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Case Report

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Hepatoprotector in cases of Dengue Hemorrhagic Fever as a prevention of hepatic damage: A case report

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Abstract: Dengue Hemorrhagic Fever (DHF) is classified as an arbovirus disease which is a public health problem in the world. The causative agent of DHF is the dengue virus, namely the RNA virus of the genus Flavivirus and the family Flaviviridae. Hepatic impairment is often observed in DHF cases with asymptomatic or asymptomatic elevations in serum transaminases up to severe manifestations in the form of acute liver failure. It was reported that DHF patients had mild hepatic impairment with clinical manifestations of mild hepatomegaly, hypoalbumin, normal SGOT/SGPT values, and clinical conditions of nausea – vomiting. To prevent worsening liver damage, combination therapy with Ursodeoxycholic Acid (UDCA) and curcumin was given as a hepatoprotector. The use of curcumin can reduce serum levels of transaminase, Malondialdehyde (MDA) or markers of oxidative stress and increase hepatic glutathione concentrations which work in free radical detoxication, while the role of UDCA is as a hepatoprotector by reducing the level of oxidative stress in liver cells.

Keywords: DHF, Liver damage, Hepatoprotector, Curcumin, UDCA

INTRODUCTION

Dengue Hemorrhagic Fever (DHF) falls within the spectrum of arboviral diseases and stands as a significant global public health challenge. Annually, a staggering 390 million cases of dengue virus infections are documented worldwide, with approximately 96 million cases displaying pronounced symptoms[1].The highest DHF incidence is observed among urban populations in tropical and subtropical regions, particularly within Southeast Asia[2]. Indonesia, an extensive endemic region for dengue, reported 73,518 DHF cases and 705 fatalities in 2021. The national tabulated Incidence Rate for DHF cases is 27 individuals per 100,000 population[3].

The etiological agent of DHF is the dengue virus, an RNA virus belonging to the Flavivirus genus within the Flaviviridae family[1]. Classified as an arbovirus

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(arthropod-borne virus), the dengue virus comprises four serotypes: dengue virus 1, 2, 3, and 4 (DENV-1, DENV-2, DENV-3, and DENV-4)[4]. All these serotypes have the potential to induce severe and fatal dengue infections, though DENV-2 and DENV-3 are more frequently associated with severe cases[5,6,7]. The primary transmission of the dengue virus is facilitated by Aedes mosquitoes, particularly Aedes aegypti and Aedes albopictus[8,9]. Additionally, non-vector transmission routes have been documented, including through blood transfusions, organ transplants, intrapartum, and breastfeeding[10]. The incubation period for dengue virus infection ranges from 4 to 10 days.

Clinical manifestations of dengue infection encompass asymptomatic cases, as well as mild flu-like syndromes termed dengue fever (DF)[11]. Severe and life-threatening forms include DHF and dengue shock syndrome[12]. Acute dengue infections manifest as fever lasting 2-7 days, accompanied by bleeding, thrombocytopenia, heightened hematocrit, ascites, pleural effusion, and hypoalbuminemia due to plasma leakage arising from hemoconcentration[13]. Although early fever phase symptoms resemble those of DF, DHF cases exhibit increased vascular permeability or plasma leakage, potentially leading to reduced intravascular volume and shock[14].

The high virulence of the dengue virus can result in multi-organ complications, including the liver[15]. Hepatic impairments are frequently observed in DHF cases, varying from asymptomatic to symptomatic elevation of serum transaminases, and even acute hepatic failure[16]. Liver dysfunction manifestations often range from mild to severe elevations in serum transaminases, presenting symptoms such as abdominal pain, nausea, vomiting, anorexia, and hepatomegaly[17,18]. Currently, no established therapeutic management exists for addressing hepatic dysfunction in DHF cases.

We present a case report of an adult patient exhibiting elevated serum transaminases and hepatosplenomegaly during inpatient care. This case report aims to explore the application of hepatoprotective agents for hepatic impairment in DHF patients.

CASE REPORT

A 62-year-old female patient was admitted to the hospital with complaints of fever fluctuating for approximately one week, occasionally accompanied by nausea. The patient reported no history of allergies. Upon examination at the Emergency Department, the patient's psychological status was cooperative, extremities were warm to touch, and no pallor was observed. Vital signs indicated a temperature of 38.4°C, blood pressure of 113/65 mmHg, heart rate of 126 beats per minute, respiratory rate of 20 breaths per minute, oxygen saturation of 96%, and random blood glucose level of 119 mg/dL, with capillary refill time < 2 seconds. The patient complained of abdominal pain with a pain intensity scale of 3 and described the pain as stabbing.

Laboratory results revealed a decreased hemoglobin level of 10.4 g/dL, normal leukocyte count of 5,770/mm3, decreased platelet count of 58,000/mm3, decreased red blood cell count of 3.42 x 1012/L, normal hematocrit level of 31.2%, normal SGOT/SGPT levels at 29 and 25 U/L, and a triglyceride level of 183 mg/dL. Positive Dengue immunoglobulin G (IgG) results indicated secondary infection. A chest X-ray impression suggested non-specific bronchitis, with no infiltrates in either lung. The radiologist suggested irritation due to acute respiratory infection. A diagnosis of pancytopenia, characterized by decreased levels of three types of blood cells resulting in anemia, leukopenia, and thrombocytopenia, was made[19]. The patient was hospitalized for seven days.

The patient received treatment that included Intravenous Fluid Drain (IVFD) Bfluid 20 drops per minute at the Emergency Department, Futrolit 20 drops per minute, one ampoule of Lansoprazole intravenously daily, one intravenous dose of Ondansetron 8 mg, three tablespoons of Sucralfate syrup daily, two capsules of

cough medication containing Paracetamol 500 mg, Acetylcysteine 200 mg, Mebhydrolin 50 mg, and Codeine 10 mg twice daily, and one 300 mg Gemfibrozil capsule at night.

On the second day, the patient still complained of fluctuating fever and nausea. The patient's general condition was weak, extremities warm, blood pressure 100/60 mmHg, hemoglobin decreased to 9.3 g/dL, platelet count decreased to 43,000/mm3, red blood cell count was normal at 3.17 x 1012/L, and hematocrit was decreased to 28.8%. The patient received a transfusion of four Thrombocyte Concentrate (TC) units (1 unit = 500 mL, 4 units = 2 L). Cough medication was not administered again due to patient refusal.

On the third day, the patient continued to experience fluctuating fever, but the nausea had decreased. The patient remained weak, extremities warm, blood pressure 111/68 mmHg, hemoglobin 8.9 g/dL, leukocyte count 3,100/mm3, platelet count 47,000/mm3, red blood cell count 3.01 x 1012/L, and albumin had decreased to 2.7 g/dL. The patient received a transfusion of four TC units and two Packed Red Cells (PRC) units.

On the fourth day, the patient was afebrile but complained of nausea and difficulty in defecation. Blood pressure was 146/80 mmHg, hemoglobin had increased to 12.2 g/dL, platelet count was still low at 44,000/mm3, and hematocrit was normal at 37.5%. The patient was diagnosed with hypertension, thrombocytopenia, non-specific bronchitis, dengue fever, and dyslipidemia. The patient received additional treatment including one daily fleet enema, three tablespoons of Lactulax thrice daily, three Inbumin tablets daily, a transfusion of four TC units, and continued other therapies.

On the fifth day, the patient complained of fatigue and ongoing fluctuating fever. Blood pressure was 140/86 mmHg, hemoglobin was 11 g/dL, and platelet count was 38,000/mm3. Abdominal ultrasound indicated mild hepatomegaly of unknown cause. No abnormalities were found in the pancreas, gallbladder, both kidneys, internal genitalia, or bladder on the abdominal ultrasound. No signs of ascites or pleural effusion were observed. The patient received a transfusion of four TC units and the doctor added Methylprednisolone 125 mg intravenously thrice daily and Trolit sachets thrice daily.

On the sixth day, the patient complained of ongoing fever, fatigue, and bloating. Blood pressure was 156/75 mmHg, hemoglobin was 11.7 g/dL, and platelet count was 47,000/mm3. The patient was diagnosed with pancytopenia, hypertension, dengue fever, non-specific bronchitis, hepatosplenomegaly, and dyslipidemia. The patient received a transfusion of four TC units and additional treatment including two Disflatyl tablets to be chewed twice daily, three Ursodeoxycholic Acid (UDCA) 500 mg tablets thrice daily, and three Curcuma tablets thrice daily.

On the seventh day, the patient reported weakness with blood pressure of 147/80 mmHg and platelet count of 30,000/mm3. The patient received a transfusion of four TC units and continued with other therapies. The patient requested discharge. Medications provided upon discharge included two daily Disflatyl tablets to be chewed, three UDCA 500 mg tablets thrice daily, three Curcuma tablets thrice daily, two daily Dexamethasone 0.5 mg tablets, one nightly Gemfibrozil 300 mg capsule, three tablespoons of cough medication thrice daily, and two daily Cefixime 100 mg tablets (for five days).

DISCUSSION

Dengue fever is classified as an acute infection caused by the dengue virus transmitted through Aedes aegypti mosquitoes. Indonesia, a tropical and subtropical country, is an endemic location for dengue infections. The classification of dengue infections and the severity levels of Dengue Hemorrhagic Fever (DHF) according to WHO are divided into Dengue Fever (DF) and DHF Grades I, II, III,

and IV. In this case, the patient was classified as having DHF Grade I, diagnosed based on fever complaints, bleeding manifestations (positive tourniquet test), evidence of plasma leakage indicated by hypoalbuminemia, and positive dengue IgG test results. Treatment for the patient was based on the Clinical Management Guidelines for Dengue by WHO (2012) and the National Guidelines for Medical Services in Adult Dengue Infections (2020), involving fluid therapy and symptomatic treatment. Additionally, a mild increase in serum transaminase levels was observed[20].

Dengue virus infection can lead to liver cell damage, characterized by an elevation in Serum Glutamic-Oxaloacetic Transaminase (SGOT) and Serum Glutamic Pyruvic Transaminase (SGPT) levels[21,22]. The detailed pathophysiology of liver dysfunction in DHF cases remains not fully understood. Among various theories, three mechanisms associated with liver dysfunction are direct cellular apoptosis, ischemic and hypoxic hepatopathy due to decreased perfusion to the liver, and immune-mediated end-organ damage[21,23]. Recent research indicates that disruptions in hepatic microcirculation and reduced portal blood flow significantly contribute to the pathogenesis of severe liver dysfunction[24]. The administered hepatoprotective therapy involved a combination of curcumin and Ursodeoxycholic Acid (UDCA).

The use of curcumin as a hepatoprotective agent in cases of DHF with liver dysfunction has been explored previously. Firmansyah (2020) reported a case involving the administration of a combination of curcumin and silymarin three times a day in a patient with DHF and acute fulminant hepatitis. After three days of treatment, SGOT improved by 12.7% and SGPT by 19.1%[25]. Moreover, curcumin has been reported to have a protective effect by preventing DNA fragmentation and preserving mitochondrial functionality[26]. Curcumin, an active component of curcumin tablets, exhibits anti-inflammatory activity used in hepatitis cases. The use of curcumin can decrease serum transaminase levels, Malondialdehyde (MDA) levels (an oxidative stress marker in the liver), and increase hepatic glutathione concentration, which contributes to free radical detoxification[27,28].

Currently, no research exists on the effectiveness of UDCA in patients with DHF-related liver dysfunction. UDCA is recommended for treating patients with primary biliary cholangitis (PBC)[29]. Furthermore, UDCA can activate anti-apoptotic pathways, providing protection to cellular structures like plasma membranes and mitochondria, thus preventing hepatocyte damage. UDCA also inhibits reactive oxygen species (ROS) formation in Kupffer cells, reducing oxidative stress levels in liver cells[30,31]. Administration of UDCA for four weeks in patients with liver dysfunction resulted in a 40% decrease in ALT enzyme levels, 34% decrease in AST levels, and 23% decrease in GGT levels[32].

CONCLUSION

The combination of UDCA and curcuma can be used as a prophylaxis for liver damage in DHF patients, but further monitoring is needed to assess the effectiveness of the therapy.

AUTHORS' CONTRIBUTIONS

Emilia Gan and Yenry Sumarlim took research data and wrote this journal. Desantika Wuryana, M. Hari Pristantiningtyas, Herya Putra Dharma and Muhammad Muchlis chose cases in the hospital that could be used as case reports, as well as guiding the writing of this journal. Jainuri Erik Pratama, Adji Prayitno Setiadi and Marisca Evalina Gondokesumo reviewed and supervised the journal. All authors have read and approved the final journal.

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DISCLOSURE STATEMENT

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