

# COVID-19 presenting with immune thrombocytopenia: A case report and review of the literature

To the Editor,

Mild thrombocytopenia (platelet counts of  $100\text{--}150 \times 10^9/\text{L}$ ) can be observed in novel coronavirus disease (COVID-19), however severe thrombocytopenia is rare.<sup>1</sup> COVID-19-associated thrombocytopenia can be due to; the direct invasion of bone marrow, cytokine release leading to hemophagocytic lymphohistiocytosis, autoimmune destruction of platelets in peripheral blood (immune thrombocytopenia [ITP]), and increased platelet consumption as a consequence of thrombi in the microvasculature.<sup>2</sup> Severe thrombocytopenia ( $<50 \times 10^9/\text{L}$ ) was related to poor prognosis in a recent COVID-19 cohort where thrombocytopenia was attributed to coagulopathy related consumption.<sup>3</sup>

We herein report a mild disease course in a patient who had COVID-19-induced severe thrombocytopenia, along with the recently published similar cases in the literature.

A 41-year-old male was presented with petechiae and nasal bleeding. He had cough and runny nose 15 days ago, which resolved recently. He was diagnosed as ITP and referred to our center after 4 days of high-dose dexamethasone therapy, which was not effective. His medical history was otherwise unremarkable. Physical examination was normal except for petechiae and purpuric rash. Upon admission, he had isolated thrombocytopenia ( $9 \times 10^9/\text{L}$ ). In the differential diagnosis of isolated thrombocytopenia, the patient did not have consumption coagulopathy or thrombotic microangiopathy with no schistocytes or blasts in the peripheral blood smear. Laboratory tests including viral hepatitis panel and rheumatological markers did not reveal any cause of thrombocytopenia, and the diagnosis of ITP was made.

Since he had cough and runny nose recently, a nasopharyngeal swab was sent for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) real time polymerase chain reaction, which came out to be positive. His chest computerized tomography showed bilateral ground glass opacities consistent with COVID-19 pneumonia. Favipiravir was prescribed as the antiviral agent, and his pneumonia gradually resolved in 5 days.

As ITP secondary to COVID-19 was the most likely diagnosis, intravenous immunoglobulin (IVIg) with a total dose of 2 g/kg was administered concomitantly with favipiravir in the first 2 days of admission. After the treatment, his platelet count was  $54 \times 10^9/\text{L}$ , and during 4-weeks of follow-up, platelet counts were between  $50$  to  $100 \times 10^9/\text{L}$ .

Recently there have been published cases of isolated severe thrombocytopenia associated with COVID-19 (Table 1). Among them,

two patients (patients #1 and #2) were presented as ITP with no fever or respiratory symptoms.<sup>4</sup> Additional two patients (patients #5 and #6) who were presented with ITP had prior fever and respiratory symptoms, starting 10 and 21 days before referral, respectively.<sup>5</sup> Similar to our patient, these four cases were also responsive to high-dose IVIg. Thrombocytopenia was detected relatively later in the other four cases (patients #3, #4, #7, and #8).<sup>4-6</sup> Patients #3 and #7 developed thrombocytopenia on the 5th and 12th days of admission respectively, and thrombocytopenia in both cases coincided with clinical deterioration. Patient #4 had used amoxicillin-clavulanic acid and low-molecular-weight-heparin before the detection of thrombocytopenia,<sup>6</sup> which might also be related to thrombocytopenia. IVIg was not effective in these patients (#3, #4, and #7). Patients #3 and #7 died because of COVID-19 progression, whereas prednisolone and eltrombopag were administered in patient #4, which induced a good response. Another patient (patient #8) developed thrombocytopenia on 16th day of admission, which was 29 days after the initiation of respiratory symptoms.<sup>7</sup> That patient had a stable disease course and was in the recovery stage. His platelet counts recovered following IVIg administration.

Thrombocytopenia has been defined as a poor prognostic factor in COVID-19,<sup>8</sup> but thrombocytopenia in the disease course is not of one kind. Cytokine release or thrombi in the microvasculature may be responsible for platelet consumption in clinically deteriorated cases. Severe thrombocytopenia in the context of ITP (patients #1, #2, #5, #6, #8, and presented case) may be a different, possibly milder entity in COVID-19 than consumption thrombocytopenia (patient #3 and #7) and it can develop on different stages of the disease. Although not frequently reported to date, SARS-CoV-2 infection can be associated with secondary ITP. When COVID-19 patients are presented or complicated with ITP related severe thrombocytopenia, IVIg could be preferred first-line treatment option for a faster recovery of platelets in comparison to corticosteroids. Other treatment options including thrombopoietin mimetics can be beneficial (patient #4),<sup>6</sup> although the data on COVID-19-induced ITP and its management are still very limited. We had the options to use hydroxychloroquine or favipiravir as the viral load-decreasing agent, of which we chose favipiravir, as thrombocytopenia is also among the uncommon side effects of hydroxychloroquine.<sup>9</sup>



## CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

**TABLE 1** All reported COVID-19 induced immune thrombocytopenia cases including the presented case

Patient (reference)	Age	Sex	Presenting symptoms	COVID symptoms	Days from symptoms to referral	Viral serology and autoimmune profile	Days from admission to thrombocytopenia/ COVID course	Platelet Nadir	Prior drugs	IVIg dose/ response	Further treatment	Platelets increased to (after treatment), d	Outcome
P#1 <sup>4</sup>	50	M	Epistaxis, generalized rash	None	Not reported	Negative	On presentation, stable COVID course	0	None	1 g/kg: 2 doses/ responsive	None	25 × 10 <sup>9</sup> /L, (2), 103 × 10 <sup>9</sup> /L, (14)	Discharged
P#2 <sup>4</sup>	49	F	Bruises, gum bleed	None	3	Negative	On presentation, stable COVID course	4 × 10 <sup>9</sup> /L	None	1 g/kg: Single dose/ responsive	None	52 × 10 <sup>9</sup> /L (2)	Discharged
P#3 <sup>4</sup>	96	F	Shortness of breath	Shortness of breath	Not reported	Negative	5th d, deteriorated	3 × 10 <sup>9</sup> /L	None	0.4 g/kg: 5 doses/ not known	None	16 × 10 <sup>9</sup> /L (2)	Died
P#4 <sup>6</sup>	65	F	Fatigue, fever, dry cough	Fatigue, fever, dry cough	4	Anti-TPO (+)	4th d, complicated with subarachnoid hemorrhage	8 × 10 <sup>9</sup> /L	Amo-Clav, LMWH	1 g/kg/ unresponsive	Prednisolone, TPO-RA	139 × 10 <sup>9</sup> /L (4)	Discharged
P#5 <sup>5</sup>	59	M	Petechiae, skin hematoma	Cough, fever	10	GPIIb (+) GPIIb IIIa (+) GPV (+)	On presentation, stable COVID course	3 × 10 <sup>9</sup> /L	None	1 g/kg: 2 doses/ responsive	Dexamethasone	47 × 10 <sup>9</sup> /L (2), 51 × 10 <sup>9</sup> (17)	Discharged
P#6 <sup>5</sup>	66	F	Petechiae, epistaxis	Fever, dyspnea, cough, diarrhea	21	Negative	On presentation, stable COVID course	2 × 10 <sup>9</sup> /L	High dose dexamethasone	1 g/kg: dose not shared/ responsive	None	32 × 10 <sup>9</sup> /L (22)	Discharged
P#7 <sup>5</sup>	67	M	Fever, cough, dyspnea	Fever, cough, dyspnea	9	Negative	12th d, deteriorated, pulmonary embolism	3 × 10 <sup>9</sup> /L	Unfractionated heparin	None	Platelet transfusion	None	Died
P#8 <sup>7</sup>	38	M	Cough, dyspnea, fever	Cough, dyspnea, fever	13	Negative	16th d, stable COVID course	2 × 10 <sup>9</sup> /L	Interferon- $\alpha$ , umifenovir,	400 mg/kg: 7 doses- responsive	Dexamethasone	60 × 10 <sup>9</sup> /L (3)	Discharged
Present case	41	M	Petechiae and purpura	Cough and runny nose	4	Negative	On presentation, stable COVID course	9 × 10 <sup>9</sup> /L	High dose dexamethasone	1 g/kg: 2 d/ responsive	None	54 × 10 <sup>9</sup> /L (2)	Discharged

Abbreviations: anti-TPO, thyroid peroxidase antibodies; Amo-Clav, amoxicillin-clavulonic acid; COVID, coronavirus disease; GP, glycoprotein (Ib, IIb/IIIa, V); IVIg, intravenous immunoglobulin; TPO-RA, thrombopoietin receptor agonist.

Ahmet Murt   
Ahmet Emre Eskazan   
Umut Yilmaz  
Tuba Ozkan  
Muhlis Cem Ar

Department of Internal Medicine, Cerrahpasa Medical Faculty,  
Istanbul University-Cerrahpasa, Istanbul, Turkey

#### Correspondence

Ahmet Emre Eskazan, Division of Hematology, Department of  
Internal Medicine, Cerrahpasa Medical Faculty, Istanbul  
University-Cerrahpasa, Istanbul 34303, Turkey.

Email: [emreeskazan@hotmail.com](mailto:emreeskazan@hotmail.com) and  
[emre.eskazan@istanbul.edu.tr](mailto:emre.eskazan@istanbul.edu.tr)

#### ORCID

Ahmet Murt  <http://orcid.org/0000-0002-1948-2914>

Ahmet Emre Eskazan  <http://orcid.org/0000-0001-9568-0894>

#### REFERENCES

1. Fan BE, Chong VCL, Chan SSW, et al. Hematologic parameters in patients with COVID-19 infection. *AJH*. 2020;95:131. <https://doi.org/10.1002/ajh.25774>
2. Xu P, Zhou Q, Xu J. Mechanism of thrombocytopenia in COVID-19 patients. *Ann Hematol*. 2020;99:1-4. <https://doi.org/10.1007/s00277-020-04019-0>
3. Yang X, Yang Q, Wang Y, et al. Thrombocytopenia and its association with mortality in patients with COVID-19. *J Thromb Haemost*. 2020; 18:1469-1472. <https://doi.org/10.1111/jth.14848>
4. Ahmed MZ, Khakwani M, Venkatadasari I, et al. Thrombocytopenia as an initial manifestation of COVID-19; case series and literature review. *BJH*. 2020. <https://doi.org/10.1111/bjh.16769>
5. Bomhof G, Mutsaers PGNJ, Leebeek FWG, et al. COVID-19 associated immune thrombocytopenia. *BJH*. 2020. <https://doi.org/10.1111/bjh.16850>
6. Zulfiqar AA, Lorenzo-Villalba N. Immune thrombocytopenic purpura in a patient with COVID-19. *NEJM*. 2020;382:43. <https://doi.org/10.1056/NEJMc2010472>
7. Chen W, Yang B, Li Z, Wang P, Chen Y, Zhou H. Sudden severe thrombocytopenia in a patient in the recovery stage of COVID-19. *Lancet Hematol*. 2020. [https://doi.org/10.1016/S2352-3026\(20\)30175-7](https://doi.org/10.1016/S2352-3026(20)30175-7)
8. Lippia G, Plebani M, Henry BM. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: a meta-analysis. *Clin Chim Acta*. 2020;506(506):145-148.
9. Antón Vázquez V, Pascual L, Corominas H, Giménez Torrecilla I. Relapsed hydroxychloroquine induced thrombocytopenia in a systemic lupus erythematosus patient. *Reumatol Clin*. 2017;13(5): 294-296. <https://doi.org/10.1016/j.reuma.2016.04.008>