



Case Report

Liver abscess with necrosis in post COVID-19: A case report

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ABSTRACT

Introduction: Coronavirus disease 2019 (COVID-19) is an acute respiratory tract infection caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2). Recent evidences mentioned the possibility of COVID-19 as a systemic infectious and inflammatory disease. Signs and symptoms of liver and gastrointestinal system are often found in post-acute COVID-19 patients. However, there are only few data found about liver abscess and necrosis in post COVID-19 patients.

Case presentation: A 49-year-old man admitted to the hospital with dyspnea, nausea, loss of appetite and epigastric pain, post confirmed SARS CoV-2 severe pneumonia 1 month ago in ICU with noninvasive ventilator (NIV), enoxaparin, tocilizumab, azithromycin, levofloxacin, hydroxychloroquine, and no preexisting liver condition. Swab PCR result was negative. The result of abdominal computed tomography (CT) scan with contrast was liver abscess formation with hemorrhages measuring about $16 \times 12 \times 11$ cm & $10 \times 9 \times 9$ cm occupying most of the right lobe liver. The patient underwent exploratory laparotomy, there were multiple liver abscesses in segment 8 with parenchymal liver necrosis and abscesses in segment 7 of liver. Necrosectomy and liver abscess drainage was performed.

Clinical discussion: Pathophysiology of liver damage in post COVID-19 are direct cytotoxicity of SARS-CoV2, immune-mediated due to severe systemic inflammatory response syndrome (SIRS) in COVID-19, hypoxemia, vascular changes due to coagulopathy, endothelitis or congestion from right heart failure, and drug-induced liver injury (DILI).

Conclusion: The possible pathophysiology of liver abscess and necrosis in post COVID-19 should be considered in monitoring and management for both COVID-19 patients and post COVID-19 patients.

Authors contribution

Aldrich Kurniawan Liemarto: study concept, data collection and interpretation.

Bernadus Parish Budiono: review of study.

Melissa Angela Chionardes: data collection, drafting and editing the paper.

Ivona Oliviera: data collection, drafting and editing the paper.

Anindita Rahmasiwi: data collection, drafting and editing the paper.

1. Introduction

Coronavirus disease 2019 is an acute respiratory infection disease

caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2) [1]. SARS-CoV2 belongs to Coronaviridae family, which is a single-stranded RNA virus. This virus has main target at angiotensin converting enzyme 2 (ACE2) receptor [2]. Therefore, respiratory system is one of the main targets of SARS-CoV2 infection. Several patients present severe symptoms and respiratory failure or acute respiratory distress syndrome (ARDS), which can lead to death [3]. In addition, ACE2 receptors are also present in liver, gastrointestinal system, heart, kidneys, pancreas, muscular and nervous systems [4,5]. Recent evidences mentioned the possibility of COVID-19 as a systemic infectious and inflammatory disease [6]. Gastrointestinal signs and symptoms are often found in post COVID-19 patients [7].

There were several previous studies regarding liver disorders in post

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SARS-CoV2 infection patients. Studies showed that SARS-CoV2 could bind to ACE2 on cholangiocytes, leading to cholangiocyte dysfunction, which triggered a systemic inflammatory response and caused liver damage [8]. Epidemiological studies showed that 43 out of 99 patients had abnormal liver function, particularly higher alanine aminotransferase (ALT) or aspartate aminotransferase (AST) levels, and 1 in 99 patients had severe liver damage [9]. In the study of Zhang et al. the incidence of liver damage was 78% of the 82 confirmed deaths from SARS-CoV2 infection [10].

2. Case presentation

A 49-year-old man admitted to hospital with chief complaint shortness of breath continuously, worsened with activity, and decreased slightly at rest; also complained cough, nausea, decreased appetite, and heartburn. Patient had history of confirmed severe SARS COV-2 pneumonia 1 month in ICU, diabetes mellitus, administration of enoxaparin, tocilizumab, azithromycin, levofloxacin, and hydroxychloroquine, AST and ALT within normal limits, no previous history of hypertension and liver disease.

At emergency room, patient was conscious, weak and short of breath, checked blood pressure, heart rate, and temperature within normal range, respiratory rate 32 times per minute, oxygen saturation 97% with nasal oxygen 4 L per minute. On physical examination, crackles were found in both lung fields and tenderness in epigastrium. Fasting blood glucose results 468 mg/dL (N:70–100), 2-h glucose post prandial 405 mg/dL (N:<140), HbA1c 8.87% (N:<5.7). The other laboratory findings were shown in Table 1. Chest X-ray revealed blurring and increased both pulmonary vascular markings, bilateral diffuse patchy opacity, as shown in Fig. 1. SARS COV-2 RT-PCR swab was negative.

On the 4th day of treatment, the patient had fever and D-dimer was 0.99 mg/dl (N: < 0.5). Enoxaparin, amikacin and imipenem/cilastatin were administered. On the 7th day, the patient complained severe abdominal pain and four times of bloody diarrhea. Physical examination revealed upper right abdominal tenderness. Abdominal CT with contrast revealed right hepatomegaly due to two liver abscesses formations with

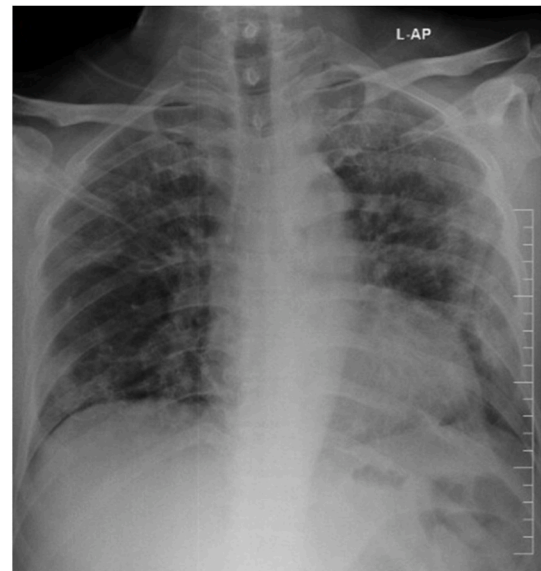


Fig. 1. Chest X-ray showed blurring and increased both pulmonary vascular marking, and bilateral diffuse patchy opacity.

hemorrhages occupying most of the right lobe of the liver, as shown in Fig. 2. The patient was scheduled for exploratory laparotomy, drainage of multiple liver abscesses, transfusion 4 units of fresh frozen plasma, administration of tranexamic acid, cefotaxim, metronidazole, pantoprazole, electrolyte and albumin correction. Paracetamol, amikacin and imipenem-cilastatin were discontinued.

On the 10th day, the patient had decreased consciousness, seizure and shortness of breath. Meropenem was administered. In laparotomy surgery by digestive surgeon, multiple liver abscesses were seen in segment 8 with parenchymal liver necrosis and abscess in segment 7 liver, then necrosectomy, abscess drainage, and chest water seal drainage were performed. There was no growth of microbe in abscess

Table 1

Laboratory findings.

Lab Parameters	Normal values	Day 1	Day 7	Day 10	Day 12	Day 14	Day 16	Day 20
Hemoglobin (g/dl)	14.0–16.0	12.1	11.3	8.0	9.5	9.3	8.7	9.0
Hematocrit (%)	40–54	34.6	31.8	23.0	27.2	28.3	27.0	29.7
Erythrocyte ($\times 10^6/\mu\text{L}$)	4.4–5.9	4.21	3.93	2.79	3.30	3.23	3.07	3.20
Leucocyte ($\times 10^3/\mu\text{L}$)	4.0–11.0	12.15	24.74	37.03	50.84	86.02	27.83	20.52
Thrombocyte ($\times 10^3/\mu\text{L}$)	150–400	390	236	126 L	110	151	84	106
Neutrophil (%)	50–70	76.1	–	–	–	93.2	93.3	89.2
Lymphocyte (%)	25–40	11.4	–	–	–	4.2	4.1	7.8
Monocyte (%)	2–8	12.3	2.5	–	1.7	2.5	2.5	2.7
Eosinophil (%)	1–4	0.0	0.0	0.0	0.0	0.0	0.0	0.1
Basophil (%)	0–1	0.2	0.0	0.0	0.0	0.1	0.1	0.2
AST (U/L)	<50	–	571	131	157	44	–	56
ALT (U/L)	<50	–	484	225	141	66	–	17
Bilirubin direct (mg/dl)	<0.2	–	0.81	–	–	0.47	–	0.48
Bilirubin indirect (mg/dl)	<0.6	–	0.01	–	–	0.03	–	0.05
Albumin (g/dl)	3.4–4.8	–	1.63	2.58	2.16	2.27	2.55	2.34
PT (second)	7.9–10.3	–	12.2	11.0	–	–	9.9	–
INR	–	–	1.25	1.14	–	–	1.04	–
APTT (second)	20.0–30.3	–	47.7	31.5	–	–	33.5	–
Fibrinogen (mg/dl)	200–400	–	–	–	–	–	172.9	–
Creatinine (mg/dl)	0.62–1.17	0.74	0.80	–	1.62	1.72	1.28	2.13
Urea (mg/dl)	19–44	18	35	–	119	184	153	182
Sodium (mmol/L)	138–146	–	121	125	133	139	159	164
Potassium (mmol/L)	3.5–4.9	–	3.1	2.9	3.2	4.4	2.0	3.2
Chloride (mmol/L)	98–109	–	81	86	94	100	102	109
Procalcitonin ($\mu\text{g/mL}$)	0.05–2.0	–	–	–	14.58	–	–	–
Hbs-Ag	Negative <0.13	–	–	Negative/0.07	–	–	–	–
Anti-Amoeba	Negative/<9	–	–	–	–	–	Positive/33.4	–

AST (aspartat aminotransferase); ALT (alanin aminotransferase); PT (Protrombin Time); INR (International Normalized Ratio); APTT (Activated Partial Thromboplastin Time); HBsAg (hepatitis B surface antigen).



Fig. 2. Abdominal CT showed two liver abscess formations with hemorrhages occupying most of the right lobe of the liver.

pus culture. Gram stain of pleural fluid showed leukocytes $>25/\text{FoV}$ and epithelium 1–3/ FoV . Sputum culture revealed *Pseudomonas aeruginosa*. Mycamin, cefoperazone sulbactam, and moxifloxacin were administered. On the 20th day, the patient's condition worsened and died. This case report has been reported in line with the SCARE Criteria [11].

3. Discussion

Post acute COVID-19 symptoms are including symptoms after 3 or 4 weeks from the acute onset of COVID-19. Gastrointestinal signs and symptoms are also frequently found [7]. Study by Jingrong et al. showed 52 (44%) of 117 patients had gastrointestinal sequelae 3 months after discharged, including lack of appetite, nausea, acid reflux, diarrhea, abdominal distension, belching, vomiting, pain abdomen, and blood stool [7]. Critically ill patients with COVID-19 showed more gastrointestinal complications and had higher risk for liver function abnormalities and hypoalbuminemia [12]. This patient presented shortness of breath, nausea, decreased appetite, and heartburn with history of confirmed severe COVID-19 pneumonia.

This patient had severe abdominal pain on day 7. Laboratory results showed elevated liver function specifically AST 571 U/L, ALT 484 U/L and hypoalbuminemia. There were several studies regarding liver disorders and elevated liver function tests in post COVID-19 patients [6]. Meta-analysis study by Yu Jun et al. showed elevated ALT in 23 studies, AST in 21 studies, serum bilirubin in 13 studies, gamma-glutamyl transpeptidase (GGT) in 3 studies, and hypoalbuminemia in 13 studies [13].

Abdominal CT Scan with contrast of this patient revealed right hepatomegaly with two liver abscess formations and hemorrhages. Multiple liver abscesses in segment 8 with hepatic parenchymal necrosis and liver abscesses in segment 7 were found during laparotomy. No microbe was found in pus culture. There was previous case report of a COVID-19 patient with liver abscess and no microbe found in the pus culture [14]. There were still lack of studies regarding liver abscess in post COVID-19 patients. Whereas liver necrosis were found in post mortem liver pathology study of COVID-19 patients by Steven et al. that 50% patients had lobular necroinflammation. In patients with right heart failure and ischemia, 78% of patients showed hepatic congestion and 40% had centrilobular ischemic necrosis [15].

The pathophysiology of liver damage caused by SARS-CoV 2 are

direct cytotoxicity of SARS-CoV2 virus replication in the liver, due to severe systemic inflammatory response syndrome (SIRS) in COVID-19, hypoxic conditions due to respiratory failure, vascular changes due to coagulopathy, endothelitis or cardiac congestion from right heart failure, drug-induced liver injury (DILI) and previous exacerbations of liver disease [2]. Otherwise, study by Chai et al. showed liver damage in COVID-19 patients was not caused directly by viral infection in hepatocytes [8]. ACE2 expression was high in cholangiocytes (59.7%) and slightly in hepatocytes (2.6%). Disorders of cholangiocytes structure and function could lead to impaired bile formation, inflammation, fibrosis and liver dysfunction, resulted in an overall increase in ACE2 expression in liver tissue which could be one of the mechanisms of liver damage caused by SARS-CoV2 infection [16]. Severe systemic inflammatory response in COVID-19 could also lead to ischemic hepatitis [13]. A cohort study of 192 COVID-19 patients showed that elevated IL-6 and IL-10 as well as decreased CD4^+ T were risk factors for severe liver damage [17]. A large number of immune cells can be overactivated and secrete excessive cytokines and chemokines, leading to ARDS and SIRS, causing ischemia and hypoxia. This causes cell damage and necrosis [12]. Patients with severe COVID-19 may develop hypoxic-ischemic liver injury (HIRI). Research by Zhong et al. showed hepatic ischemia–reperfusion can activate Kupffer cells, neutrophils, and platelets causing cellular destructive reactions that result in inflammation and cell damage [18]. Impaired microcirculation due to hepatic sinusoidal endothelial cells damage will also exacerbate hepatic ischemia and oxygen deficiency [18]. Hypoxia and inflammation are common in patients with severe COVID-19, which play a major role in the regulation of hepatocellular ACE2 expression [2]. This explains the cause of extrapulmonary SARS-CoV2 dissemination in ARDS and hypoxia patients. *Hypercoagulable state* in COVID-19 patients also contributes to liver damage with the incidence of pulmonary thrombotic complications that exacerbates acute right heart failure caused by high pulmonary vascular resistance during ARDS, and results in hepatic congestion [19]. Several drugs for severe COVID-19 can also cause DILI [12]. In a retrospective study, lopinavir/ritonavir had 7 times greater risk of liver damage [20]. DILI was also reported in administration of tocilizumab for COVID-19 patients and might be related to IL-6 pathway that played role in liver regeneration [21]. In this patient, there was administration of tocilizumab, azithromycin, levofloxacin, and hydroxychloroquine 1 month ago while being treated for COVID-19.

It is very important to fix the etiology by giving oxygen supplementation to reduce the damage caused by hypoxia, maintaining hemodynamic and coagulation stability, stopping hepatotoxic drugs, giving adjuvant hepatoprotective therapy, drainage of abscesses and targeted antibiotic therapy can be considered [14].

4. Conclusion

In this case, liver abscess with necrosis were found in post severe COVID-19 pneumonia patient and currently had a negative PCR swab test. The pathophysiology of post COVID-19 liver damage can help in considering the treatment that should be given to the patient. The possibility of liver damage should also be a special consideration in post COVID-19 patients, both in terms of monitoring and patient care management.

Conflicts of interest

None.

Source of funding

None.

Ethical approval

This article type (case report) does not require a formal ethical committee approval.

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Patient perspective

The patient did not present his point of view.

Research registration number

N/A.

Guarantor

Aldrich Kurniawan Liemarto and Bernadus Parish Budiono.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2021.103107>.

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