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SEVERE THROMBOCYTOPENIA IN A PATIENT WITH COVID-19: A CASE REPORT AND REVIEW OF LITERATURE.

Irenawati SAMAD[1], Vui Heng CHONG[2], Noorainun YUSOF[1], Muhammad Syafiq Abdullah[1], Rosmonaliza ASLI[1], Babu Ivan MANI[2], Riamiza Natalie MOMIN[2], Pui Lin CHONG[1].

[1]Raja Isteri Pengiran Anak Saleha Hospital, Jalan Putera Al-Muhtadee Billah, Bandar Seri Begawan, BA 1710, Brunei Darussalam.
[2]Pengiran Muda Mahkota Pengiran Muda Haji Al-Muhtadee Billah Hospital, Jalan Sungai Basong, Tutong, TA 1341, Brunei Darussalam.

ABSTRACT

Approximately one-third of patients with COVID-19 develop thrombocytopenia, and it is more commonly seen in those with severe infection. We present a 66-year-old gentleman with confirmed COVID-19 who developed severe thrombocytopenia during his admission. He was asymptomatic at diagnosis. He developed petechial rash over both arms, root of the mouth and under the tongue and was confirmed to have thrombocytopaenia. This was managed by Platelet transfusion. Thrombocytopenia is usually mild in patients with COVID-19 unlike our case. Nonetheless, a comprehensive evaluation of thrombocytopenia remains important as treatment of the underlying cause may reduce the risk of potentially catastrophic consequences. Clinicians should remain vigilant of the association between COVID-19 and thrombocytopenia, and instigate prompt supportive treatment accordingly.

Keywords: Brunei, COVID-19, Platelet transfusion, SARS-CoV-2, Thrombocytopenia.

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Keywords: Brunei, COVID-19, Platelet transfusion, SARS-CoV-2, Thrombocytopenia.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a novel infectious disease first reported in Wuhan, China in December 2019. Given its highly transmissible nature, COVID-19 was declared a pandemic on 11th March 2020 by WHO.[1] COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and is associated with flu-like symptoms and respiratory illness which may progress to pneumonia and acute respiratory distress syndrome (ARDS). Haematological changes such as lymphopenia and thrombocytopenia have been observed in patients with COVID-19. Thrombocytopenia is associated with higher risk of severe COVID-19 disease and increased mortality.[2] We report a case of severe thrombocytopenia in a patient with COVID-19 who recovered with prompt treatment.

Correspondence: Dr Pui Lin Chong (BM, MRCP UK, MRCP Diabetes & Endocrinology, MD), Department of Internal Medicine, Raja Isteri Pengiran Anak Saleha Hospital**,** Jalan Putera Al-Muhtadee Billah, Bandar Seri Begawan, BA 1710, Brunei Darussalam.
Email: lina.chong@moh.gov.bn
Tel: +673 2242424 ext 6230

CASE REPORT

A 66-year-old retired army officer, normally fit and well, was admitted with confirmed COVID -19 (positive SARS-CoV-2 real time polymerase chain reaction on nasopharyngeal swab) diagnosed as part of contact tracing. He was asymptomatic and clinical examination was unremarkable at the time of admission. Initial laboratory results and chest radiograph were normal.

On day 7 of admission, he developed a fever (38°C). Ground glass opacities in the left lower zone was observed on repeat chest radiograph. Full blood count and procalcitonin were normal (0.15ng/mL; normal range [NR] <0.5), and C-reactive protein was 1.1 mg/dL (NR 0.0-0.9). Lopinavir/ritonavir (400mg/100mg 2 tablets twice daily) and intravenous amoxicillin-clavulanic acid (1.2g 8-hourly) were started. Blood tests the next day showed an uptrending CRP (1.9mg/dL), lymphopenia (absolute lymphocyte count $0.4x10^9$/L; NR 1.2-4.4) and thrombocytopenia ($126x10^3$/uL; NR 174-430). As fever persisted, hydroxychloroquine (400mg twice daily day 1 and 200mg twice daily day 2-5) was added a day after the initiation of antiviral and antibiotic treatment.

On day 11, he developed a dry cough with petechial rash over both arms, on the roof of his mouth and under his tongue. Thrombocytopenia worsened from $126x10^3$/uL to $2x10^3$/uL requiring platelet transfusion. Further platelet transfusion was administered the following day as severe thrombocytopenia persisted.

Relevant investigations include sterile blood and urine cultures, dengue (IgM, IgG NS1 antigen), and malarial screening, all of which were negative. Microcytic red cells, target cells and severe thrombocytopenia on a background of thalassaemia trait were reported on peripheral blood film. Lupus anticoagulant screen was absent whilst extractable nuclear antigen antibodies (ENA) and antinuclear antibody (ANA) were negative. Prothrombin time was mildly elevated (12.6 seconds), and activated partial thromboplastin time and international normalised ratio were within normal limits.

Although drug-induced thrombocytopenia was unlikely, due to the severity of thrombocytopenia, hydroxychloroquine was stopped after 3 days. With resolution of fever, normal procalcitonin and normal septic workup, antibiotic therapy was discontinued 4 days after initiation. Thrombocytopenia continued to improve without the need for further platelet transfusion. Upon discharge on day 19, the platelet count was near normal ($131x10^3$/uL). Figure 1 illustrates platelet count trend during the period of hospitalisation.

DISCUSSION

The spectrum of clinical presentation of COVID-19 varies from asymptomatic or mild disease to severe illness which may result in death. In a large Chinese series, the majority of patients have mild disease (81%), 14% have severe disease and 5% were critically ill.[3] Thrombocytopenia can be associated with any viral illness. Approximately 36.2% of patients with COVID-19 develop thrombocytopenia and the rate rises further in those with severe disease (57.7.%).[4] However, thrombocytopenia encountered was generally mild rather than severe as in our patient.

Mechanisms underlying thrombocytopenia in COVID-19 remain unknown. It has been postulated that direct infection of bone marrow cells with resultant abnormal haematopoiesis may decrease platelet production; lung injury due to SARS-CoV-2 may cause platelet aggregation and consumption; and increased autoantibodies and immune complexes may lead to destruction of platelet.[5] Different treatments of thrombocytopenia have been reported, and Table I summarises the treatment and outcome of severe thrombocytopenia in patients with COVID-19 published to date.[6-15]

The likely cause of thrombocytopenia in our patient is SARS-CoV-2 infection given the onset of thrombocytopenia in relation to the onset of viral symptoms, the absence of pseudothrombocytopenia, the absence of autoimmune antibodies, and the absence of

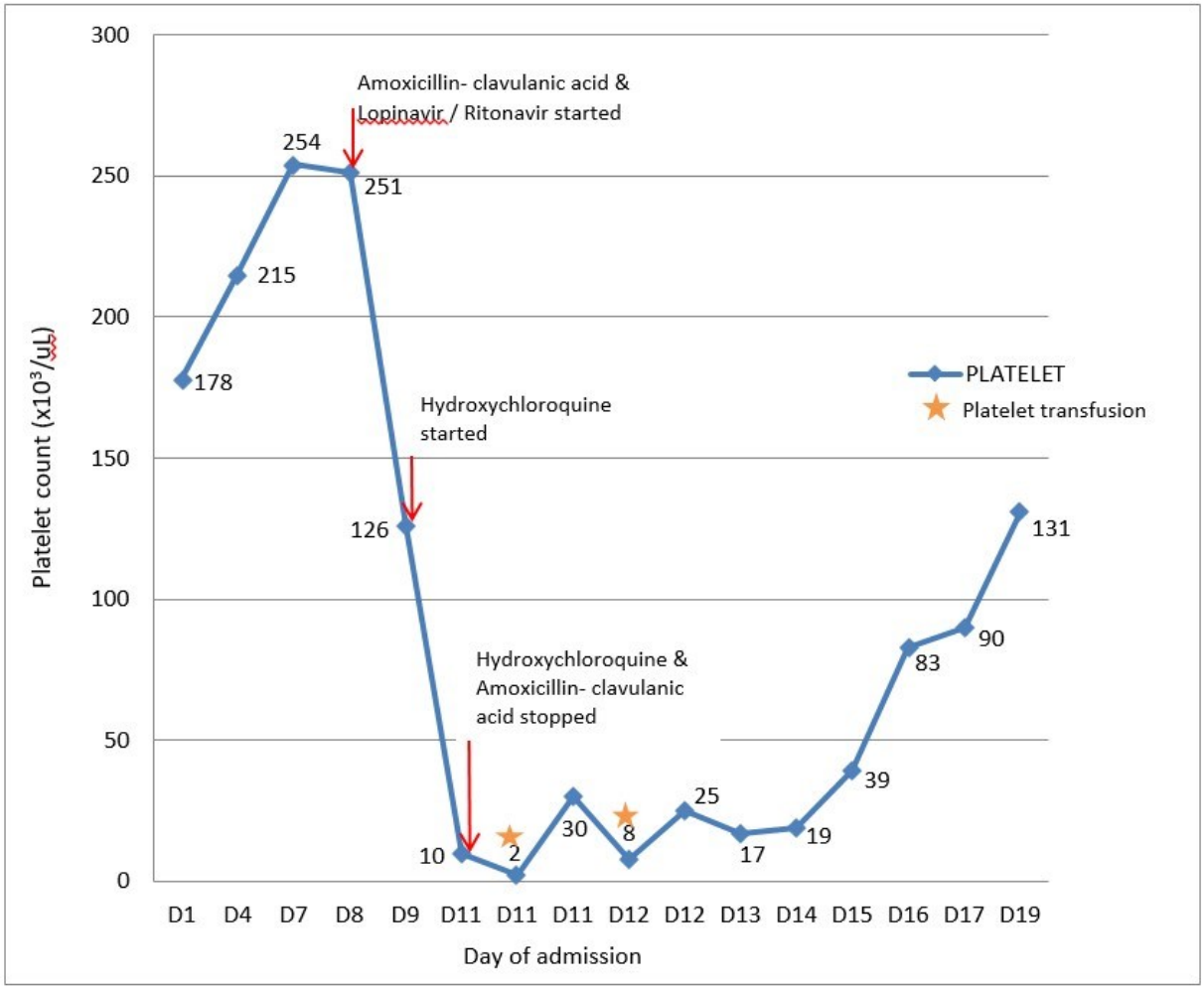

Figure 1: Trend of Platelet Count During Admission.

autoimmune antibodies, and the absence of other infection associated with thrombocytopenia. SARS-CoV-2 may inhibit haematopoiesis in the bone marrow leading to decreased platelet formation and thrombocytopenia. In addition, lung injury secondary to viral infection may result in damaged pulmonary capillary beds which impairs megakaryotecyte rupture and indirectly, leads to decreased platelet release into systemic circulation.[5]

Drug-induced thrombocytopenia has been reported with lopinavir/ritonavir[16], hydroxychloroquine[17] and amoxicillin-clavulanic acid[18] use. However, such drug reaction is rare and it is doubtful that these medications were the cause of thrombocytopenia in this case. Moreover, in the hydroxychloroquine case report, the patient was also on heparin.[17]

CONCLUSION

Clinicians must maintain a heightened awareness of thrombocytopenia in patients with COVID-19 as its occurrence is associated with severe COVID-19 disease and increased mortality. Close monitoring and assessment for the development of ARDS and organ dysfunction, with prompt treatment may reduce mortality. In addition, evaluation of underlying causes of thrombocytopenia should be undertaken instead of attributing to viral infection alone. Our patient developed severe thrombocytopenia requiring platelet transfusion and recovered uneventfully. If left untreated, severe thrombocytopenia may lead to serious bleeding complications and death.

Table I: Summary of Severe Thrombocytopenia associated with SARS-CoV-2 infection.

Patient	Age	Gender	Initial Presentation	Nadir Platelet	Thrombocytopenia Treatment	Outcome
#1[4]	65	F	Fatigue, fever, dry cough and abdominal discomfort	1 x $10x^9$/L	IVIG, Prednisolone and TPO-RA	Recovered
#2[5]	31	F	Fever, dry cough and decreased fetal movement (23 weeks gestation)	23 x $10x^9$/L	Platelet transfusion	Recovered
#3[6]	12	F	Fever, dry cough, shortness of breath, vomiting and haematuria	<10 x $10x^9$/L	IVIG and Dexamethasone	Recovered
#4[7]	50	M	Epistaxis and generalised petechial rash	0 x $10x^9$/L	IVIG	Recovered
#5[7]	49	F	Gum bleeding and generalised bruising	4 x $10x^9$/L	IVIG	Recovered
#6[7]	91	F	Shortness of breath	3 x $10x^9$/L	IVIG	Death
#7[8]	59	M	Oral mucosa petechiae, spontaneous skin haematomas, cough and fever	<3 x $10x^9$/L	IVIG and Dexamethasone	Recovered
#8[8]	66	F	Petechiae, epistaxis, bleeding from haemorrhoids, fever, shortness of breath, cough, diarrhoea and vomiting	2 x $10x^9$/L	Platelet transfusion and Dexamethasone	Recovered
#9[8]	67	M	Fever, shortness of breath and cough	3 x $10x^9$/L	Platelet transfusion	Death
#10[9]	16	M	Fever, generalised seizure and haemodynamic shock (Thrombocytopenia associated multiple organ failure)	42 x $10x^9$/L	Plasma exchange	Recovered
#11[10]	38	M	Cough, nasal bleed, fever and muscle aches	2 x $10x^9$/L	IVIG and Dexamethasone	Recovered
#12[11]	57	F	Headaches and malaise	16 x $10x^9$/L	No treatment	Recovered
#13[12]	72	F	Productive cough and fever; history of ITP on treatment	6 x $10x^9$/L	IVIG, platelet transfusion and Methylprednisolone	Recovered
#14[13]	41	M	Petechiae, nasal bleed, cough and runny nose	9 x $10x^9$/L	IVIG and Dexamethasone	Recovered

IVIG – intravenous immunoglobulin; TPO-RA – thrombopoietin receptor agonist; ITP – idiopathic thrombocytopenic purpura

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DECLARATION

None of the authors have any conflict of interest to declare.

CONSENT

Consent has been obtained from patient for permission to publish this case report.

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