INTRODUCTION

Dengue is a seasonal endemic viral infection found in various tropical countries, including Indonesia, which usually escalates during the rainy season. Dengue has various degrees of severity, ranging from mild flu-like fever to severe, including multiorgan failure syndrome. The availability of dengue serological tests has made the diagnosis of dengue in endemic areas relatively straightforward. However, since the introduction of the multisystem inflammatory syndrome in children (MIS-C) at the start of the novel coronavirus disease 2019 (COVID-19) pandemic, there has been a dilemma in establishing the diagnosis of dengue. Initially reported as a severe inflammatory syndrome similar to Kawasaki disease and toxic shock syndrome, known as MIS-C, has clinical manifestations very closely resembling dengue shock syndrome (DSS), especially fever, abdominal pain, rash, shock, multiorgan failure, and bicytopenia. In the rainy season in October, amid the COVID-19 endemic in Indonesia, we found a case with overlapping DSS and MIS-C. This case report aims to describe a 17-year-old girl with DSS and MIS-C.

CASE REPORT

A 17-year-old female came to the emergency department of a referral hospital and presented with shock. The patient complained of a fever four days before admission. The fever continued throughout the day and did not improve, although she took oral paracetamol. The patient also complains of yellowish discolored skin and sclera. The abdomen did not appear distended, no ascites were found, bowel sounds were within normal limits, the liver and spleen were unpalpable, and there was tenderness in the epigastric region. The extremities were cold, capillary refill time was >2 seconds, and no pitting edema

ABSTRACT

Background: Dengue and coronavirus disease 2019 (COVID-19) have recently become endemic in various tropical countries. Multisystem inflammatory syndrome in children (MIS-C) is a clinical manifestation of COVID-19 with a life-threatening syndrome of hyperinflammation, multiorgan failure, and shock, and it closely resembles the manifestations of severe dengue. Many attempts have been made in research to differentiate the two. Here we aims to describe a case of a patient with dengue coinfection with MIS-C.

Case Presentation: A 17-year-old woman came in a state of shock, with cold extremities, fever, jaundice, shortness of breath, acute abdominal pain, and hematuria, decreased urine output. Further investigations reveal increased parameters of hepato-renal organ damage, c-reactive protein, and anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) immunoglobulin G (IgG). Patient was positive for anti-dengue IgM and IgG, but negative for COVID-19 based on SARS-CoV-2 antigen and polymerase chain reaction.

Conclusion: This case demonstrates the possibility of dengue coinfection and MIS-C co-occurring, causing the patient to develop a hyperinflammatory syndrome and clinical deterioration.
was found in all four extremities. There are no petechiae on the skin, but the skin looks icteric. The initial urine output from the urinary catheters was 1.8 cc/kg/hour. Initial treatment in the emergency room includes oxygen supplementation of 2 liters per minute with a nasal cannula, fluid resuscitation with ringer lactate solution, insertion of two intravenous lines, 25 mg norepinephrine drip at a rate of 1 ml/hour, 2 ml KCL drip, 55 ml paracetamol and 2 grams cefoperazone intravenously, and ursodeoxycholic acid orally.

A complete blood count showed no abnormalities other than a low platelet count (28,000/µL). Blood gas analysis reveals decreased arterial oxygen saturation (86%), with decreased HCO₃⁻ and pCO₂, with a blood pH of 7.36 (compensated metabolic acidosis). On electrolyte examination, hyponatremia (126 mg/dL) and hypokalemia (2.8 mg/dL) were present. Erythrocytes (+2) and bilirubin (+1) were found on semi-quantitative urinalysis. Renal function parameters showed increased urea (87.4 mg/dL) and serum creatinine (3.52 mg/dL). Increased liver function parameters were also present, with SGPT 119 mg/dL and SGOT 116 mg/dL, accompanied by increases in total (5.81 mg/dL), direct (4.70 mg/dL), and indirect (1.11 mg/dL) bilirubin. While the result for the SARS-CoV-2 antigen was negative, the anti-SARS-CoV-2 immunoglobulin G (IgG) level was significantly increased (4744.4 AU/mL), with positive dengue IgM and IgG. Based on the clinical data found, the patient was initially diagnosed with decompensated dengue shock syndrome (DSS), cholestatic hepatitis, failure stage acute kidney injury (AKI), electrolyte imbalance (hyponatremia and hypokalemia), and compensated metabolic acidosis. The patient was differential diagnosed with MIS-C, considering the high levels of anti-SARS-CoV-2 IgG.

On the second day of treatment at the pediatric intensive care unit, vital signs improved. However, there was a decrease in urine output (0.66 cc/kg/hour) and worsening of kidney function parameters, including serum creatinine (3.54 mg/dL) and urea (126.4 mg/dL). The patient was referred to a Tertiary Hospital for further management and the possible need for hemodialysis. Follow-up investigations in the Tertiary Hospital found a high level of c-reactive protein (CRP) (94.40 mg/dL). Complete blood count showed increased in white blood cells (25.73 x 10³/µL), anemia (Hb 9.40 g/dL) and low platelet count (14,000/µL). Echocardiography showed decreased left ventricular systolic function with decreased cardiac output and systemic vascular resistance index. The patient was diagnosed with MIS-C, secondary hepatic injury, acute kidney injury stage failure with rapidly progressive glomerulonephritis, and bicitopenia (mild microcytic normochromic anemia with severe thrombocytopenia).

At the tertiary hospital, the patient received intravenous high-dose methylprednisolone (30 mg/kg BW each) and intravenous immunoglobulin (IVIG) at 2 grams/kg BW each. The high dose of methylprednisolone was tapered off on the fourth and sixth day to 20 mg/kg BW each and 2 mg/kg BW each, respectively. Then, on day nine, the methylprednisolone was changed to 12 mg orally. Intravenous immunoglobulin was given in stages, first 1 ml/kg BW/hour, 2 ml/kg BW/hour, and 4 ml/kg BW/hour, then continued at 172 ml/hour until finished. On the tenth day of treatment, the patient was free of fever for nine days, had no subjective complaints, had vital signs within normal limits, and was discharged for outpatient care.

DISCUSSION

The diagnosis of dengue, in this case, was quite simple. The patient’s clinical findings during admission supported the diagnosis of dengue, especially the lasting fever and low platelet levels, and were further supported by positive dengue IgM and IgG results. A fever on the fourth day may indicate the patient is in the critical phase of dengue, although theoretically, there should be a defervescence in the critical phase.³

This case is challenging due to the involvement of the hepatobiliary system and urinary tract in the clinical manifestations of DSS, accompanied by the high level of anti-SARS-CoV-2 IgG. According to the World Health Organization and CDC criteria, the diagnosis of MIS-C requires positive results or a history of COVID-19 within four weeks before the symptoms appear.⁶ While the patient denies any history or contact with COVID-19 patients, accompanied by a negative result for the SARS-CoV-2 antigen and PCR, the high levels of SARS-CoV-2 antibodies and CRP in the patient point to the possibility of post-COVID-19 MIS-C.

Studies comparing dengue and MIS-C found that both had clinical manifestations of fever, edema, abdominal pain, shock, and acute kidney injury, with no statistically significant differences. Hepatic dysfunction was significantly more common in dengue [odd ratio (OR) = 1.94]. Significantly different laboratory results of dengue and MIS-C were seen in lower platelet levels (range 16-47 x10⁹/µL in dengue vs. 70-210 x10⁹/µL in MIS-C), SGOT (range 161.5-1470 IU/L in dengue vs. 27.5-120.5 IU/L in MIS-C) and c-reactive protein (CRP) [range 1.2-17.9 mg/L in dengue vs. 21-204 mg/L on MIS-C]. The authors concluded that mucocutaneous involvement and high CRP elevation could be used to differentiate MIS-C from dengue.⁷ Reflecting on this comparative study, overlapping clinical and laboratory results found in this case did not rule out the possibility of simultaneous dengue infection with MIS-C. Jaundice (hyperbilirubinemia) observed in this case is also one of the clinical manifestations that can occur in dengue and MIS-C,⁸,⁹ although the mechanism is not known for certain in MIS-C.

The initial management of patients given patients includes the installation of intravenous lines for two accesses. Isotonic fluids and norepinephrine were given to treat shock, paracetamol to reduce fever, and KCL drip to treat hypokalemia. The patient’s vital signs improved on the second day of treatment. However, urine production had decreased, accompanied by worsening kidney function parameters. In anticipation of worsening kidney function, the patient was referred to a tertiary hospital for further management and preparation for hemodialysis. The patient received high doses of methylprednisolone and IVIG during treatment at the referral hospital. This recent systematic review study reported...
that the most frequently administered anti-inflammatory agent in MIS-C was IVIG (63%), followed by intravenous steroids (44%). 10 Although anti-inflammatory therapy has been found to improve the patient’s condition, no data is available regarding the effectiveness of therapy when given alone or in combination. 11,12 Previous observational studies found clinical improvement in some patients despite not receiving IVIG. 13

CONCLUSION
Endemic COVID-19 and dengue have become diagnostic challenges in many tropical countries. Although the two manifestations are very similar, many attempts have been made to differentiate between them. It is undeniable that there is a possibility that both occur together. Multisystem inflammatory syndrome in children is a severe and life-threatening condition; therefore, the possibility of MIS-C should always be considered. In this patient, the possibility of a previous history of asymptomatic/mild COVID-19 was also unable to be ruled out. The coinfection with dengue could induce the pro-inflammatory mediators that trigger MIS-C.

CONFLICT OF INTEREST
There is no conflict of interest in writing this case report.

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