



Idiopathic thrombocytopenic purpura as a hematologic manifestation of COVID-19 infection: A case report

Azadeh Laali^a, Zohreh Kermanshah^{b,*}, Hossein Keyvani^{c,d}, Vahid Kaveh^e,
Sajad Karampoor^{c,d,**}

^a Department of Infectious Diseases, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran

^b School of Medicine, Iran University of Medical Sciences, Tehran, Iran

^c Gastrointestinal and Liver Diseases Research Center, Iran University of Medical Sciences, Tehran, Iran

^d Department of Virology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

^e Department of Hematology and Oncology, Iran University of Medical Sciences, Tehran, Iran

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ABSTRACT

The hematologic system is one of the vulnerable parts of the human body in coronavirus disease-2019 (COVID-19) infection. Lymphopenia and disseminated intravascular coagulation (DIC) are among the most frequent consequences of COVID-19. Idiopathic thrombocytopenic purpura is one of the common causes of thrombocytopenia in adults. It is defined by thrombocytopenia when platelet counts $<10^5/\mu\text{l}$ in the absence of anemia and leukopenia. Traditionally, infections, typically viral, have been known as the main culprits of low platelet counts before the involvement of ITP. According to the literature, C virus (HCV), HIV, varicella-zoster virus (VZV), and cytomegalovirus (CMV) are considered secondary causative agents for the development of ITP. In this study, we reported a case that was afflicted with concurrent severe thrombocytopenia diagnosed as ITP and COVID-19 infection.

1. Introduction

As the number of cases diagnosed with SARS-coV-2 (known as COVID-19) in December 2019, COVID-19 became a pandemic within four months and affected almost all countries in the world. COVID-19 infection mainly affects the respiratory system [1–3] and is characterized by various symptoms such as fever, dry cough, dyspnea, fatigue, less commonly myalgia, sore throat, and nasal congestion [4–6]. However, apart from these clinical signs, other complications, such as stroke, seizures, diarrhea, and organ failure, are among the less reported symptoms indicating the involvement of neurological, gastrointestinal, cardiovascular, and renal systems [7]. The hematologic system is one of the vulnerable sites of the human body in COVID-19 infection. Studies reported some cases with lymphopenia, prolonged prothrombin time (PT), activated partial thromboplastin time (aPTT), and disseminated intravascular coagulation (DIC) [8].

Idiopathic thrombocytopenic purpura (ITP, also called immune thrombocytopenic purpura) is one of the common causes of thrombocytopenia in adults. It is defined by thrombocytopenia when the number

of platelets is less than $10^5/\mu\text{l}$, in the absence of anemia and leukopenia, and the diagnosis is made by excluding other potential causes for thrombocytopenia [9–12]. ITP is characterized by bleeding, typically occurring in the skin or mucous membranes (also called "platelet type" bleeding pattern) with petechiae, purpura, and epistaxis. Uncommonly, patients can also be diagnosed with severe hemorrhage [13]. Traditionally, infections, typically viral, have been known as the main causative agents of low platelet counts before the involvement of ITP. According to the literature, hepatitis C virus (HCV), HIV, varicella-zoster virus (VZV), and cytomegalovirus (CMV) are among the most causative agents of secondary ITP [14–17]. To the best of our knowledge, COVID-19-related ITP has been reported in two case-series studies [18, 19]. In this study, we reported a case with concomitant severe thrombocytopenia diagnosed as ITP and COVID-19 infection.

2. Case presentation

A 77-year-old male patient was referred to the Emergency Department of Firoozgar Hospital with hematochezia and gross hematuria. He

* Corresponding author.

** Corresponding author. Gastrointestinal and Liver Diseases Research Center, Iran University of Medical Sciences, Tehran, Iran.,

E-mail addresses: z.kermanshah97@gmail.com (Z. Kermanshah), sajadkarampoor1987@gmail.com, karampoor.s@iums.ac.ir (S. Karampoor).

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had a known history of congestive heart failure, diabetes mellitus, ischemic heart disease, aortic valve replacement, and mitral valve repair surgery. He also had petechial lesions on all four extremities. He had a history of malaise and undocumented fever four days before the admission. His vital signs at the time of admission were as follows; BP (blood pressure) = 144/95 mmHg, HR (heart rate) = 120, RR (respiratory rate) = 14, and oral temperature = 37 °C. Due to his valve repair history, he was under warfarin treatment at a dose of 5mg and 2.5 mg intermittently every other day. His complete blood count results at the time of admission were as follows: WBC (white blood cell) = 7.7×10^3 per mm^3 , RBC (red blood cell) = 3.22×10^3 per mm^3 , Hb (hemoglobin) = 9.5 g/dL, Hct (hematocrit) = 28.5%, MCV (mean corpuscular volume) = 87.9 fL, MCH (mean corpuscular hemoglobin) = 29.5 Pg, MCHC (mean corpuscular hemoglobin concentration) = 33.6%, platelet = 4×10^3 per mm^3 , RDW (red cell distribution width) = 16.2%. For hematochezia work-up, an endoscopic examination was performed, which showed mild esophagitis and gastritis. Regarding the history of cardiac valve replacement and repair, endocarditis was also assessed in the patient. The echocardiography results showed no evidence of endocarditis, and the blood culture obtained from the patient was negative. Also, drug-induced thrombocytopenia was also ruled out. Afterward, a peripheral blood smear was obtained to rule out other causes of thrombocytopenia and examine the presence of ITP. The viral markers for HIV (human immunodeficiency virus) and HCV (hepatitis C virus) were negative. Laboratory tests for lupus anticoagulant, anti-cardiolipin antibody, anti-ds-DNA, and ANCA were also negative. According to these clinical findings, the diagnosis of primary ITP was made; thus, the treatment procedures were continued with the prescription of IVIG and dexamethasone.

As part of the hospital policy regarding the coronavirus pandemic, the patient underwent oropharyngeal swab testing for the presence of SARS-CoV-2 using real-time RT-PCR upon the hospital admission, and the result of the laboratory test was positive. It is noteworthy that the patient had neither pulmonary involvement in CT-scan/chest X-ray nor any signs/symptoms of upper respiratory tract infection. Hence, the treatment of COVID-19 infection was initiated using the prescription of hydroxychloroquine and atazanavir one day before starting the administration of IVIG and dexamethasone.

After one day of treatment with hydroxychloroquine and atazanavir, the platelet count was increased from 49×10^3 to 83×10^3 per mm^3 . On the fourth day of treatment with IVIG, dexamethasone, atazanavir, and hydroxychloroquine, the number of platelets was elevated as high as 148×10^3 per mm^3 . The patient was discharged two days later with acceptable general conditions and a platelet count of 170×10^3 per mm^3 and was asked to visit the Infectious Diseases Clinic two weeks later for the follow-up of the COVID-19 treatment.

3. Discussion

In a case-series study conducted by Ahmed et al., they presented three positive patients with COVID-19 who were concomitantly afflicted with thrombocytopenia, two of whom were diagnosed with ITP. One case was a 50-year-old male with no history of comorbidity, presenting generalized petechial lesions and oral blisters. Another case was a 49-year-old female with no prior comorbidity presenting gum bleeding and generalized bruises. None of these two patients had any respiratory signs/symptoms or pulmonary involvement in CXR. Both of them were subsequently diagnosed with COVID-19 using real-time PCR by throat swab testing. They received conventional treatment (IVIG) for ITP and were discharged with stable conditions [18]. Another case-series study performed by Bomhof et al. showed three cases that were concurrently diagnosed with COVID-19 and ITP. The first case was a 59-year-old male with a history of neuroendocrine malignancy for ten years, presenting oral mucosal petechiae and skin hematomas. Ten days before the manifestations of symptoms mentioned earlier, he was diagnosed with COVID-19 using real-time PCR by a nasopharyngeal swab testing. He

was treated with platelet transfusion, IVIG, and dexamethasone and exhibited a favorable response to treatment. The second patient, a 66-year-old female with a history of hypertension, presented petechial lesions, epistaxis, and bleeding hemorrhoids. She also had a history of fever, dyspnea, and cough. She was diagnosed with COVID-19 using real-time PCR by oropharyngeal swab testing. She also responded well to treatment with IVIG and dexamethasone. The third patient, a 67-year-old male with a history of hypertension and diabetes mellitus, presented cough, fever, and dyspnea, and he was diagnosed with COVID-19 using real-time PCR by an oropharyngeal swab testing. He was admitted to ICU and intubated due to deteriorating conditions, while he suffered from low platelet counts during the treatment course. Eventually, the development of ITP was ascribed to COVID-19 infection in that patient. Notably, he died of intracerebral bleeding 24 hours later [19].

Infections, especially viral, are among the most frequent causes of secondary ITP. Antibodies produced against viral antigens may cross-react with normal human platelet antigens through molecular mimicry and cause ITP. Infections with HCV, HIV, VZV, and CMV have been reported to cause ITP [14–17]. HIV and HCV are routinely examined during the diagnosis procedures of ITP. It can be postulated that infection with COVID-19 can also cause ITP through a similar mechanism.

Among its various extra-pulmonary manifestations, COVID-19 interferes with the immune system as well, causing dysregulation in the host immune response. Studies demonstrated that T-cell lymphopenia and over-activation of innate immunity are the most hallmarks of hematologic complications in COVID-19 infection [20]. It is now known that immune system alteration is one of the consequences of ITP. For example, loss of peripheral tolerance can produce self-reactive antibodies that may cause ITP, anti-phospholipid syndrome, and systemic lupus erythematosus [21,22]. Another proposed immune-related mechanism in the development of ITP is a defect in the number and/or function of regulatory T cells, resulting in the dysregulated cytotoxic activity of T cells [23–26]. It seems that COVID-19 infection influences T lymphocytes to generate cytotoxic agents against platelets and develop ITP. However, further studies are warranted to elucidate the precise immune-mediated mechanism of COVID-19 in the development of ITP, and the screen for the presence of SARS-CoV-2 is required in patients diagnosed with ITP.

4. Conclusion

As the pandemic continues, COVID-19 infection exhibits new versions of clinical manifestations that have been so far uncommon. Further reports on the concurrent development of ITP and COVID-19 infection corroborate that ITP could be considered as a possible complication of COVID-19. This would help out physicians to gain better insight into the etiology of ITP in patients.

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Ethics approval

Informed consent was obtained from the patient, and it is available upon request.

Authors' contributions

S.K. drafted the manuscript, F.A. conducted the medical examinations and collected the required data, and A.L. designed the study and drafted the manuscript. All authors read and approved the final version of the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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