Delayed hypercoagulable state in COVID-19 adolescent patient: a case report

Respirology Case Report,2021, Vol 9, Issue 7

doi: 10.1002/rcr2.793

Desdiani Desdiani1,2 , Nita Yulianti3 & Anindita Basuki4

1 Faculty of Medicine, Universitas Sultan Ageng Tirtayasa, Cilegon, Indonesia.

2 Department of Pulmonology and Respiratory Medicine, Bhayangkara Brimob Hospital, Depok, Indonesia.

3 Department of Clinical Pathology, Bhayangkara Brimob Hospital, Depok, Indonesia. 4 Department of Radiology, Bhayangkara Brimob Hospital, Depok, Indonesia

Received: 25 March 2021; Revised: 17 May 2021; Accepted: 17 May 2021;

Daftar Isi

Daftar Isi 2
Manuscript Submission 23 Maret 2021 3
Manuscript Submitted 5
Authorship Consent 23 Maret 2021 12
Re : Authorship Consent 13
Manuscript Submitted 25 Maret 2021 14
Quote for Puiblication Charge 1 April 2021 16
Manuscript Revision 15 April 2021 17
Revision Reminder 6 Mei 2021 19
Revision Submitted 17 Mei 2021 21
Decision on Manuscript 19 Mei 2021 23
Decision Letter 19 Mei 2021 24
Manuscript Acceptance 20 Mei 2021 25
Article Proof 20 Mei 2021 26
Article Production 23 Mei 2021 35
Publication 23 Mei 2021 36
Article Proof 26 Mei 2021 37
Correction Successfully Submitted 26 Mei 2021 39
Re : Correction Successfully Submitted 28 Mei 2021 40
Author to Editor : Agreement 28 Mei 2021 41
Article Accepted 42
Published Article 8 Juni 2021 45

Manuscript Submission 23 Maret 2021

Respirology Case Reports - Manuscript ID RCR-21-065 [email ref: SE-6-a]

Dari: Respirology Case Reports (onbehalfof@manuscriptcentral.com)

Kepada: desdiani@ymail.com

Cc: desdiani@ymail.com; nitayulianti_hmt@yahoo.com; aninditabasukidr@gmail.com

Tanggal: Selasa, 23 Maret 2021 pukul 14.20 GMT+7

23-Mar-2021

Dear Dr. Desdiani:
CC all authors,

Your manuscript entitled "Delayed hypercoagulable state in COVID-19 adolescent patient: A case report" by Desdiani, Desdiani; Yulianti, Nita; Basuki, Anindita, has been submitted online and is currently under-review in Respirology Case Reports.

The editorial office staff will be in touch shortly if any essential information is missing for your submission.

The submitting author is the contact author for this paper, as such all further correspondence will be sent to Dr. Desdiani Desdiani.

Co-authors: Please contact the Editorial Office as soon as possible if you disagree with being listed as a co-author for this manuscript.

Your manuscript ID is RCR-21-065.

Please mention the above manuscript ID in all future correspondence or when calling the office for questions. If there are any changes in your street address or e-mail address, please log in to ScholarOne Manuscripts at https://mc.manuscriptcentral.com/respirolcasereports and edit your user information as appropriate.

You can also view the status of your manuscript at any time by checking your Author Center after logging in to https://mc.manuscriptcentral.com/respirolcasereports.

PUBLICATION CHARGE AND DISCOUNT:
The Wiley Open Access Payment team will contact you shortly after your manuscript has been processed with a quote for the publication charge for your article.

Did you know that members of the Asian Pacific Society of Respirology (APSR) and of Societies with en-bloc APSR membership receive a 50% discount of the Open Access Publication Charge for case reports and case series?
For more information on Publication Charges and discount and which Societies qualify for a discount, please visit:
https://onlinelibrary.wiley.com/page/journal/20513380/homepage/article_publication_charges_and_discounts.htm

If you are a member of the Asian Pacific Society of Respirology (APSR) or any of its en-bloc Societies, make sure that you have indicated your membership number and provided proof of membership upon submission. If you forgot, please contact the Editorial Office now:
respcasereports@resphealth.uwa.edu.au

If you are not a member, why not join? Please visit: http://www.apsresp.org/membership.html for more information.

IMPORTANT NOTE:
To simplify the submission process for you, the Editorial Office staff will check your submission and will notify you shortly only if anything essential is missing to your submission.
Any adjustment to the text or figures format will be required only if your manuscript is accepted for publication. We strongly recommend that you use our self-explanatory templates to guide you for your submission and ensure you have provided all the necessary information.

Please also note that your figures may be deemed appropriate for peer-review but that you may be requested to provide better quality figures if your manuscript is accepted for publication. The requirements for figure quality needed for publication are highlighted in the following Wiley author service page (see sections on Technical Specifications, Line Art requirements, Color Artwork and Mode Usage reminders):
https://authorservices.wiley.com/author-resources/book-authors/prepare-your-manuscript/artwork.html

Thank you for submitting your manuscript to Respirology Case Reports.

Sincerely,
Respirology Case Reports Editorial Office

Manuscript Submitted

Delayed hypercoagulable state in COVID-19 adolescent patient: A case report

Desdiani Desdiani[1,2*], Nita Yulianti[3], Anindita Basuki[4]

[1]Faculty of Medicine, Universitas Sultan Ageng Tirtayasa, Cilegon, Banten, Indonesia

[2]Department of Pulmonology and Respiratory Medicine, Bhayangkara Brimob Hospital, Cimanggis, Depok, Indonesia

[3]Department of Clinical Pathology, Bhayangkara Brimob Hospital, Cimanggis, Depok, Indonesia

[4]Department of Radiology, Bhayangkara Brimob Hospital, Cimanggis, Depok, Indonesia

[*]Corresponding author**:** Desdiani Desdiani

Faculty of Medicine, Universitas Sultan Ageng Tirtayasa, Jalan Jend. Sudirman No.20, RT.10/RW.5, Kotabumi, Cilegon, Banten, Indonesia 42434.

Tel +62254280330, Fax: +62254281254

E-mail : desdiani@ymail.com

Short title: Hypercoagulable State in COVID-19 Adolescent Patient

Keywords: COVID-19…….

Abstract

Background: Hypercoagulable state in COVID-19 adolescent patient is a rare case. COVID-19 is a systemic hyperinflammation disease which can cause severe respiratory symptoms and also extrapulmonary manifestations. such as pulmonary embolism, ischemic stroke, deep vein thrombosis, or arterial thrombosis.

Case presentation: A 16-year-old Indonesian boy with mild COVID-19 symptoms was admitted to the emergency department in our hospital. The patient was treated with azithromycin, N-acetyl cysteine, etc. Within several days of the treatment, the patient showed clinical improvement. However, on day 15, the patient experienced hypercoagulation and stroke-like symptoms. The patient was then subjected to additional drugs, including low-molecular-weight heparin (LMWH), and peripheral neuropathy vitamin therapy after consulting a neurologist. On day 20 of the treatment, the clinical symptoms reduced. The patient was able to move the limbs again and the tingling sensation reduced. The D-dimer value of 460 ng/mL, quantitative CRP of 6.1 mg/L, lymphocytes 13%, and the other parameters were within normal ranges.

Conclusion: The association between COVID-19 and stroke in young population and the use of anticoagulants to prevent thrombotic events need to be studied further. Young patients with hypercoagulation and stroke symptoms but not yet confirmed with COVID-19 need to be thoroughly investigated, including the patients with mild COVID-19 symptoms, especially if new neurological symptoms arise.

Introduction

COVID-19 is a disease which can cause systemic hyperinflammation and has spread worldwide. The usual symptoms are fever, cough, malaise, anosmia, loss of appetite, diarrhea, and other varying symptoms [1]. To date, there is no definitive treatment which can cure the disease. Elderly patients or patients with existing comorbidities have increased risks of severe illness from COVID-19. Most of the reported cases are those with some complications, such as hypercoagulation. Some cases reported that this condition could occur in young patients when the potency of virus infection has started to decrease. Endothelial injury due to COVID-19 can trigger hypercoagulable state. We report a case of an adolescent patient with mild symptoms of COVID-19 who was already in recovery state, but later developed hypercoagulable state and stroke-like symptoms.

Case Report

A 16-year-old Indonesian boy with fever and cough, and a medical history of close contact with a confirmed case COVID-19 patient was admitted to the emergency department in Bhayangkara Brimob Hospital (Depok, Indonesia). From anamnesis, there was no comorbidity (e.g. hypertension, diabetes mellitus, autoimmune disease, or malignancy). Vital signs and oxygen saturation were in normal ranges. Nasopharyngeal swab PCR tests was conducted and the result was positive for COVID-19 with CT values of RdrP: 28.05, E: 27.08. Laboratory tests revealed leucocytes of 3,720 cell/µL, lymphocytes of 10%, monocytes of 13%, NLR 7.1, ALC 780 µL, D-dimer of 269 ng/ml, quantitative CRP < 5 mg/L, prothrombin time (PT) 13.1 second, INR 0.96,

and partial thromboplastin time 23.7. The PA chest X-ray showed no radiological abnormalities in the heart and lungs (Fig. 1). The CT scan of the chest also showed no visible acute lung inflammation, lung mass, or mediastinal tumor (Fig. 2). The patient was given treatments with azithromycin, N-acetyl cysteine, multivitamins, and other supporting medications.

Within several days of the treatment, the patient showed clinical improvement. On day 13 of the treatment, the patient had a nasopharyngeal swab PCR examination. The result was positive with CT values of RdrP: 33.79, E: 33.77. On day 15, the patient suddenly had a high fever accompanied by severe and throbbing headaches, flatulence, nausea and vomiting, abdominal pain, numbness of arms, and tingling and immobility of legs. The oxygen saturation was 93%. The patient was then subjected to additional drugs, such as meropenem, dexamethasone, remdesivir, low-molecular-weight heparin (LMWH), ondansentron, omeprazole, and supplements (e.g. vitamin C, zinc, and vitamin D3). Laboratory tests showed leucocytes of 12,220 cells µ/L, monocytes of 12%, NLR 17.72, lymphocytes of 4.4%, D-dimer of 16,180 ng/mL, quantitative CRP 26.4 mg/L, APTT 19.9 seconds, potassium 3.2, AST of 51 U/L. Radiology examination revealed no radiological abnormalities in the heart and lungs. CT scan of the chest showed solitary ground-glass opacity (GGO) nodules on S6 left lung (Fig. 3 and Fig. 4). We consulted a neurologist, and the patient was then given additional peripheral neuropathy vitamin therapy. Furthermore, the patient was subsequently given oxygen therapy and he felt better after that.

On day 20, clinical symptoms improved. The patient was able to move the limbs again and the tingling sensation reduced. The D-dimer, quantitative CRP, and lymphocytes were 460 ng/mL, 6.1 mg/L, and 13%, respectively. The other parameters were within normal ranges, although the PCR result was still positive. At the end of the third week, the patient was discharged from the

hospital. The patient's PCR result was negative. The laboratory and radiology results also had improved.

Discussion

Pisano et al. (2020) reported an African-American 33-year-old female COVID-19 patient with acute malignant middle cerebral artery infarction. The SARS-CoV-2 virus was reported to cause a thrombotic event [2]. COVID-19 patients might experience thrombocytopenia, prolonged PT, increased fibrinogen, and high D-dimers [3]. Other markers of coagulation and inflammation that can be abnormal include ferritin, von Willebrand Factor (VWF), C-reactive protein (CRP), complement, and cytokines. Thrombotic events occur in one-third of COVID-19 patients which are dominated by pulmonary embolism and associated with the severity of disease and increased mortality [4]. A study on the five patients infected with COVID-19 under 50 years old who did not have risk factors for vascular diseases and were hospitalized with symptoms such as stroke showed that these cases have increased sevenfold compared with the previous year and were associated with COVID-19. The patient's laboratory results in our case showed a hypercoagulable state, leading to the postulation that stroke observed in the young patient may be associated with SARS-CoV-2. The clinical symptoms of COVID-19 patients with hypercoagulable state and stroke-like symptoms are worse than non-COVID-19 stroke patients because they are related to the pathophysiology of the COVID-19 disease [5].

To date, data which support the association between COVID-19 and stroke in young population without specific risk factors (sometimes only mild respiratory symptoms) are increasing. Further studies are necessary to investigate this association and the use of anticoagulants to prevent thrombotic events. Our case underlines young patients with hypercoagulation and stroke symptoms, but not yet confirmed with COVID-19, need to be

thoroughly investigated, including the patients with mild COVID-19 symptoms, especially if new neurological symptoms arise.

Disclosure Statement

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

Acknowledgments

The authors would like to thank all staff of Bhayangkara Brimob Hospital who have contributed in providing medical data and records as well as our patient who were involved in this report.

Author Contribution Statement

Desdiani Desdiani : Conceptualization, acquisition of information, analysis or interpretation of the data, drafting the manuscript, final approval of the version to be published

Nita Yulianti : Analysis or interpretation of the data

Anindita Basuki : Analysis or interpretation of the data

Conflict of interest: None to declare.

Funding: No funding

References

1) Kichloo A, Dettloff K, Aljadah M, et al. COVID-19 and hypercoagulability: a review. Clin Appl Thromb Hemost. 2020;26:1-9.

2) Pisano TJ, Hakkinen I, Rybinnik I. Large vessel occlusion secondary to COVID-19 hypercoagulability in young patient: a case report and literature review. J Stroke Cerebrovasc Dis. 2020;29:1-6.
3) Bao J, Li C, Zhang K, et al. Comparative analysis of laboratory indexes of severe and non-severe patients infected with COVID-19. Clin Chim Acta 2020;509:180-94.
4) Klok FA, Kruip MJHA, van der Meer NJM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res. 2020;191:145-7.
5) Oxley TJ, Mocco J, Majidi S, et al. Large-vessel stroke as a presenting feature of COVID-19 in the young. N Engl J Med. 2020;382:60.

Fig. 1. The PA chest X-ray showed no radiological abnormalities in the heart and lungs.

Fig. 2. CT scan of the chest at the time showed no visible acute lung inflammation, lung mass, or mediastinal tumor.

Fig. 3. The PA chest X-ray showed no radiological abnormalities in the heart and lungs.

Fig. 4. CT scan of the chest showed solitary ground-glass opacity nodules on S6 left lung.

Authorship Consent 23 Maret 2021

Consent Form and Authorship

Dari: desdiani - (desdiani@ymail.com)

Kepada: respcasereports@resphealth.uwa.edu.au

Tanggal: Selasa, 23 Maret 2021 pukul 14.33 GMT+7

Dear Managing Editors,
I would like to send consent form and authorship of my manuscript. Thank you for your attention

Best Regards
Desdiani Desdiani, MD, PhD

Change-to-authorship-letter (1).docx
110.9kB

RCR_patient_consent_form.docx
299.5kB

Re : Authorship Consent

RE: Consent Form and Authorship

Dari: Managing Editors Respirology Case Reports (respcasereports@resphealth.uwa.edu.au)

Kepada: desdiani@ymail.com

Tanggal: Kamis, 25 Maret 2021 pukul 12.52 GMT+7

Dear Dr Desdani,

I think that you have misunderstood our request. We do not need the patient consent form or the change of authorship form.
To complete your submission to our Journal you must submit your manuscript in our template for case reports, I attach the template for your convenience.
Can you please copy and paste the text from your manuscript into this template and fill the boxes that are currently missing in your manuscript file (title, authors, etc...)?

We use a digital workflow, so all the manuscripts need to be submitted in our template and it also helps our Editors and Reviewers.

Please email me if you need more explanation or if you do not understand what is required.

I look forward to receiving your manuscript again.
Kindest regards,
Christel

Christel Norman, PhD
Deputy Managing Editor
Respirology and Respirology Case Reports Editorial Office
Please note I work Monday, Tuesday and Thursday
T: +61-8-61510807
E: respcasereports@resphealth.uwa.edu.au
http://onlinelibrary.wiley.com/journal/10.1002/(ISSN)2051-3380
Submit a manuscript: https://mc.manuscriptcentral.com/respirolcasereports

From: desdiani - <desdiani@ymail.com>
Sent: Tuesday, 23 March 2021 3:34 PM
To: Managing Editors Respirology Case Reports <respcasereports@resphealth.uwa.edu.au>
Subject: Consent Form and Authorship

Dear Managing Editors,

I would like to send consent form and authorship of my manuscript. Thank you for your attention

Best Regards

Desdiani Desdiani, MD, PhD

Manuscript Submitted 25 Maret 2021

Respirology Case Reports - Manuscript ID RCR-21-065 [email ref: SE-6-a]

Dari: Respirology Case Reports (onbehalfof@manuscriptcentral.com)

Kepada: desdiani@ymail.com

Cc: desdiani@ymail.com; nitayulianti_hmt@yahoo.com; aninditabasukidr@gmail.com

Tanggal: Kamis, 25 Maret 2021 pukul 20.11 GMT+7

25-Mar-2021

Dear Dr. Desdiani:
CC all authors,

Your manuscript entitled "Delayed hypercoagulable state in COVID-19 adolescent patient: A case report" by Desdiani, Desdiani; Yulianti, Nita; Basuki, Anindita, has been submitted online and is currently under-review in Respirology Case Reports.

The editorial office staff will be in touch shortly if any essential information is missing for your submission.

The submitting author is the contact author for this paper, as such all further correspondence will be sent to Dr. Desdiani Desdiani.

Co-authors: Please contact the Editorial Office as soon as possible if you disagree with being listed as a co-author for this manuscript.

Your manuscript ID is RCR-21-065.

Please mention the above manuscript ID in all future correspondence or when calling the office for questions. If there are any changes in your street address or e-mail address, please log in to ScholarOne Manuscripts at https://mc.manuscriptcentral.com/respirolcasereports and edit your user information as appropriate.

You can also view the status of your manuscript at any time by checking your Author Center after logging in to https://mc.manuscriptcentral.com/respirolcasereports.

PUBLICATION CHARGE AND DISCOUNT:
The Wiley Open Access Payment team will contact you shortly after your manuscript has been processed with a quote for the publication charge for your article.

Did you know that members of the Asian Pacific Society of Respirology (APSR) and of Societies with en-bloc APSR membership receive a 50% discount of the Open Access Publication Charge for case reports and case series?
For more information on Publication Charges and discount and which Societies qualify for a discount, please visit:
https://onlinelibrary.wiley.com/page/journal/20513380/homepage/article_publication_charges_and_discounts.htm

If you are a member of the Asian Pacific Society of Respirology (APSR) or any of its en-bloc Societies, make sure that you have indicated your membership number and provided proof of membership upon submission. If you forgot, please contact the Editorial Office now:
respcasereports@resphealth.uwa.edu.au

If you are not a member, why not join? Please visit: http://www.apsresp.org/membership.html for more information.

IMPORTANT NOTE:
To simplify the submission process for you, the Editorial Office staff will check your submission and will notify you shortly only if anything essential is missing to your submission.
Any adjustment to the text or figures format will be required only if your manuscript is accepted for publication. We strongly recommend that you use our self-explanatory templates to guide you for your submission and ensure you have provided all the necessary information.

Please also note that your figures may be deemed appropriate for peer-review but that you may be requested to provide better quality figures if your manuscript is accepted for publication. The requirements for figure quality needed for publication are highlighted in the following Wiley author service page (see sections on Technical Specifications, Line Art requirements, Color Artwork and Mode Usage reminders):
https://authorservices.wiley.com/author-resources/book-authors/prepare-your-manuscript/artwork.html

Thank you for submitting your manuscript to Respirology Case Reports.

Sincerely,
Respirology Case Reports Editorial Office

Quote for Puiblication Charge 1 April 2021

Respirology Case Reports - Quote for Article Publication Charge - RCR-21-065

Dari: cs-openaccess@wiley.com

Kepada: DESDIANI@YMAIL.COM

Tanggal: Kamis, 1 April 2021 pukul 05.33 GMT+7

Dear Dr. Desdiani Desdiani,

Thank you for your recent submission to Respirology Case Reports. Respirology Case Reports is an open access journal that levies article publication charges; therefore, I am writing to confirm the article publication charge based on the information you supplied during the submission of the following manuscript:

Article Title: Delayed hypercoagulable state in COVID-19 adolescent patient: A case report

Manuscript ID: RCR-21-065

If your manuscript is accepted for publication in Respirology Case Reports, you will be asked to pay the following:

Total Payable: 500 USD

Society Name: APSR society with en bloc memberships

Society Member Discount: 50%

Article Publication Charge: 1000 USD

Upon invoicing, tax will be applied where applicable. If you are a tax-exempt individual or institution, you will be asked to provide your relevant tax information at that time. Please see http://www.wileyopenaccess.com/details/content/12f25d2979e/Authors.html for more information on publication charges and applicable taxes. You may provide an alternative billing address at the time of payment if an institution or another individual is paying the publication charge for your manuscript.

If you have questions about the status of your manuscript, please contact the Respirology Case Reports Editorial Office respcasereports@resphealth.uwa.edu.au.

Thank you for submitting your manuscript to Respirology Case Reports.

Sincerely,

Sheila Marie Arcilla

Wiley Open Access

cs-openaccess@wiley.com

ref: QTE - QTP

Manuscript Revision 15 April 2021

Respirology Case Reports - Decision on Manuscript ID RCR-21-065 [email ref: DL-SW-3-a]

Dari: Respirology Case Reports (onbehalfof@manuscriptcentral.com)

Kepada: desdiani@ymail.com

Cc: desdiani@ymail.com; nitayulianti_hmt@yahoo.com; aninditabasukidr@gmail.com

Tanggal: Kamis, 15 April 2021 pukul 10.36 GMT+7

14-Apr-2021

Dear Dr. Desdiani:

Manuscript ID RCR-21-065 entitled "Delayed hypercoagulable state in COVID-19 adolescent patient: A case report" which you submitted to Respirology Case Reports, has been reviewed. Some revisions to your manuscript have been recommended. Therefore, I invite you to respond to the comments appended below and revise your manuscript by the date showing in your author centre.

Before submitting your revisions:

1. Prepare a response to the reviewer comments appended below in point-by-point fashion. In order to expedite the processing of the revised manuscript, please be as specific as possible in your response and indicate the page numbers in the manuscript where you have addressed each comment.

2. Prepare a revised manuscript (word document), highlighting the changes you've made. Save this new document on your computer as you will be asked to upload it during the revision submission process. NOTE: Please be sure to keep in mind reviewer comments and incorporate your responses within the manuscript. There may well be areas where you disagree; for example, you may want to write, "A reviewer suggests that... However, I disagree because...". In any case, please try to address all of the concerns that are raised within the manuscript.

3. In addition to your revised manuscript with changes highlighted, please also save a "clean" copy where the changes are not marked.

To submit your revised manuscript:

1. Log in by clicking on the link below

*** PLEASE NOTE: This is a two-step process. After clicking on the link, you will be directed to a webpage to confirm. ***

https://mc.manuscriptcentral.com/respirolcasereports?URL_MASK=13c4da6e2d8e440fb89ea2d4f4c212d5

OR

Log into https://mc.manuscriptcentral.com/respirolcasereports and click on Author Center. Under author resources, use the button "Click here to submit a revision". PLEASE DO NOT SUBMIT YOUR REVISIONS AS A NEW MANUSCRIPT.

2. Follow the on-screen instructions. First you will be asked to provide your "Response to Decision Letter"—this is the response to reviewer comments that you prepared earlier.

3. Click through the next few screens to verify that all previously provided information is correct.

4. File Upload: Delete any files that you will be replacing (this includes your old manuscript). Upload your new revised manuscript file with changes highlighted, a "clean" copy of your revised manuscript file, any replacement figures/tables, or any new files. Once this is complete, the list of files in the "My Files" section should ONLY contain the final versions of everything. REMEMBER: figures should be in tiff, or eps format.

5. Review and submit: please be sure to double-check everything carefully so that your manuscript can be processed as quickly as possible.

Case Reports and I look forward to receiving your revision.

Deadlines:
Because we are trying to facilitate timely publication of manuscripts submitted to Respirology Case Reports, your revised manuscript should be uploaded as soon as possible. If it is not possible for you to submit your revision in the time allowed, we may have to consider your paper as a new submission. If you feel that you will be unable to submit your revision within the time allowed please contact me to discuss the possibility of extending the revision time.

Once again, thank you for submitting your manuscript to Respirology Case Reports and I look forward to receiving your revision.

Sincerely,
Dr. Trevor Williams
Associate Editor, Respirology Case Reports

Associate Editor's comments to Author:
Associate Editor
Comments to the Author (Required):
This is potentially a notable case but a great deal of important information is not included. The reviewer has provided an excellent list of comments which will enhance the report. If the requested data/clarification is not available then as it stands the report falls below the standard required for publication

If applicable:
Reviewer(s)' Comments to Author:

Reviewer: 1

Comments to the Author
In the manuscript 'Delayed hypercoagulable state in COVID-19 adolescent patient: A case report' Desdiani et al report the case of an adolescent with a post Covid-19 coagulation syndrome. The novel nature of the case is that this is a young patient who was recovering from a mild COVID infection that then deteriorated after developing a hypercoagulable state. There are a number of questions raised in the manuscript that require clarification:
MAJOR
Did the patient have heparin prior to deterioration – a HIT like syndrome has been associated with vaccines and may be associated with the clinical clotting syndrome (BMJ 2021;373:n954 http://dx.doi.org/10.1136/bmj.n954)
Did the platelet trajectory mimic a HIT like syndrome
How long was he treated with LMWH? switched to an alternative
What did the CT brain/MRI brain show?
Please discuss potential differentials or confounders to the diagnosis that this is a thrombotic event related to COVID -19
Was a lumbar puncture performed to rule out alternative causes of neurological compromise?
While the patient has no risk factors are there any risk factors in his family that might increase his propensity to clotting.
MINOR
Case
Acronyms need to be expanded or defined when first encountered in the manuscript
All supporting medications need to be listed (oage 4 of 10 – 1st paragraph)
……, the patient showed clinical improvement. On day 13 the patient had a nasopharyngeal swab PCR examination with a COVID-19 positive result of CT values …...
…, and the patient was then given additional peripheral neuropathy vitamin therapy – please name any treatments given
…the third week, the patient was discharged from the hospital- please mention the exact length of stay
…The patient's PCR result was negative…- was this the first and only time that the PCR was negative? Was the patient shedding COVID-19 for 3/52?
Do we know if there were different strains involved or what the original strain was – (Wuhan vs UK Vs South African etc.)- please confirm that the patient had not previously received a vaccine against one of the strains.
Was the patient kept in isolation all this time- did anyone else in contact with him get sick with similar symptoms
I cannot see a platelet count mentioned in the manuscript
Discussion
….The clinical PRESENTATIONS of COVID-19 patients with hypercoagulable state and strokelike symptoms were worse than non-COVID-19 s

Revision Reminder 6 Mei 2021

Reminder: Respirology Case Reports [email ref: AR-SW-2-a]

Dari: Respirology Case Reports (onbehalfof@manuscriptcentral.com)

Kepada: desdiani@ymail.com

Tanggal: Kamis, 6 Mei 2021 pukul 13.06 GMT+7

06-May-2021

This is an automatically-generated reminder/notification. Please ignore this reminder if you have already taken action

Dear Dr. Desdiani:

We recognise that the impact of the COVID-19 pandemic may affect your ability to return your revised manuscript to us within the requested timeframe. If this is the case, please let us know.

Recently, you received a decision on Manuscript ID RCR-21-065, entitled "Delayed hypercoagulable state in COVID-19 adolescent patient: A case report." The manuscript and decision letter are located in your Author Center at https://mc.manuscriptcentral.com/respirolcasereports.

This e-mail is simply a reminder that your revision is due in two weeks. If it is not possible for you to submit your revision within two weeks, please contact me as it may be possible to extend the revision time allowed. Otherwise we will consider your paper as a new submission.

There are two ways to submit your revised manuscript. You may use the link below to submit your revision online with no need to enter log in details:

*** PLEASE NOTE: This is a two-step process. After clicking on the link, you will be directed to a webpage to confirm. ***

https://mc.manuscriptcentral.com/respirolcasereports?URL_MASK=7cf7f2aedf374dbfb72d4cb5534404ed

Alternatively log into https://mc.manuscriptcentral.com/respirolcasereports and enter your Author Center. You can use the revision link or you will find your manuscript title listed under "Manuscripts with Decisions." Under "Actions," click on "Create a Revision." Your manuscript number has been appended to denote a revision. Please DO NOT upload your revised manuscripts as a new submission.

Sincerely,
Editorial Office
Respirology Case Reports Editorial Office
respcasereports@resphealth.uwa.edu.au

Revision Submitted 17 Mei 2021

Respirology Case Reports - Manuscript ID RCR-21-065.R1 [email ref: SE-8-a]

Dari: Respirology Case Reports (onbehalfof@manuscriptcentral.com)

Kepada: desdiani@ymail.com

Cc: desdiani@ymail.com; nitayulianti_hmt@yahoo.com; aninditabasukidr@gmail.com

Tanggal: Senin, 17 Mei 2021 pukul 06.48 GMT+7

16-May-2021

Dear Dr. Desdiani:
CC all authors,

Your revised manuscript entitled "Delayed hypercoagulable state in COVID-19 adolescent patient: A case report" by Desdiani, Desdiani; Yulianti, Nita; Basuki, Anindita, has been submitted online and is presently under review in Respirology Case Reports.

The submitting author is the contact author for this paper, as such all further correspondence will be sent to Dr. Desdiani Desdiani.

Co-authors: Please contact the Editorial Office as soon as possible if you disagree with being listed as a co-author for this manuscript.

Your manuscript ID is RCR-21-065.R1.

For your reference: the manuscript number of the PREVIOUS manuscript version is: RCR-21-065.

Please mention the above manuscript ID in all future correspondence or when calling the office for questions. If there are any changes in your street address or e-mail address, please log in to ScholarOne Manuscripts at https://mc.manuscriptcentral.com/respirolcasereports and edit your user information as appropriate.

You can also view the status of your manuscript at any time by checking your Author Center after logging in to https://mc.manuscriptcentral.com/respirolcasereports.

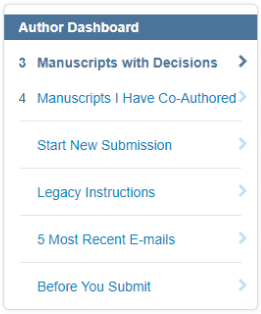
PUBLICATION CHARGE AND DISCOUNT:
The Wiley Open Access Payment team will contact you shortly after your manuscript has been processed with a quote for the publication charge for your article.

Did you know that members of the Asian Pacific Society of Respirology (APSR) and of Societies with en-bloc APSR membership receive a 50% discount of the Open Access Publication Charge for case reports and case series?
For more information on Publication Charges and discount and which Societies qualify for a discount, please visit:
https://onlinelibrary.wiley.com/page/journal/20513380/homepage/article_publication_charges_and_discounts.htm

If you are a member of the Asian Pacific Society of Respirology (APSR) or any of its en-bloc Societies, make sure that you have indicated your membership number and provided proof of membership upon submission. If you forgot, please contact the Editorial Office now:
respcasereports@resphealth.uwa.edu.au

If you are not a member, why not join? Please visit: http://www.apsresp.org/membership.html for more information.

IMPORTANT NOTE:
To simplify the submission process for you, the Editorial Office staff will check your submission and will notify you shortly only if anything essential is missing to your submission.
Any adjustment to the text or figures format will be required only if your manuscript is accepted for publication. We strongly recommend that you use our self-explanatory templates to guide you for your submission and ensue you have provided all the necessary information.
Please also note that your figures may be deemed appropriate for peer-review but that you may be requested to provide better quality figures if your manuscript is accepted for publication. The requirements for figure quality needed for



Manuscripts with Decisions

ACTION	STATUS	ID	TITLE	SUBMITTED	DECISIONED
	Contact Journal ADM: Case Reports, Respirology • Reject (08-Dec-2021) view decision letter	RCR-21-255	COVID-19 patient with a late diagnosis of HIV View Submission	05-Dec-2021	08-Dec-2021
	Contact Journal ADM: Case Reports, Respirology • Accept (19-May-2021) *Archiving completed on 21-May-2023* view decision letter	RCR-21-065.R1	Delayed hypercoagulable state in COVID-19 adolescent patient: A case report *Files Archived*	17-May-2021	19-May-2021
a revision has been submitted (RCR-21-065.R1)	Contact Journal ADM: Case Reports, Respirology • Major Revision (14-Apr-2021) • a revision has been submitted *Archiving completed on 21-May-2023* view decision letter	RCR-21-065	Delayed hypercoagulable state in COVID-19 adolescent patient: A case report *Files Archived*	25-Mar-2021	14-Apr-2021

E-mail author to editor dikirim melalui sistem, sedangkan file pada sistem telah di archieved.

Decision on Manuscript 19 Mei 2021

Respirology Case Reports - Decision on Manuscript ID RCR-21-065.R1 [email ref: DL-RW-1-a]

Dari: Respirology Case Reports (onbehalfof@manuscriptcentral.com)

Kepada: desdiani@ymail.com

Cc: desdiani@ymail.com; nitayulianti_hmt@yahoo.com; aninditabasukidr@gmail.com

Tanggal: Rabu, 19 Mei 2021 pukul 12.31 GMT+7

19-May-2021

Dear Dr. Desdiani:

It is a pleasure to accept your manuscript entitled "Delayed hypercoagulable state in COVID-19 adolescent patient: A case report" in its current form for publication in Respirology Case Reports.

Please note although the manuscript is accepted the files will now be checked to ensure that everything is ready for publication, and you may be contacted if final versions of files for publication are required.

Respirology Case Reports is the official case reports journal of the Asian Pacific Society of Respirology (APSR). If you are not already a member of the APSR, we encourage you to consider joining and enjoy the many benefits membership offers including discounted open access publication fee for Respirology Case Reports, free access to Respirology content, discounted registration fees for the annual APSR congress and discounted membership fees for other respiratory societies. Full details on APSR membership categories can be found at www.apsresp.org/membership.html Details about cost of membership and discounts can be found at:
http://www.apsresp.org/members/application/dues.html
For the APSR Membership Application online, please go to: http://www.apsresp.org/members/application/input.php

Thank you for your fine contribution. On behalf of the Editors of Respirology Case Reports, we look forward to your continued contributions to the Journal.

Sincerely,
Dr. Trevor Williams
Associate Editor, Respirology Case Reports

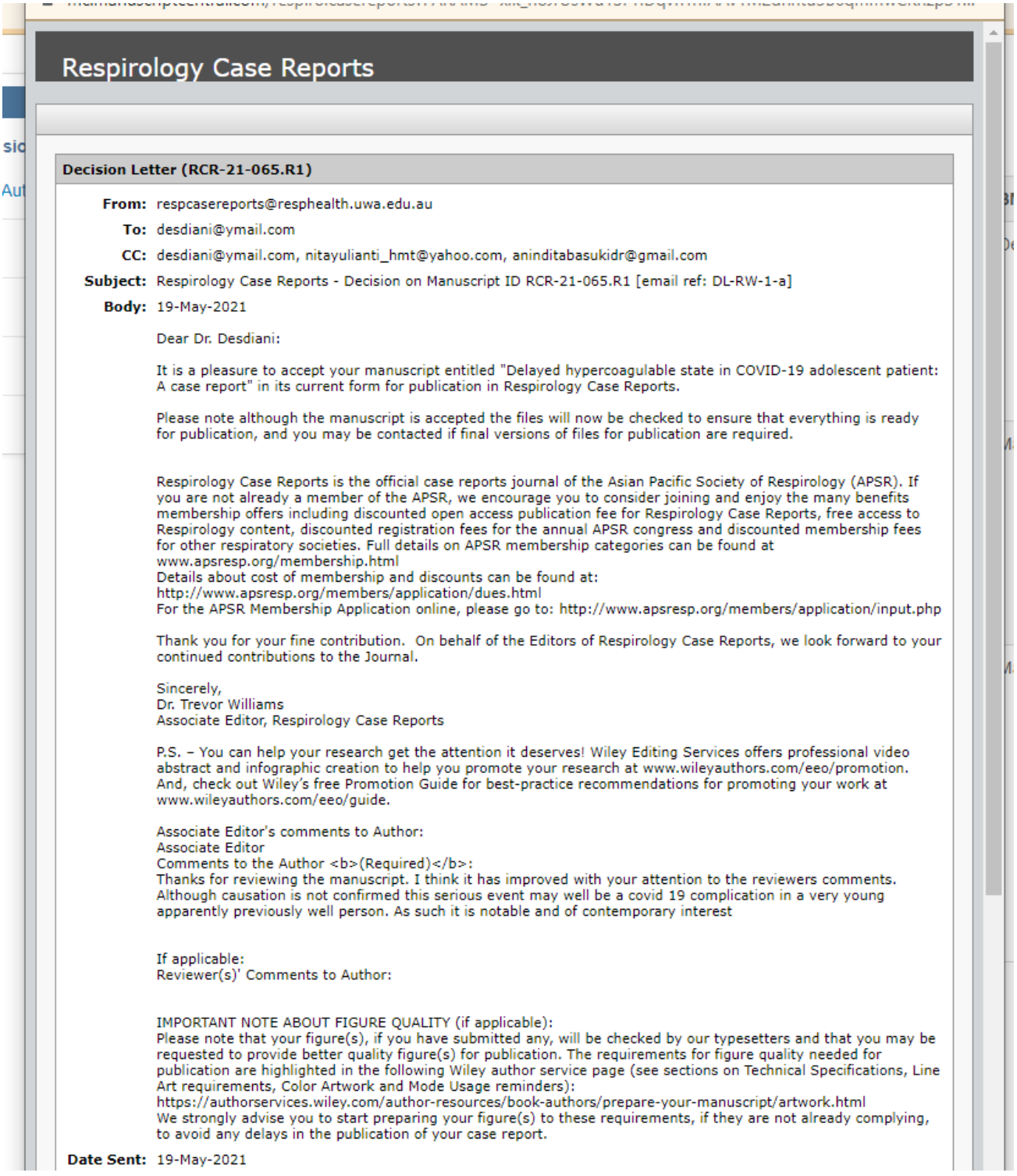
P.S. – You can help your research get the attention it deserves! Wiley Editing Services offers professional video abstract and infographic creation to help you promote your research at www.wileyauthors.com/eeo/promotion. And, check out Wiley's free Promotion Guide for best-practice recommendations for promoting your work at www.wileyauthors.com/eeo/guide.

Associate Editor's comments to Author:
Associate Editor
Comments to the Author (Required):
Thanks for reviewing the manuscript. I think it has improved with your attention to the reviewers comments. Although causation is not confirmed this serious event may well be a covid 19 complication in a very young apparently previously well person. As such it is notable and of contemporary interest

If applicable:
Reviewer(s)' Comments to Author:

IMPORTANT NOTE ABOUT FIGURE QUALITY (if applicable):
Please note that your figure(s), if you have submitted any, will be checked by our typesetters and that you may be requested to provide better quality figure(s) for publication. The requirements for figure quality needed for publication are

Decision Letter 19 Mei 2021



Respirology Case Reports

Decision Letter (RCR-21-065.R1)

From: respcasereports@resphealth.uwa.edu.au

To: desdiani@ymail.com

CC: desdiani@ymail.com, nitayulianti_hmt@yahoo.com, aninditabasukidr@gmail.com

Subject: Respirology Case Reports - Decision on Manuscript ID RCR-21-065.R1 [email ref: DL-RW-1-a]

Body: 19-May-2021

Dear Dr. Desdiani:

It is a pleasure to accept your manuscript entitled "Delayed hypercoagulable state in COVID-19 adolescent patient: A case report" in its current form for publication in Respirology Case Reports.

Please note although the manuscript is accepted the files will now be checked to ensure that everything is ready for publication, and you may be contacted if final versions of files for publication are required.

Respirology Case Reports is the official case reports journal of the Asian Pacific Society of Respirology (APSR). If you are not already a member of the APSR, we encourage you to consider joining and enjoy the many benefits membership offers including discounted open access publication fee for Respirology Case Reports, free access to Respirology content, discounted registration fees for the annual APSR congress and discounted membership fees for other respiratory societies. Full details on APSR membership categories can be found at www.apsresp.org/membership.html
Details about cost of membership and discounts can be found at:
http://www.apsresp.org/members/application/dues.html
For the APSR Membership Application online, please go to: http://www.apsresp.org/members/application/input.php

Thank you for your fine contribution. On behalf of the Editors of Respirology Case Reports, we look forward to your continued contributions to the Journal.

Sincerely,
Dr. Trevor Williams
Associate Editor, Respirology Case Reports

P.S. – You can help your research get the attention it deserves! Wiley Editing Services offers professional video abstract and infographic creation to help you promote your research at www.wileyauthors.com/eeo/promotion. And, check out Wiley's free Promotion Guide for best-practice recommendations for promoting your work at www.wileyauthors.com/eeo/guide.

Associate Editor's comments to Author:
Associate Editor
Comments to the Author (Required):
Thanks for reviewing the manuscript. I think it has improved with your attention to the reviewers comments. Although causation is not confirmed this serious event may well be a covid 19 complication in a very young apparently previously well person. As such it is notable and of contemporary interest

If applicable:
Reviewer(s)' Comments to Author:

IMPORTANT NOTE ABOUT FIGURE QUALITY (if applicable):
Please note that your figure(s), if you have submitted any, will be checked by our typesetters and that you may be requested to provide better quality figure(s) for publication. The requirements for figure quality needed for publication are highlighted in the following Wiley author service page (see sections on Technical Specifications, Line Art requirements, Color Artwork and Mode Usage reminders):
https://authorservices.wiley.com/author-resources/book-authors/prepare-your-manuscript/artwork.html
We strongly advise you to start preparing your figure(s) to these requirements, if they are not already complying, to avoid any delays in the publication of your case report.

Date Sent: 19-May-2021

Manuscript Acceptance 20 Mei 2021

Respirology Case Reports - Welcome to our reviewer database

Dari: Respirology Case Reports (onbehalfof@manuscriptcentral.com)

Kepada: desdiani@ymail.com

Tanggal: Kamis, 20 Mei 2021 pukul 13.04 GMT+7

20-May-2021

RCR-21-065.R1 - Delayed hypercoagulable state in COVID-19 adolescent patient: A case report

Dear Dr. Desdiani:

Congratulations on the acceptance of your manuscript for publication in Respirology Case Reports.

Upon submission you indicated that you would be interested in being added to our reviewer database.

We have now added your contact details to the database and we ask that you take a few minutes to login to your account and check that your keywords best describe your area(s) of expertise.
This will be extremely helpful for our Associate Editors so they can select and invite you when they receive an appropriate manuscript for peer-review.

To access your account, your Respirology Case Reports - ScholarOne Manuscripts account information is as follows:
SITE URL: https://mc.manuscriptcentral.com/respirolcasereports
USER ID: desdiani@ymail.com
PASSWORD: If you are unsure of your password you can click the link below which will take you directly to the option for setting a new password
https://mc.manuscriptcentral.com/respirolcasereports?URL_MASK=b31a84acc41e4002945c3c2c3f575262

In agreeing to act as a reviewer, you agree that we may store your details in ScholarOne Manuscripts for access only by editors of Respirology Case Reports for the purpose of selecting reviewers. If you change your mind and no longer wish to receive invitations to review manuscripts for the Journal, please do not hesitate to contact me and we will ensure that you are excluded from further reviewer invitations.
Thank you for your participation.

Sincerely,

The Editorial Team
Respirology Case Reports
https://mc.manuscriptcentral.com/respirolcasereports

Links to ScholarOne's Terms and Conditions of Use and Privacy Policy can be found at the bottom of the page on every ScholarOne Manuscripts site.

By submitting a manuscript to or reviewing for this publication, your name, email address, and affiliation, and other contact details the publication might require, will be used for the regular operations of the publication, including sharing with the publisher (Wiley) and partners for production, publication and improvements to the authoring process. The publication and the publisher recognize the importance of protecting the personal information collected from users in the operation of these services, and have practices in place to ensure that steps are taken to maintain the security, integrity, and privacy of the personal data collected and processed. You can learn more at www.wiley.com/privacy. In case you don't want to be contacted by this publication again, please send an email to

Article Proof 20 Mei 2021

Notification of publication

Dari: Respirology Case Reports (onbehalfof@manuscriptcentral.com)

Kepada: desdiani@ymail.com

Cc: desdiani@ymail.com; nitayulianti_hmt@yahoo.com; aninditabasukidr@gmail.com

Tanggal: Kamis, 20 Mei 2021 pukul 13.04 GMT+7

20-May-2021

Dear Dr. Desdiani:

It is a pleasure to inform you that your manuscript entitled "Delayed hypercoagulable state in COVID-19 adolescent patient: A case report" will be published in a forthcoming issue of Respirology Case Reports.

To maintain consistency of style within the Journal the Editors reserve the right to change the English expression of your manuscript without altering the scientific content. The responsibility for the final editing lies with the Editor-in-Chief.

Your article cannot be published until the publisher has received the appropriate signed license agreement. The corresponding author will shortly receive an email from Wiley's Author Services system which will ask them to log in and will present them with the appropriate license for completion.

Please find attached the final version of your manuscript for you to save as a reference.
If you find that any corrections need to be made, please do NOT return the corrections to us but wait for the official typeset galley proofs to arrive in due course to make your corrections. WE ENCOURAGE ALL AUTHORS TO CHECK THE SPELLING OF THEIR NAME AND FLAG ANY MISTAKES TO THE CORRESPONDING AUTHOR.

Galley proofs of your manuscript will be sent to you in due course. The proofs will be accessible on the web and all the details will be sent to you by our publisher, Wiley. Further instructions will be sent with the proof (see note below regarding figure quality). In your absence, please arrange for a colleague to access your email to retrieve the proofs and check them on your behalf. Authors should note that no correction is possible once the article has been published online therefore the corresponding author should be carefully and thoroughly checking the proofs before approving them for publication, in particular the correct spelling of all authors names.

Shortly after you have sent your corrections on the proofs back to our publisher and providing all payment has been finalised with the payment team for the open access fee, your manuscript will be published online at:
http://onlinelibrary.wiley.com/journal/10.1002/(ISSN)2051-3380

To help with increasing readership and citations of your paper, please find attached an author checklist for your reference.

We sincerely thank you for your contribution to Respirology Case Reports. Your interest is greatly appreciated and we look forward to receiving other manuscripts from you in due course.

Sincerely,
Prof. Christopher Lai
Editor-in-chief, Respirology Case Reports

IMPORTANT NOTE ABOUT FIGURE QUALITY (if applicable):
Please note that your figure(s), if you have submitted any, will be checked by our publisher, Wiley, and that you may be requested to provide better quality figure(s) for publication. The requirements for figure quality needed for publication are highlighted in the following Wiley author service page (see sections on Technical Specifications, Line Art requirements, Color Artwork and Mode Usage reminders):
https://authorservices.wiley.com/author-resources/book-authors/prepare-your-manuscript/artwork.html
We strongly advise you to start preparing your figure(s) to these requirements, if they are not already complying, to avoid any delays in the publication of your case report.

Official Case Reports Journal of the Asian Pacific Society of Respirology
Respirology Case Reports OPEN ACCESS

Delayed hypercoagulable state in COVID-19 adolescent patient: A case report

Journal:	*Respirology Case Reports*
Manuscript ID	RCR-21-065.R1
Wiley - Manuscript type:	Case Report
Date Submitted by the Author:	17-May-2021
Complete List of Authors:	Desdiani, Desdiani; Universitas Sultan Ageng Tirtayasa, Department of Pulmonology and Respiratory Medicine, Faculty of Medicine; Bhayangkara Brimob Hospital, Pulmonology and Respiratory Medicine Yulianti, Nita; Bhayangkara Brimob Hospital, Department of Clinical Pathology Basuki, Anindita; Bhayangkara Brimob Hospital, Department of Radiology
Key Words:	COVID-19, hypercoagulation, adolescent patient
Abstract:	COVID-19 is a systemic hyper inflammation disease that can cause severe respiratory symptoms and extrapulmonary manifestations. Hypercoagulable state in COVID-19 adolescent patient is a rare case. We present the case of a 16-year-old Indonesian boy with mild COVID-19 symptoms. Initially, the patient was treated with azithromycin, N-acetyl cysteine, etc. Within several days of the treatment, there was a clinical improvement. However, on day 15, the patient experienced hypercoagulation and stroke-like symptoms. The patient was then subjected to additional drugs, including low-molecular-weight heparin (LMWH), and peripheral neuropathy vitamin therapy. On day 20, the clinical symptoms reduced. This case demonstrates the need for further study of the association between COVID-19 and stroke in the young population and the use of anticoagulants to prevent thrombotic events.

RCR-21-065.R1

Title:

Delayed hypercoagulable state in COVID-19 adolescent patient: A case report

Authors' names:

Desdiani Desdiani[1,2*], Nita Yulianti[3], Anindita Basuki[4]

Authors' affiliations:

[1]Faculty of Medicine, Universitas Sultan Ageng Tirtayasa, Cilegon, Banten, Indonesia

[2]Department of Pulmonology and Respiratory Medicine, Bhayangkara Brimob Hospital, Cimanggis, Depok, Indonesia

[3]Department of Clinical Pathology, Bhayangkara Brimob Hospital, Cimanggis, Depok, Indonesia

[4]Department of Radiology, Bhayangkara Brimob Hospital, Cimanggis, Depok, Indonesia

Corresponding author:

Desdiani Desdiani

Faculty of Medicine, Universitas Sultan Ageng Tirtayasa, Jalan Jend. Sudirman No.20, RT.10/RW.5, Kotabumi, Cilegon, Banten, Indonesia 42434.

E-mail : desdiani@ymail.com

Short title:

Hypercoagulable in COVID-19 Adolescent

Keywords:

COVID-19, hypercoagulation, adolescent patient

Abstract:

COVID-19 is a systemic hyperinflammation disease which can cause severe respiratory symptoms and extrapulmonary manifestations. Hypercoagulable state in COVID-19 adolescent patient is a rare case. We present the case of a 16-year-old Indonesian boy with

mild COVID-19 symptoms. Initially, the patient was treated with azithromycin, N-acetyl cysteine, etc. Within several days of the treatment, there was clinical improvement. However, on day 15, the patient experienced hypercoagulation and stroke-like symptoms. The patient was then subjected to additional drugs, including low-molecular-weight heparin (LMWH), and peripheral neuropathy vitamin therapy. On day 20, the clinical symptoms reduced. This case demonstrates the need for further study of the association between COVID-19 and stroke in young population and the use of anticoagulants to prevent thrombotic events.

Text:

Introduction

COVID-19 is a disease which can cause systemic hyperinflammation and has spread worldwide. The usual symptoms are fever, cough, malaise, anosmia, loss of appetite, diarrhea, and other varying symptoms [1]. To date, there is no definitive treatment which can cure the disease. Elderly patients or patients with existing comorbidities have increased risks of severe illness from COVID-19. Most of the reported cases are those with some complications, such as hypercoagulation. Some cases reported that this condition could occur in young patients when the potency of virus infection has started to decrease. Endothelial injury due to COVID-19 can trigger hypercoagulable state. We report a case of an adolescent patient with mild symptoms of COVID-19 who was already in recovery state, but suddenly experienced hypercoagulable state and stroke-like symptoms.

Case Report

A 16-year-old Indonesian boy with fever and cough, and a history of close contact with a confirmed case COVID-19 patient was admitted to the emergency department in our hospital. From anamnesis, there was no comorbidity (e.g. hypertension, diabetes mellitus,

autoimmune disease, or malignancy). Vital signs and oxygen saturation were in normal ranges. Laboratory, radiology, and nasopharyngeal swab polymerase chain reaction (PCR) tests were conducted and the results were positive for COVID-19 with CT values of RdrP: 28.05, E: 27.08. Laboratory examination showed leucocytes of 3,720 cell/µL, Platelet 241,000 cell/µL, lymphocytes 10%, monocytes 13%, Neutrophil to Lymphocyte Ratio (NLR) 7.1, absolute lymphocyte count (ALC) 780 µL, D-dimer 269 ng/ml, quantitative C-reactive Protein (CRP) < 5 mg/L, prothrombin time 13.1 second, the international normalized ratio (INR) 0.96, and partial thromboplastin time 23.7. The posteroanterior (PA) chest X-ray showed no radiological abnormalities in the heart and lungs (Fig. 1). The Computed Tomography (CT) scan of the chest at the time also showed no visible acute lung inflammation, lung mass, or mediastinal tumor (Fig. 2). The patient was given treatments with azithromycin, N-acetyl cysteine, paracetamol and other supporting medications such as zinc, vitamin D3, vitamin C and curcumin.

Within several days of the treatment, the patient showed clinical improvement. On day 13 the patient had a nasopharyngeal swab PCR examination with a positive result of CT values of RdrP: 33.79, E: 33.77. On day 15 of the treatment, the patient suddenly had a high fever accompanied by severe and throbbing headaches, flatulence, nausea and vomiting, abdominal pain, numbness of arms, tingling and immobility of legs, and oxygen saturation of 93%.

The patient was then subjected to additional drugs, such as meropenem, dexamethasone, remdesivir, low-molecular-weight heparin (LMWH) for 5 days, ondansentron, omeprazole, and supplements (e.g. vitamin C, zinc, and vitamin D3). Laboratory examination showed leukocytes of 12,220 cells µ/L, platelet 260,000 cell/µL, monocytes 12%, NLR 17.72, lymphocytes 4.4%, D-dimer 16,180 ng/mL, quantitative CRP

26.4 mg/L, activated partial thromboplastin time (APTT) 19.9 seconds, potassium 3.2, Aspartate aminotransferase (AST) 51 U/L. Radiology examination showed no radiological abnormalities both in the heart and lungs. CT scan of the chest showed solitary ground-glass opacity nodules on S6 left lung (Fig. 3 and Fig. 4). We consulted a neurologist, and the patient was then given additional peripheral neuropathy vitamin therapy such as methylcobalamin and vitamin B1 for 5 days. Furthermore, the patient was also given oxygen therapy and he felt better after that.

On day 20 of the treatment, the clinical symptoms reduced. The patient was able to move the limbs again and the tingling sensation reduced. The D-dimer value of 460 ng/mL, quantitative CRP of 6.1 mg/L, lymphocytes 13%, platelet 284,000 cell/µL and the other parameters were within normal ranges, although the PCR result was still positive. At the end of the third week, the patient was discharged from the hospital. The patient's PCR result was negative. The laboratory and radiology results also had improved.

Discussion

Pisano et al. (2020) reported an African-American 33-year-old female COVID-19 patient with acute malignant middle cerebral artery infarction. The SARS-CoV-2 virus was reported to cause a thrombotic event [2]. COVID-19 patients might experience thrombocytopenia, prolonged prothrombin time, increased fibrinogen, and D-dimers [3]. Other markers of coagulation and inflammation that can be abnormal include ferritin, von Willebrand Factor (VWF), C-reactive protein (CRP), complement, and cytokines. Thrombotic events occur in one-third of COVID-19 patients which are dominated by pulmonary embolism and associated with the severity of disease and increased mortality [4]. A study on the five patients infected with COVID-19 under 50 years old who did not have risk factors for

vascular diseases and were hospitalized with symptoms such as stroke showed that these cases have increased sevenfold compared with the previous year and were associated with COVID-19. The patient's laboratory results in our case showed a hypercoagulable state, leading to the postulation that stroke observed in the young patient may be associated with SARS-CoV-2. This patient had never previously received vaccines and heparin. The clinical of COVID-19 patients with hypercoagulable state and stroke-like symptoms were worse than non-COVID-19 stroke patients because it is related to the pathophysiology of the COVID-19 disease [5].

To date, data which support the association between COVID-19 and stroke in young population without specific risk factors (sometimes only mild respiratory symptoms) are increasing. Further studies are necessary to investigate this association and the use of anticoagulants to prevent thrombotic events. Our case underlines young patients with hypercoagulation and stroke symptoms but not yet confirmed with COVID-19 need to be thoroughly investigated, including the patients with mild COVID-19 symptoms, especially if new neurological symptoms arise.

References:

1) Kichloo A, Dettloff K, Aljadah M, et al. COVID-19 and hypercoagulability: a review. Clin Appl Thromb Hemost. 2020;26:1-9.
2) Pisano TJ, Hakkinen I, Rybinnik I. Large vessel occlusion secondary to COVID-19 hypercoagulability in young patient: a case report and literature review. J Stroke Cerebrovasc Dis. 2020;29:1-6.
3) Bao J, Li C, Zhang K, et al. Comparative analysis of laboratory indexes of severe and non-severe patients infected with COVID-19. Clin Chim Acta 2020;509:180-94.

4) Klok FA, Kruip MJHA, van der Meer NJM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res. 2020;191:145-7.

5) Oxley TJ, Mocco J, Majidi S, et al. Large-vessel stroke as a presenting feature of COVID-19 in the young. N Engl J Med. 2020;382:60.

Figure legends:

Figure 1. Chest Imaging. (A) Chest radiography showing no radiological abnormalities both in the heart and lungs. (B) CT scan of the chest at that time showed no visible picture of acute lung inflammation, lung mass or mediastinal tumor

Figure 2. Chest Imaging (A) Chest radiography no radiological abnormalities both in the heart and lungs. (B) CT scan of the chest showed a solitary nodular Ground Glass Opacity in S6 left lung (red arrow)

Disclosure statement

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

Author contribution statement:

Desdiani Desdiani : Conception, acquisition of information, analysis or interpretation data, drafting the manuscript, final approval of the version to be published

Nita Yulianti : Analysis or interpretation of laboratories data

Anindita Basuki : Analysis or interpretation of radiography data

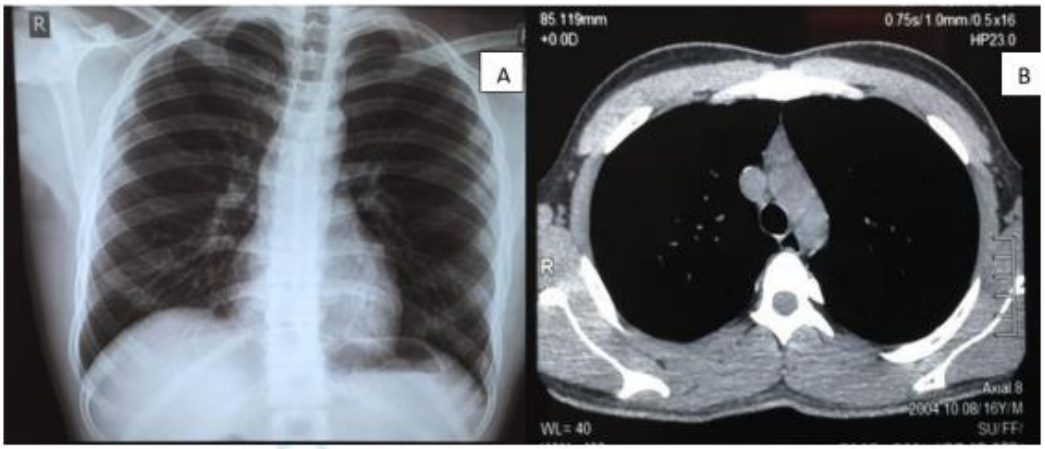


Figure 1. Chest Imaging. (A) Chest radiography showing no radiological abnormalities both in the heart and lungs. (B) CT scan of the chest at that time showed no visible picture of acute lung inflammation, lung mass or mediastinal tumor

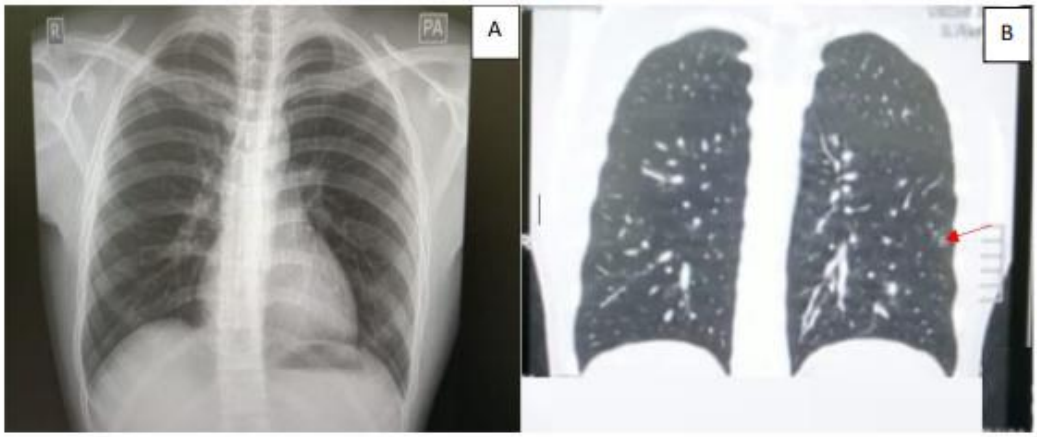


Figure 2. Chest Imaging (A) Chest radiography no radiological abnormalities both in the heart and lungs. (B) CT scan of the chest showed a solitary nodular Ground Glass Opacity in S6 left lung (red arrow)

Article Production 23 Mei 2021

Information: Production Editor Contact Respirology Case Reports | Delayed hypercoagulable state in COVID-19 adolescent patient: A case report

Dari: jpcms@spi-global.com

Kepada: desdiani@ymail.com

Tanggal: Minggu, 23 Mei 2021 pukul 07.30 GMT+7

Dear Dr. Desdiani Desdiani,

We are in the process of preparing "Delayed hypercoagulable state in COVID-19 adolescent patient: A case report" for publication. Your production editor, Abigail Cabela, will support you and your article throughout the process.

Please get in touch with your Production Editor at acabela@wiley.com if you have any questions.

Sincerely,
Booking-in Team,
On behalf of Wiley

Article ID: RCR2_793
Article DOI: 10.1002/RCR2.793

Publication 23 Mei 2021

In Production: Your article accepted in Respirology Case Reports

Dari: cs-author@wiley.com

Kepada: desdiani@ymail.com

Tanggal: Minggu, 23 Mei 2021 pukul 08.40 GMT+7

Dear Desdiani Desdiani,

Article ID: RCR2793
Article DOI: 10.1002/rcr2.793
Internal Article ID: 17117470
Article: Delayed hypercoagulable state in COVID-19 adolescent patient: A case report
Journal: Respirology Case Reports

Congratulations on the acceptance of your article for publication in Respirology Case Reports.

Your article has been received and the production process is now underway. We look forward to working with you and publishing your article. Using Wiley Author Services, you can track your article's progress.

Please click below to login - if you are using a different email address than this one, you will need to manually assign this article to your Dashboard (see How do I assign a missing article to My Dashboard?):

https://authorservices.wiley.com/index.html#login?campaign=email_invitation-new

If applicable, a list of available actions will appear below – check out your Author Services Dashboard for all actions related to your articles.

Sign your license agreement (REQUIRED) -- you will receive an email when this task is ready on your dashboard.
Pay your article publication charge (REQUIRED)
Track your article's progress to publication
Access your published article
Share your published article with colleagues

If you need any assistance, please click here to view our Help section.

Sincerely,
Wiley Author Services

Article Proof 26 Mei 2021

Action: Proof of RCR2_EV_RCR2793 for Respirology Case Reports ready for review

Dari: Wiley Online Proofing (onlineproofing@eproofing.in)
Kepada: desdiani@ymail.com
Tanggal: Rabu, 26 Mei 2021 pukul 00.56 GMT+7

Review your proof

Dear **Dr. Desdiani Desdiani,**

The proof of your **Respirology Case Reports** article **Delayed hypercoagulable state in COVID-19 adolescent patient: a case report** is now available for review:

Edit Article

To review your article, please complete the following steps, ideally within 48 hours*, so we can publish your article as quickly as possible.

1. Open your proof in the online proofing system using the button above.
2. Check the article for correctness and respond to all queries. For instructions on using the system, please see the "Help" menu in the upper right corner.
3. Submit your changes by clicking the "Submit" button in the proofing system.
4. Don't forget to pay your open access Article Publication Charge (APC). We can't publish your article without it. LOG IN TO PAY (BUTTON/Link https://authorservices.wiley.com/index.html#dashboard)

Helpful Tips

- Your manuscript has been formatted following the style requirements for the journal. Any requested changes that go against journal style will not be made.
- Your proof will include queries. These must be replied to using the system before the proof can be submitted.
- The only acceptable changes at this stage are corrections to grammatical errors or data accuracy, or to provide higher resolution figure files (if requested by the typesetter).

- Any changes to scientific content or authorship will require editorial review and approval.
- Once your changes are complete, submit the article after which no additional corrections can be requested.
- Most authors complete their corrections within 48 hours. Returning any corrections promptly will accelerate publication of your article.

If you encounter any problems or have questions, please contact the production office at (RCR2@wiley.com). For the quickest response, include the journal name and your article ID (found in the subject line) in all correspondence.

Best regards,
Respirology Case Reports Production Office

* We appreciate that the COVID-19 pandemic may create conditions for you that make it difficult for you to review your proof within standard timeframes. If you have any problems keeping to this schedule, please reach out to me at (RCR2@wiley.com) to discuss alternatives.

Correction Successfully Submitted 26 Mei 2021

Corrections successfully submitted for RCR2_EV_RCR2793, Delayed hypercoagulable state in COVID-19 adolescent patient: a case report.

Dari: Wiley Online Proofing (notifications@eproofing.in)
Kepada: desdiani@ymail.com
Cc: RCR2@wiley.com
Tanggal: Rabu, 26 Mei 2021 pukul 07.38 GMT+7

Corrections successfully submitted

Dear **Dr. Desdiani Desdiani,**

Thank you for reviewing the proof of the **Respirology Case Reports** article **Delayed hypercoagulable state in COVID-19 adolescent patient: a case report**.

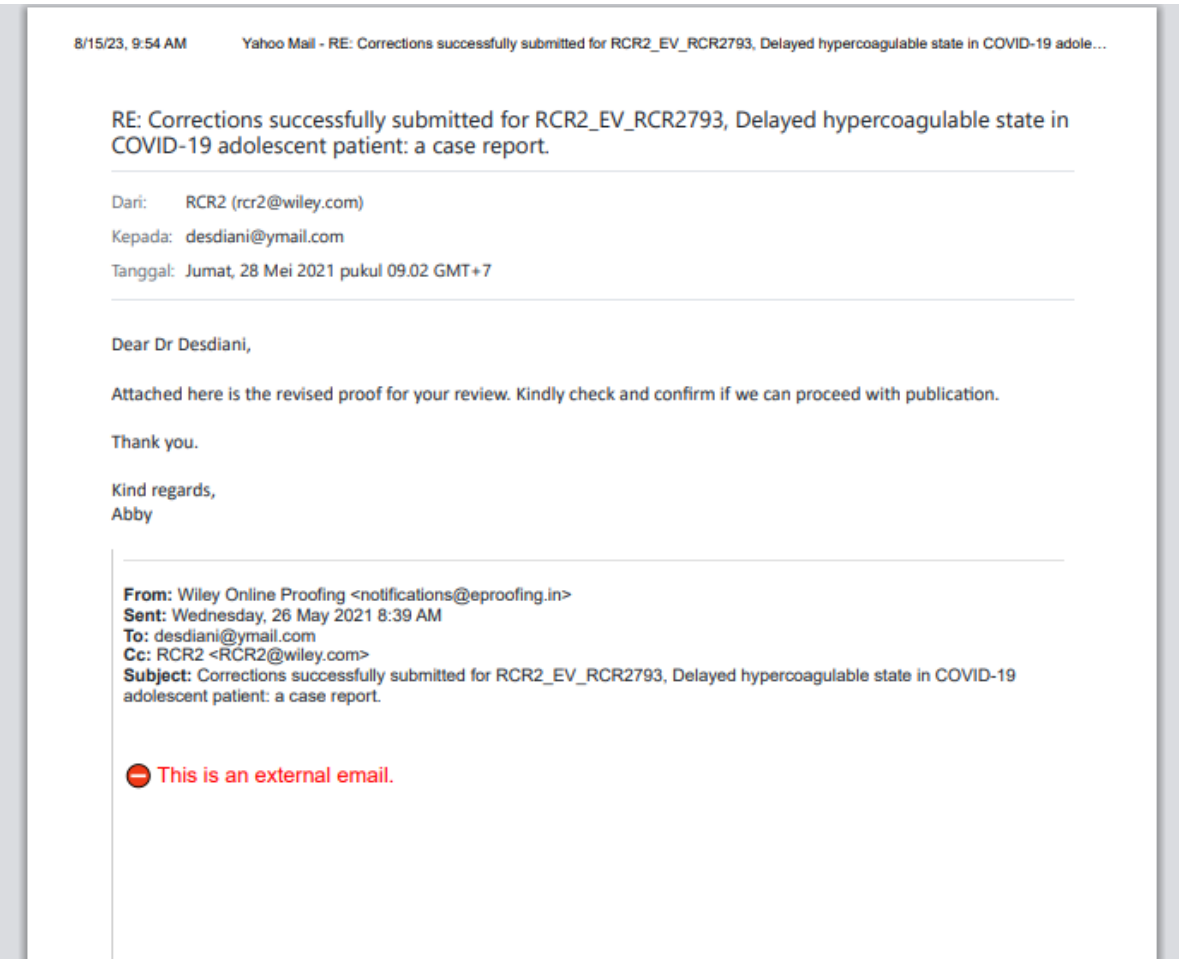
View Article

This is a read-only version of your article with the corrections you have marked up.

If you encounter any problems or have questions please contact us at (RCR2@wiley.com). For the quickest response include the journal name and your article ID (found in the subject line) in all correspondence.

Best regards,
Respirology Case Reports

Re : Correction Successfully Submitted 28 Mei 2021



8/15/23, 9:54 AM Yahoo Mail - RE: Corrections successfully submitted for RCR2_EV_RCR2793, Delayed hypercoagulable state in COVID-19 adole…

RE: Corrections successfully submitted for RCR2_EV_RCR2793, Delayed hypercoagulable state in COVID-19 adolescent patient: a case report.

Dari: RCR2 (rcr2@wiley.com)
Kepada: desdiani@ymail.com
Tanggal: Jumat, 28 Mei 2021 pukul 09.02 GMT+7

Dear Dr Desdiani,

Attached here is the revised proof for your review. Kindly check and confirm if we can proceed with publication.

Thank you.

Kind regards,
Abby

From: Wiley Online Proofing <notifications@eproofing.in>
Sent: Wednesday, 26 May 2021 8:39 AM
To: desdiani@ymail.com
Cc: RCR2 <RCR2@wiley.com>
Subject: Corrections successfully submitted for RCR2_EV_RCR2793, Delayed hypercoagulable state in COVID-19 adolescent patient: a case report.

⛔ This is an external email.

Author to Editor : Agreement 28 Mei 2021

Re: Corrections successfully submitted for RCR2_EV_RCR2793, Delayed hypercoagulable state in COVID-19 adolescent patient: a case report.

Dari: desdiani - (desdiani@ymail.com)

Kepada: RCR2@wiley.com

Tanggal: Jumat, 28 Mei 2021 pukul 13.41 GMT+7

Dear Abby,
I agree with the revised proof of my manuscript.
Thank you.

Best regards,
Desdiani Desdiani

Pada Jumat, 28 Mei 2021 09.02.21 GMT+7, RCR2 <rcr2@wiley.com> menulis:

> Dear Dr Desdiani,
>
> Attached here is the revised proof for your review. Kindly check and confirm if we can proceed with publication.
>
> Thank you.
>
> Kind regards,
> Abby
>
> **From:** Wiley Online Proofing <notifications@eproofing.in>
> **Sent:** Wednesday, 26 May 2021 8:39 AM
> **To:** desdiani@ymail.com
> **Cc:** RCR2 <RCR2@wiley.com>
> **Subject:** Corrections successfully submitted for RCR2_EV_RCR2793, Delayed hypercoagulable state in COVID-19 adolescent patient: a case report.
>
> This is an external email.

Article Accepted

Official Case Reports Journal of the Asian Pacific Society of Respirology

Respirology Case Reports OPEN ACCESS APSR

Delayed hypercoagulable state in COVID-19 adolescent patient: a case report

Desdiani Desdiani[1,2], Nita Yulianti[3] & Anindita Basuki[4]

[1]Faculty of Medicine, Universitas Sultan Ageng Tirtayasa, Cilegon, Indonesia.
[2]Department of Pulmonology and Respiratory Medicine, Bhayangkara Brimob Hospital, Depok, Indonesia.
[3]Department of Clinical Pathology, Bhayangkara Brimob Hospital, Depok, Indonesia.
[4]Department of Radiology, Bhayangkara Brimob Hospital, Depok, Indonesia.

Keywords
Adolescent patient, COVID-19, hypercoagulation.

Correspondence
Desdiani Desdiani, Faculty of Medicine, Universitas Sultan Ageng Tirtayasa, Jalan Jend. Sudirman No. 20, RT.10/RW.5, Kotabumi, Cilegon, Banten 42434, Indonesia. E-mail: desdiani@ymail.com

Received: 25 March 2021; Revised: 17 May 2021; Accepted: 17 May 2021; Associate Editor: Trevor Williams.

***Respirology Case Reports*, 9 (7), 2021, e00793**

doi: 10.1002/rcr2.793

Abstract

Coronavirus disease 2019 (COVID-19) is a systemic hyperinflammation disease which can cause severe respiratory symptoms and extrapulmonary manifestations. Hypercoagulable state in COVID-19 adolescent patient is a rare case. We present the case of a 16-year-old Indonesian boy with mild COVID-19 symptoms. Initially, the patient was treated with azithromycin, N-acetyl cysteine, etc. After several days of the treatment, there was clinical improvement. However, on day 15, the patient experienced hypercoagulation and stroke-like symptoms. The patient was then subjected to additional drugs, including low-molecular weight heparin (LMWH), and peripheral neuropathy vitamin therapy. On day 20, the clinical symptoms reduced. This case demonstrates the need for further study of the association between COVID-19 and stroke in young population and the use of anticoagulants to prevent thrombotic events.

Introduction

Coronavirus disease 2019 (COVID-19) is a disease which can cause systemic hyperinflammation and has spread worldwide. The usual symptoms are fever, cough, malaise, anosmia, loss of appetite, diarrhoea, and other varying symptoms [1]. To date, there is no definitive treatment which can cure the disease. Elderly patients or patients with existing comorbidities have increased risks of severe illness from COVID-19. Most of the reported cases are those with some complications, such as hypercoagulation. Some cases reported that this condition could occur in young patients when the potency of virus infection has started to decrease. Endothelial injury due to COVID-19 can trigger hypercoagulable state. We report a case of an adolescent patient with mild symptoms of COVID-19 who was already in recovery state, but suddenly experienced hypercoagulable state and stroke-like symptoms.

Case Report

A 16-year-old Indonesian boy with fever and cough, and a history of close contact with a confirmed case COVID-19 patient was admitted to the emergency department in our hospital. From anamnesis, there was no comorbidity (e.g. hypertension, diabetes mellitus, autoimmune disease, or malignancy). Vital signs and oxygen saturation were in normal ranges. Laboratory, radiology, and nasopharyngeal swab polymerase chain reaction (PCR) tests were conducted and the results were positive for COVID-19 with CT values of RdrP: 28.05, E: 27.08. Laboratory examination showed leucocytes of 3720 cells/μL, platelet 241,000 cells/μL, lymphocytes 10%, monocytes 13%, neutrophil-to-lymphocyte ratio (NLR) 7.1, absolute lymphocyte count (ALC) 780 μL, D-dimer 269 ng/mL, quantitative C-reactive protein (CRP) < 5 mg/L, prothrombin time 13.1 sec, the international normalized ratio (INR) 0.96, and partial thromboplastin of time 23.7. The posteroanterior (PA) chest X-ray showed no radiological abnormalities in the heart and lungs (Fig. 1A). Computed tomography (CT) scan of the chest at the time also showed no visible acute lung inflammation, lung mass, or mediastinal tumour (Fig. 1B). The patient was treated with azithromycin, N-acetyl cysteine, paracetamol, and other supporting medications such as zinc, vitamin D3, vitamin C, and curcumin.

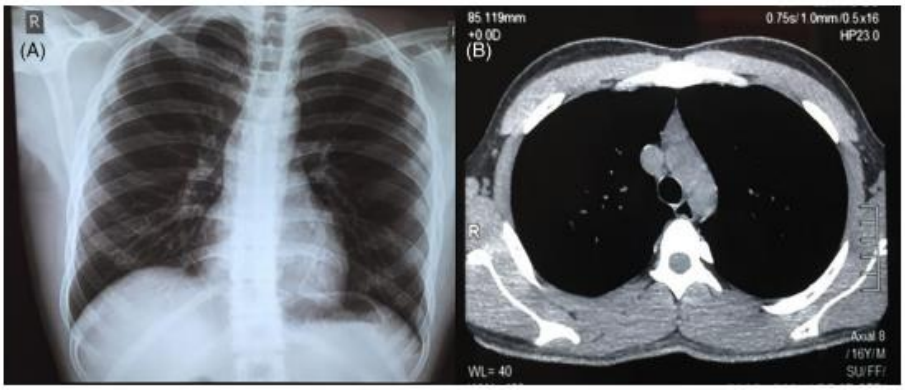


Figure 1. Chest imaging. (A) Chest radiography showing no radiological abnormalities both in the heart and lungs. (B) Computed tomography (CT) scan of the chest at that time showed no visible picture of acute lung inflammation, lung mass, or mediastinal tumour.

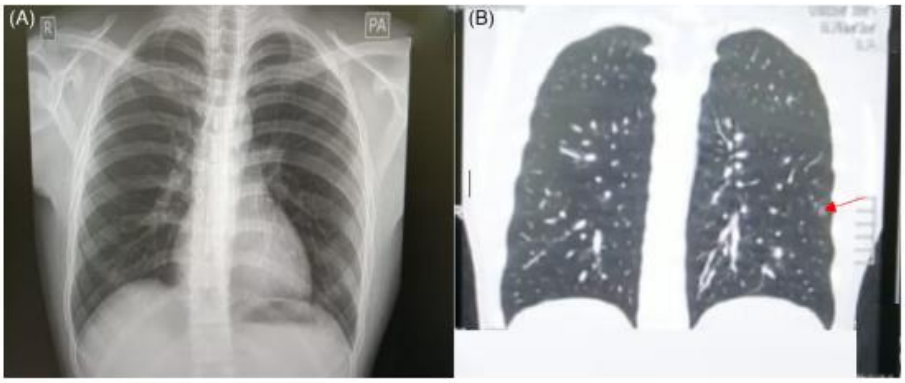


Figure 2. Chest imaging. (A) Chest radiography showing no radiological abnormalities both in the heart and lungs. (B) Computed tomography (CT) scan of the chest showed a solitary nodular ground-glass opacity in S6 left lung (red arrow).

After several days of the treatment, the patient showed clinical improvement. On day 13, the patient had a nasopharyngeal swab PCR examination with a positive result of CT values of RdrP: 33.79, E: 33.77. On day 15 of the treatment, the patient suddenly had a high fever accompanied by severe and throbbing headaches, flatulence, nausea and vomiting, abdominal pain, numbness of arms, tingling and immobility of legs, and oxygen saturation of 93%.

The patient was then subjected to additional drugs, such as meropenem, dexamethasone, remdesivir, low-molecular weight heparin (LMWH) for five days, ondansetron, omeprazole, and supplements (e.g. vitamin C, zinc, and vitamin D3). Laboratory examination showed leucocytes of 12,220 cells/μL, platelet 260,000 cell/μL, monocytes 12%, NLR 17.72, lymphocytes 4.4%, D-dimer 16,180 ng/mL, quantitative CRP 26.4 mg/L, activated partial thromboplastin time (APTT) 19.9 sec, potassium 3.2, and aspartate aminotransferase (AST) of 51 U/L. Radiology examination showed no radiological abnormalities both in the heart and lungs (Fig. 2A). CT scan of the chest showed solitary ground-glass opacity nodules on S6 left lung (Fig. 2B). We consulted a neurologist, and the patient was then given additional peripheral neuropathy vitamin therapy such as methylcobalamin and vitamin B1 for five days.

Furthermore, the patient was also given oxygen therapy and he felt better after that.

On day 20 of the treatment, the clinical symptoms reduced. The patient was able to move the limbs again and the tingling sensation reduced. The D-dimer value of 460 ng/mL, quantitative CRP of 6.1 mg/L, lymphocytes 13%, platelet 284,000 cell/μL and the other parameters were within normal ranges, although the PCR result was still positive. At the end of the third week, the patient was discharged from the hospital. The patient's PCR result was negative. The laboratory and radiology results had also improved.

Discussion

Pisano et al. reported an African-American 33-year-old female COVID-19 patient with acute malignant middle cerebral artery infarction. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was reported to cause a thrombotic event [2]. COVID-19 patients might experience thrombocytopenia, prolonged prothrombin time, increased fibrinogen, and D-dimers [3]. Other markers of coagulation and inflammation that can be abnormal include ferritin, von Willebrand factor (VWF), CRP, complement, and cytokines. Thrombotic events occur in one-third of COVID-19 patients which are dominated by pulmonary embolism and associated with the severity of disease and increased mortality [4]. A study of five patients (younger than 50 years) infected with COVID-19 who did not have risk factors for vascular diseases and were hospitalized with symptoms such as stroke showed that these cases have increased sevenfold compared with the previous year and were associated with COVID-19. The patient's laboratory results in our case showed a hypercoagulable state, leading to the postulation that stroke observed in the young patient may be associated with SARS-CoV-2. This patient had never previously received vaccines and heparin. The clinical status of COVID-19 patients with hypercoagulable state and stroke-like symptoms was worse than non-COVID-19 stroke patients because it is related to the pathophysiology of the COVID-19 [5].

To date, data which support the association between COVID-19 and stroke in young population without specific risk factors (sometimes only mild respiratory symptoms) are increasing. Further studies are necessary to investigate this association and the use of anticoagulants to prevent thrombotic events. Our case underlines young patients with hypercoagulation and stroke symptoms but not yet confirmed with COVID-19 need to be thoroughly investigated, including the patients with mild COVID-19 symptoms, especially if new neurological symptoms arise.

Disclosure Statement

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

Author Contribution Statement

Desdiani Desdiani: Conception, acquisition of information, analysis or interpretation data, drafting the manuscript, and final approval of the version to be published. Nita Yulianti: Analysis or interpretation of laboratory data. Anindita Basuki: Analysis or interpretation of radiography data.

References

1. Kichloo A, Dettloff K, Aljadah M, et al. 2020. COVID-19 and hypercoagulability: a review. Clin. Appl. Thromb. Hemost. 26:1–9.
2. Pisano TJ, Hakkinen I, and Rybinnik I. 2020. Large vessel occlusion secondary to COVID-19 hypercoagulability in young patient: a case report and literature review. J. Stroke Cerebrovasc. Dis. 29:1–6. https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.105307.
3. Bao J, Li C, Zhang K, et al. 2020. Comparative analysis of laboratory indexes of severe and non-severe patients infected with COVID-19. Clin. Chim. Acta 509:180–194. https://doi.org/10.1016/j.cca.2020.06.009.
4. Klok FA, Kruip MJHA, van der Meer NJM, et al. 2020. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb. Res. 191:145–147.
5. Oxley TJ, Mocco J, Majidi S, et al. 2020. Large-vessel stroke as a presenting feature of COVID-19 in the young. N. Engl. J. Med. 382:60.

Published Article 8 Juni 2021

Published: Your article is published in an issue

Dari: cs-author@wiley.com

Kepada: desdiani@ymail.com

Tanggal: Selasa, 8 Juni 2021 pukul 22.37 GMT+7

Dear Desdiani Desdiani,

Your article Delayed hypercoagulable state in COVID-19 adolescent patient: A case report in Respirology Case Reports has the following publication status: Published in Issue

To access your article, please click the following link to register or log in:

https://authorservices.wiley.com/index.html#register

You can also access your published article via this link: http://dx.doi.org/10.1002/rcr2.793

If you need any assistance, please click here to view our Help section.

Sincerely,

Wiley Author Services

To unsubscribe from these emails, target="_blank">click here.

Link : https://onlinelibrary.wiley.com/doi/10.1002/rcr2.793