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A Fatal Outcome of SARS-COV-2 Infection: A Case Report of A 60 Years Old Man with Multiple Organ Failure

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Abstract

The infection of Corona Virus Disease – 19 (COVID-19) has spread out in Indonesia. The number of deaths has increased in recent months. Cases of infection are followed by comorbidities such as diabetes, hypertension, cardiovascular and cerebrovascular condition have higher risk to develop severe illness. These conditions also give the higher risk of death in patients. Herein, we reported a 60 years old man that was infected with Sar-Cov-2 and had no comorbidities. Before the infection, patient was healthy. In the early phase of infection, clinical manifestations were seen in patients such as fever, cough, nausea and vomiting. A few days after being admitted to the hospital, the condition began to get worse which led to multiple organ failure. Acute kidney injury, liver injury, dysregulation of glucose level and acid base disorder were shown from laboratory tests. Unfortunately, clinical manifestations were poor and the patient passed away.

1. Introduction

The Corona Virus Disease–19 (COVID-19) outbreaks has become a pandemic, including Indonesia. In Indonesia, as of July 28, 2021, more than 3.2 million people have tested positive for COVID-19, with more than 80,000 death case (Fisher & Heymann, 2020). The number of deaths has increased in recent months. The increase in cases also occurred in Bengkulu Province. In April 2021, the Fatmawati room at the M. Yunus Hospital which became a referral isolation room for the province was no longer sufficient to treat all patients with COVID-19. This hospital becomes a referral hospital, especially for severe cases that require a ventilator. in Bengkulu Province, M.Yunus Hospital is the only hospital equipped with central oxygen which makes it easier to treat patients with ventilators.

COVID-19 is caused by infection with SARS-CoV-2 which can spread very quickly. This virus is thought to have originated from Wuhan, an area in China which then spread throughout the world until it was categorized by WHO as a pandemic. This pandemic also hit Indonesia and Bengkulu Province (in Indonesia). Proper case handling and adequate facilities are needed to deal with this pandemic. The hospital is also an important element that will become a place for the community to ask for help.

Common cold symptoms have been found in the mild cases. However, in severe cases it was reported that COVID-19 infection was also accompanied by multiple organs failure such as the lungs, liver and kidneys. These cases have been reported in several deaths (Mokhtari et al., 2020). In some previous reports, damage to these organs was experienced by some people with comorbidities such as diabetes, hypertension or cardiovascular and cerebrovascular condition (Sanyaolu et al., 2020). The severity of the infection is likely to be related to comorbid factors. However, what we report now is the incidence of multiple organ failure after Sar-Cov-2 infection without any comorbidity factors. Therefore, it is necessary to obtain further study about the pathophysiology of injury to these organs. This report discusses the damage to several important organs and metabolic disorder that were only seen after several days of the patient being hospitalized.

2. Case Report

Laboratory parameter checking of the patient was carried out twice. the first check at the time of admission to Bhayangkara Hospital, Bengkulu Province and the second check was carried out after the patient was referred to M. Yunus Hospital, Bengkulu City. This patient has no comorbidities. Laboratory tests showed some abnormals in hematologic parameters. It was significant for leucocytosis with lymphopenia. Neutrophil-Lymphocyte count ratio was 11.12, indicating ongoing severe infection. The D-dimer was a marker of fibrin formation and degradation, especially a reflective of pathological activation of the hemostatic pathways in the case of COVID-19. In this patient, D-dimer was significantly elevated more than 10.000 ng/mL. Blood chemistry laboratory also gave poor result in some parameters. The patient got elevated hepatic enzymes. The increasing of aspartate aminotransferase and alanine aminotransferase enzymes indicated a liver damage. Despite no history of diabetic, blood glucose was also not in normal range. The result of random blood glucose was 266. This patient also developed an acute kidney injury (stage III) with a rise in creatinine more than three times of baseline. Urine secretion in 24 hours was significantly low due to poor clearance function of the kidneys. Arterial blood gas analysis revealed a metabolic acidosis without compensation with poorly oxygen saturation (Table 1). This condition indicates the occurrence of multiple organ failure in these patients.Supporting investigations were needed as an important diagnostic tool. There were two chest X-ray of the patient. On 4th May 2021, the chest X-ray showed any sign of infiltrate on bilateral lung tissue that was dominated in subpleural and lower zone. The patient also suffered from cardiomegaly with cardiothoracic ratio near to 0.6. Second X-ray was obtained on 3rd April 2021. In addition, nasopharyngeal swab for SARS-CoV-2 RNA was positive.

Table 1. Summary of laboratory results of the patient infected with COVID-19

Items	At admissions	1st review
HEMATOLOGY		
White blood cell count (x103 cells/L); normal range (4-10)	8300	14000 (↑)
Segmented Neutrophil (%); (normal range 35-70)	79 (↑)	88 (↑)
Band Neutrophil (%); (normal range 3-5)	1	1
Lymphocyte (%); (normal range 20-45)	15 (↓)	8 (↓)
Eosinophil (%); (normal range 1-6)	0	0
Hemoglobin (g/L); (male normal range 13-18)	13.8	13.4
HEMOSTASIS		
PT (second); (normal range 9.7-13.1)		14.8 (↑)
APTT (second); (normal range 25.5-42.1)		42.5 (↑)
D-dimer (ng/mL); (normal range <0.5)		>10.000 (↑)
LIVER FUNCTION		
Albumin (g/dL); (normal range 3.8-4.8)		4
Alanine aminotransferase (U/L); (normal range <50)		138 (↑)
Aspartate aminotransferase (U/L); (normal range <50)		132 (↑)
KIDNEY FUNCTION		
Urea (mg/dL); (normal range 20-40)	44.9 (↑)	413 (↑)
Creatinine (mg/dL); (normal range 0.5-1.2)	1.8 (↑)	14.7 (↑)
Glucose (mg/dL); (normal range <160)	82 (↓)	266 (↑)
ARTERIAL BLOOD GAS		
PH (normal range 7.35-7.45)		7.21 (↓)
PO2 (mmHg); (normal range 71-104)		42 (↓)
PCO2 (mmHg); (normal range 33-44)		37
HCO3 (mmol/L); (normal range 22-29)		14 (↓)
Base Excess		-13
O2 Saturation (%); (normal range 94-99)		67 (↓)
ELECTROLYTE		
Natrium (mmol/L); (normal range 135-145)		135
Kalium (mmol/L); (normal range 3.4-5.3)		3.8
Chlorida (mmol/L); (normal range 50-200)		108

(↑) above normal range; (↓) below normal range. At admisssion, April 28th 2021; 1st review, May 4th 2021.

3. Result and Discussion

3.1 Acute Kidney Injury

Acute kidney injury (AKI) is a clinical syndrome caused by impairment of structure and functional of the kidney within 48 hours. This condition can worsen the outcome of hospitalized patients. The clinician has to identify the existance of AKI as soon as possible. Recent evidence suggests that even relatively mild injury,

marked by small changes in serum creatinine and/or urine secretion, is a predictor of serious clinical consequences. AKI can be related to some conditions affecting kidney impairment in pre-renal, intrinsic and post renal. In **pre-renal AKI**, there is no damage in renal parenchyma but hypoperfusion leads to a decreased GFR. This is part of adaptive response to various extra-renal insults. Hypovolaemia, impaired cardiac function, systemic vasodilatation, and increased vascular resistance are the main cause that had a profound impact on renal perfusion. Meanwhile intrinsic AKI is caused by some nephrotoxic drugs, endogenous toxins,infection and autoimmune disease. Post renal AKI is related to intra and post renal obstruction (Makris & Spanou, 2016).

Various causes of AKI indicate that it can be related to intra or extra renal conditions. Early diagnosis was so crucial to improve the patient outcome. Unfortunately, initial report indicated that rates of acute kidney injury (AKI) were still negligible. Growing evidence has demonstrated that AKI was also found among patients with COVID-19. More than 20% of hospitalized patients and 50% of patients in the ICU were suffered from COVID-19 with acute renal injury. AKI is now recognized as a common complication of COVID-19. COVID-19-associated AKI (COVID-19 AKI) is associated with adverse outcomes, including the development or worsening comorbid disease (Makris & Spanou, 2016).

This patient developed an acute kidney injury marked by elevated creatinine serum level. At first, laboratory was obtained on 28th April. The concentration of creatinine was 1.8 mg/dl, indicating that an acute kidney injury was at stage I (in this case, creatinine serum elevated 1.5 times from baseline). On May 4th, the result changed with creatinine level to 18.6 mg/dL, revealing an acute kidney injury stage III. AKI stage was progressively increasing within 6 days in this patient. The pathogenesis of COVID-19-associated AKI was likely multifactorial involving both the direct effects of the SARS-CoV-2 virus on the kidney and the indirect mechanisms resulted from systemic consequences of viral infection.

Recent research found the role of APOL1 gene in COVID-19-associated AKI. First, the SARS-CoV2 RNA was not detected in the renal samples from two COVID-19 patients with high-risk APOL1 genotype. Further investigation identified collapsing focal segmental glomerulosclerosis in the pathologic features. In addition, the cytokine strom also played a role in podocyte damage by enhancing the gene expression of APOL1. Another research observed postmortem renal tissues from six COVID-19 patients with AKI. It found severe acute tubular necrosis caused by infiltration of macrophage and lymphocyte. Then, the N-protein of SARS-CoV2 was successfully identified in renal tubules, podocytes and tubular epithelium. From those research, it suggested that SARS-CoV2 could cause AKI by directly invading the renal cells or indirect mechanism involving the cytokine strom (Abbate et al., 2020; Diao et al., 2021; Farkash et al., 2020; Kissling et al., 2020; Su et al., 2020).

The other indirect mechanisms were possibly obtained from decreasing kidney density using CT. Additionally, edema and inflammation of the renal parenchyma were also identified. Activation of complement components could also be related to parenchymal damages of renal tissue. Deposition of C5b-9 was identified on the tubular cells, glomeruli and capillaries. Then, others inflammatory cells (CD4+ T cells, CD68+ macrophages, and CD56+ natural killer cells) were observed in the tubules and interstitial tissue of patients. Those inflammatory cells

and complement components caused apoptosis in epithelial cells, fibrosis and impaired the microvascular system (Diao et al., 2021; Saffarzadeh et al., 2012).

3.2 Liver Injury

Elevation of liver transaminases (ALT and AST) was also experienced by this patient. The incidence of elevated liver transaminases was about 2.5% to 76.3% in COVID-19 patients. The rising of bilirubin level was also found in 35% of cases. Recent investigation has proved that SARS-CoV-2 infection directly impaired liver function by cytotoxicity due to replication of the virus. The expression of ACE2 as a receptor of Spike-I Glycoprotein of COVID-19 was increased in cholangiocytes (59.7% of cells) and in hepatocytes (2.6% of cells). Another study shows that the renin-angiotensin system and peroxisome proliferator-activated receptor signaling pathway potentially enhance the infection. Several studies have proved that immunological inflammatory response as a pathological pathway in SARS-CoV-2 infection induced liver injury. High level of D-dimers (>10.000 ng/mL) in this patient as inflammatory marker was also confirmed of this pathological pathway. This phenomenon conveys that cytokine storm syndrome may be fundamental role in the presence of liver injury in this patient. Some antiviral agents, antibiotics, antipyretics or steroids used in the treatment of COVID-19 might also impair the liver function (Kulkarni et al., 2020; Kumar-M et al., 2020; Paliogiannis & Zinellu, 2020; Yadav et al., 2021).

3.3 Dysregulation of Glucose Level

Diabetes is one of comorbid and risk factor of severe SARS-CoV-2 infection. Some patients with no history of diabetes show hyperglicemic level. This new onset of diabetes is associated with SARS-CoV-2 infection. Some researchers found new onset of diabetes, including diabetic ketoacidosis and hyperosmolarity in patients with SARS-CoV-2 infection. Same mechanism with kidney and liver injury is related to SARS-CoV-2 infection. This virus binds to angiotensin-converting enzyme 2 (ACE2) receptors which are also expressed in pancreatic beta cells. On other hand, this patient experienced hypoglicemic level at admission (82 mg/dL). As the hypoglicemic management, D40% was given to increase the blood glucose. After 1 flc of D40% , blood glucose significantly increased to 266 mg/dL. This reveals a dysregulation of glucose level. Although some studies have observed new onset diabetes in patient with SARS-CoV-2 infection, but in this case we observed dysregulation of blood glucose. Thus, one of the manifestations that can occur in patients infected with Sar-Cov-2 is abnormalities in blood glucose levels. Further research about the mechanism of blood glucose dysregulation was needed for optimal management of SARS-CoV-2 infection (Hamming et al., 2004; Yang et al., 2010).

In the earlier studies, there are some findings say that the virus also impair the glucose regulation by Na+/H+ exchanger (NHE) and lactate pathways. The virus induces cellular hypoxia and generates reactive oxygen species. This process results in endothelial damage and insulin resistance. Several mechanism of exocrine and endocrine damage, such as virus binding to ACE2 receptors, the exocrine pancreas injury, systemic inflammation caused by severe SARS-CoV-2 infection, virus mediated injury to the islet cells, are induced by cytokine storm due to excessive immune response, virus-induced lipotoxicity from UFAs, and NSAID-corticosteroids induced pancreatic injury (Samanta et al., 2020).

3.3 Acid-Base Disorder

Acid–base disorders are common in severe disease. Acid-base disorders are pathologic changes in carbon dioxide partial pressure (PCo2) or serum bicarbonate (HCO3−) that typically produce abnormal arterial pH values. Patients with SARS-CoV-2 infection also experienced acid-base disorders. These cases were reflected by the severity of the underlying pathologic process. Acid–base disorder was found in 79.7% of the patients. Metabolic alkalosis (33.6%) was the main alteration followed by respiratory alkalosis (30.3%), combined alkalosis (9.4%), respiratory acidosis (3.3%), metabolic acidosis (2.8%) and other compensated acid–base disturbances (3.6%) (Alfano et al., 2021).

Patients in this case are having metabolic acidosis. Previous study reported that metabolic acidosis occurred in subjects with renal impairment. This patient had an increased value in creatinine level, indicating the renal impairment. Ammonia excretion impairment and decreased tubular reabsorption of bicarbonate are the leading cause of metabolic acidosis. This acid-base disorder bothers the cardiovascular system, such as reduce cardiac contractility, cardiac output and induce arterial vasodilation (Jung et al., 2011; Kovesdy, 2014; Raikou, 2016).

4. Conclusion

The case demonstrates that there were abnormalities of functions in important organs such as kidney and liver. Cytokine storm and the rising of inflammation possibly caused organ failure. In addition, there were some indications of metabolism disturbance those which possibly are related to SAR-COVID infection, such as electrolyte, dysregulation of glucose level (possibly related to cellular hypoxia), metabolic acidosis in subjects with renal impairment. Infection of SAR-COV-2 could induce development of comorbid disease in this patient. Therefore, special monitoring is needed for patients with clinical conditions that lead to an increased incidence of inflammation.

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