilateral bibasal infiltrates. The nasopharyngeal swab was positive for SARS-CoV-2. The patient was admitted and treated with lopinavir/ritonavir, hydroxychloroquine, and ceftriaxone.

After six days, he deteriorated radiologically with increasing oxygen requirements, with PLT around 50,000–85,000/mm^3. He received a high dose of corticosteroids and a single dose of tocilizumab. After 24 h, he reached PLT – 340,000/mm^3 and the clinical improvement was observed, with a progressive decrease in oxygen requirement. He was discharged after 10 days with PLT – 666,000/mm^3 and without oxygen.

Case 3

A 38-year-old female patient, with no relevant medical history, was diagnosed with ITP from the age of 4. She was splenectomized in June 2017 for a lack of response to treatment with corticosteroids and romiplostim. In October 2019, she was diagnosed with complete thrombosis of the left jugular vein. She was anticoagulated with acenocoumarol at the time of inclusion. A study of hereditary and acquired thrombophilia revealed heterozygous mutation of the prothrombin gene. In March 2020, she came to the emergency room due to bruising with minimal trauma and petechiae in legs without other associated symptoms since 3 weeks of evolution. Laboratory tests revealed PLT – 11,000/mm^3. Acenocoumarol was discontinued and treatment with Immunoglobulins 1 g/kg/day × 2 doses and prednisone 40 mg/day were started. Four days later, she was admitted to the emergency room because of respiratory worsening with fever and cough. A chest radiograph showed bilateral opacities in lower fields compatible with COVID-19. Blood tests revealed counts of lymphocytes – 1.2 x 10^3/mm^3, PLT – 372,000/mm^3, and D dimer – 0.54 g/dL. Discharged from the emergency department after having been administered with levofloxacin and hydroxychloroquine for seven days, he was monitored closely by telephone follow-up and treatment. Anticoagulation was restarted with enoxaparin 1.5 mg/kg, and prednisone was decreased to 30 mg/24 h until suspension on April 30. The serological SARS-CoV-2 test showed negative IgM and positive IgG antibodies. Since then she has remained stable with PLT around 90,000/mm^3.

Discussion

Our patients presented with mild-severe thrombocytopenia but no evidence of severe active bleeding. The response to immunoglobulins and corticosteroids treatment was rapid and satisfactory. The temporal sequence suggests that the cause of immune thrombocytopenia was related to SARS-CoV-2 [2]. However, there are not yet sufficient data that demonstrate the physiopathology of this phenomenon. Given the current pandemic, we suggest screening for SARS-CoV-2 in all patients with new-onset cytopenias.

Authors' contributions

According to the ICMJE criteria for authorship, all authors have participated in similar conditions in the article preparation.

Conflict of interest

The authors have no conflicts of interest to declare.

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We do not have any financial support.

Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments; Uniform requirements for manuscripts submitted to biomedical journals.

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