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A case report: Maternal complications from severe dengue. What can happen?

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ABSTRACT

Dengue fever (DHF) is an acute infectious disease caused by dengue virus. Thrombocytopenia results from viral suppression in the bone marrow, and platelet destruction occurs. Damaged platelets worsen plasma leakage. When the amount of filtration fluid exceeds the ability and fluid trapped in the interstitium eventually enters the alveoli, there is an increase in alveolar capillaries, resulting in pulmonary edema. The patient was referred with complaints of fever for 5 days, dizziness (+), shortness of breath (+), nausea (+), and vomiting (+). Laboratory examination showed platelets 109 x 103/µL, positive Ig G DHF Immuno Serology, and thorax X-ray with pulmonary edema. Cesarean section and IUD insertion were performed. During and after surgery, there were no complications.

Introduction

Dengue viruses (DENVs) form dengue complex in the genus Flavivirus, family Flaviviridae, and consist of four antigenically related but distinct DENV serotypes (DENV-1, DENV-2, DENV-2, DENV-3, and DENV-4). These DENVs can cause a spectrum of illnesses ranging from asymptomatic dengue infection to dengue fever (DF) to dengue hemorrhagic fever (DHF) to dengue shock syndrome (DSS). It is estimated that close to 3.6 billion are at risk, with 390 million infections, of which 96 million are symptomatic. Among the 96 million symptomatic cases, 2 million end in severe forms of infections, that is, DHF and DSS, and around 21,000 fatal cases occur annually around the world. Most of these infections occur in developing and underdeveloped countries where the surveillance network for infectious diseases is not robust, which means there is a possibility of gross underreporting of dengue (Iskandar, 2022). In this chapter, we will discuss the evolution of the virus and its vector, the epidemiology of dengue, the molecular and genomic structure of DENV, their pathogenesis, the immune response of the host to the infection, laboratory diagnosis, management, and recent developments in dengue drug and vaccine development (Thergarajan & Sekaran, 2023).

Dengue is endemic to the Southeastern geographical area of Asia (SEA) and spreads through the mosquito vector Aedes aegypti (Organization, 1997). Globally, the incidence of dengue increased from 30,668,000 in 1990 to 56,879,000 in 2019 (Murugesan &

Manoharan, 2020). In SEA alone, there were 7,700,000 cases of dengue in 2019 (Tian et al., 2022).

It was reported that dengue is the most common cause of fever during pregnancy (46%) in Vientiane, Laos (Chansamouth et al., 2016). In 2015, 82,000 patients in Vietnam had dengue infection nqw /i25 deaths. The mortality rate for severe dengue fever is 0.8–2.5%, and pregnancy should be recognized as a coexisting risk factor for severe infection. However, the maternal and fetal outcomes remain not fully understood. The first systemic review could not determine whether maternal dengue infection is a risk for adverse effects because there were few comparative studies (Pouliot et al., 2010). Recently, the first systematic review on outcomes of neonates born to mothers with dengue fever was reported, and it demonstrated that preterm birth and low birthweight were reported to be the most common adverse pregnancy outcomes; however, dengue fever was not significantly associated with these adverse outcomes, suggesting that symptomatic dengue fever may indicate risk (Paixão, Teixeira, Maria da Conceição, & Rodrigues, 2016).

The picture of DHF cases in 2023 in Madiun City has affected 144 people, with 1 case of death. The dengue morbidity rate in 2023 was 80.75/100,000 population, and the dengue mortality rate in 2023 was 0.69%. And the DHF mortality rate in 2023 was 0.69%. Data for 2024 up to 16 February 2024 show that 66 cases of DHF have been reported, 1 case of death, a morbidity rate of 36.89/100,000 population, and a mortality rate of 1.52% (Astuti, Dwiningwarni, Atmojo, Masfufa, & Yanesty, 2023).

Case report of Mrs. E, 26 years old, referral from a private hospital, gravida 3, the first child aged 8 years, abortion 1x. With complaints of fever for 5 days, accompanied by dizziness (+), headache (+), weakness (+), nausea (+), vomiting (+) 3 times today, and shortness (-). Mucus comes out of the birth canal. Bleeding complaints such as nosebleeds or bleeding gums are denied. Complaints of red spots on the skin are denied (Amanda, Wiratmo, & Utami, 2023). Complaints of tightness - tightness and feeling of fluid seeping from the birth canal are denied. Paien is 37-38 weeks pregnant from HPHT. Blood pressure 105/72, pulse 115 times/minute, respiratory rate 20 times/minute, temperature 36.5 degrees Celsius, SpO2 100%. Physical examination found anemis in the conjunctiva. From the obstetric examination, Leopold I inspection palpable soft, non-bouncy, podium fundus height of 30 cm; Leopold II palpable flat part on the right side of the mother; Leopold III palpable round, hard, bouncy part; Leopold IV Not yet entered the upper pelvic door (PAP), Fetal movement: present, DJJ: 134 x/min, His: (-), VT: Opening 0/10 cm; 0% eff. The results of the reactive NST reading category 1. Ultrasound examination of a single live baby, head position, estimated fetal weight of 2900 grams. Laboratory examination results of Hemoglobin 9.3 x 103, Platelets 136 x 103.

Method

The method used is a case report.

Results and Discussion

Dengue hemorrhagic fever is a dengue virus infection with four serotypes: Den-1, Den-2, Den-3, and Den-4. It is characterized by a sudden fever of 2-7 days, which can be accompanied by joint pain, retroorbital pain, heartburn, nausea, and vomiting. Bleeding, thrombocytopenia, and evidence of fluid permeation into the interstitial are also present.

The exact mechanism of the pathophysiology and pathogenesis of dengue hemorrhagic fever is still unknown, but most adhere to the "secondary heterologous infection hypothesis", which says that dengue fever can occur if a person after the first dengue infection gets reinfected with a different type of dengue virus for a certain period which is estimated to be between 6 months and 5 years.

As a result of a second infection by a different type of dengue virus in a patient with low levels of anti-dengue antibodies, the anamnestic antibody response that will be caught in a few days results in the proliferation and transformation of immune lymphocytes by producing high-titer anti-dengue IgG antibodies. Dengue virus replication occurs as a result of the presence of a large number of viruses. All of these things will form an antibody-antigen complex, further activating the complement system. The release of C3a and C5a due to the activating of C3 and C5 causes increased permeability of the blood vessel wall and the seepage of plasma through the endothelium of the blood vessel wall. In people with severe shock, plasma volume can be reduced to more than 30% and lasts 24-48 hours.

Shocks that are not adequately treated can cause tissue anoxia, metabolic acidosis, and death. Thrombocytopenia is a hematological disorder found in most dengue patients. The platelet value decreases during fever and reaches its lowest value during shock. The number of thrombocytes rapidly increases during convalescence, and average values are usually reached by the 10th day after the onset of the disease.

The endothelium has a vital function, namely maintaining vascular tone, preventing blood clots and cell migration, producing chemoattractants, and maintaining the permeability of blood vessels. This function is needed to maintain the blood supply to the body's organs. In order to function correctly, endothelial cells must remain stable. The links between cells composed of protein molecules maintain the stability of vascular endothelial cells. The links between endothelial cells that play the most role are tight junctions and adherens junctions. The links between endothelial cells form a narrow gap between endothelial (paracellular pathways). They can only be passed through small molecules < 2 nm in diameter, such as water, urea, glucose, electrolytes, etc. However, if the gap widens, the gap between the endothelium can pass through larger molecules and blood cells (plasma leakage).

In dengue, there is a plasma leak. The release of interleukin (IL)-1, IL-6, tumor necrosis factor-alpha (TNF-α), histamine, bradykinin, anaphylaxis C3a and C5a, vascular endothelial growth factor (VEGF), activation of complements, thrombin, and antibodies during infection can cause activation and contraction of capillary endothelial cell filament actin. The contraction that occurs makes the link proteins between endothelial cells (tight

junction and adherens junction) enter the cell, making the gap between cells widen and subsequently causing plasma leakage.

Non-cardiac pulmonary edema is an abnormal or excessive accumulation of fluid in the interstitial and alveolar spaces of the lungs due to increased microvascular permeability. Pulmonary edema occurs when the capillary alveoli membrane filtration rate increases beyond the capacity of lymphatic duct flow.

Under normal circumstances, the mechanisms that maintain the pulmonary alveoli remain in a fluid-free state by feeding are regulated by the anatomy and physiology of the lungs themselves, namely the balance of capillary pressure and osmotic pressure of plasma fluid, as well as the state of permeability of the capillary wall that remains normal.

In general, pulmonary edema occurs due to an increase in pulmonary microvessels due to an increase in pulmonary veins, generally due to mitral stenosis and left ventricle decompensation, known as cardiopulmonary edema. Another cause of pulmonary edema is an increase in capillary alveoli, caused by toxic substances from inside and outside the lungs due to inhalation of toxic gases. In this state, there is a buildup of protein and fluid in the pulmonary intertidal without an increase in microvascular, known as non-cardiac pulmonary edema.

Management of DHF with pulmonary edema in pregnancy

Spreading dengue to the ovaries by its endemic vector can increase the incidence of dengue hemorrhagic fever. The increase in the number of cases also occurred due to overcrowding of residents, movement from one place without reporting, poor environmental sanitation, travel in endemic areas, and ineffective vector eradication (Organization, 1997). WHO divides the clinical manifestations of dengue hemorrhagic fever by degrees one to four, according to the manifestations caused.

Acute pulmonary edema is a significant cause of morbidity and mortality in pregnant and recently pregnant women (Wilkinson, 2011). It is characterized by sudden onset breathlessness, may be accompanied by agitation, and is often the clinically severe manifestation of various pathophysiological processes. The Scottish Confidential Audit of Severe Maternal Morbidity, one of the most extensive maternal morbidity audits, reported that acute pulmonary edema was the fourth most common form of maternal morbidity (Wilkinson, 2011). It is also frequently the reason for intensive care admission (Pollock, 2010) and may occur during the antenatal, intrapartum, or postpartum periods.

Estimated rates of acute pulmonary edema in pregnancy vary from 0.08% to 0.5% (Dunne, 2008; Altman, 2008). The wide ranges reported are due to the poor reporting of maternal morbidity and the lack of minimal reporting datasets of key outcomes in pregnancy and the postpartum period (Tornton, 2011).

Iatrogenic causes remain an essential factor for acute pulmonary edema without hypertension. The management of preterm labor with the use of tocolytic agents such as adrenoceptor antagonists (terbutaline and salbutamol) has been associated with acute pulmonary edema. Important mechanisms in this setting include effects on capillary permeability, reduced myocardial contractility, and fluid administration.

Britain and Ireland during tocolytic therapy and the concurrent use of steroid medication. Newer single agents such as nifedipine are associated with less acute pulmonary edema (level 1++ evidence). Magnesium sulfate and corticosteroids have both been implicated as precipitators of acute pulmonary edema in pregnant or postpartum women. Women in whom magnesium sulfate infusions are administered for fetal neuroprotection in preterm labor (level 1++ evidence) need to be carefully monitored and their fluid balance meticulously recorded.

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Inhaling toxic gases in this state can cause toxic substances to build up inside and outside the lungs. This buildup of proteins and fluids in the intertidal lungs without an increase in microvascular blood flow is known as non-cardiac pulmonary edema.

The administration of diuretics aims to reduce the pre-load that becomes a burden on the ventricles. In situations where hypotension occurs with low pulmonary capillary wedge pressure requiring fluid resuscitation to increase blood pressure and tissue perfusion, if there is no response to inotropic administration, it may be considered.

The triggering factors of non-cardiac pulmonary edema must be identified and managed optimally. Causes of pulmonary edema with normal microvascular pressure include inhalation of toxic gases (Nitrogen dioxide, CO, Sulfur dioxide, etc.), gastric fluid aspiration, and pulmonary edema due to altitude. Pulmonary edema should be treated in the intensive care unit to monitor and evaluate blood gas analysis, fluid balance, blood pressure, and radiological picture. Specific treatment refers to the underlying cause of >40,000 cases of pulmonary edema unless obstetric or termination measures cannot be avoided in the next six hours.

Attention if urine output is minimal, persistent vomiting, lethargy, weak pulse, slow filling of capillaries >2 seconds, liver enlargement >2cm, mucosal hemorrhage (epistaxis, gum bleeding, petechiae, and vaginal bleeding and increased hematocrit >20% from the baseline line), these symptoms are DHF with warning signs (Group B). Check your vital signs every hour to know exactly how much urine you will output each hour. (urine target 0.5ml/kg/hour).

Intensive fluid resuscitation is carried out with normal fluid saline bolus 5-7 cc/kg/hour within 1-2 hours; if the situation improves, continue to administer 3-5ml/Kg/hour in 2-4 hours, gradually reducing to 2-3ml/Kg/hour in 2 to 4 hours. If the situation improves, stop fluid therapy at 48 hours. Evaluate urine output and pulse pressure and avoid induction of labor or surgical planning in this phase.3 DHF with shock

on admission is categorized in group C. Patients in this category require Intensive Unit Care (ICU).

Conclusion

Dengue infection is significant in pregnancy. Viral infection can affect the incidence of morbidity and mortality rates in femtometers. Case recognition to establish the correct diagnosis of fluid therapy administration is not delayed. DHF in pregnant women can cause preterm birth, intrauterine fetal death, placental abruption, pulmonary edema, and miscarriage in early pregnancy. Childbirth is performed by cesarean section due to the presence of pulmonary edema to evaluate, and pregnancy is highly dependent on obstetric indications as well as the choice of termination method. It is not recommended to perform labor induction or surgery planning in the critical phase because it will cause heavy bleeding. Platelet administration is also not recommended to be done routinely without any accompanying indications. The administration of PRC is prepared and can be given immediately if bleeding occurs after termination. The administration does not wait for the loss of blood volume to reach 500 cc, which will make the hematocrit drop to the lowest level. Postoperative care is carried out in the ICU room due to the presence of pulmonary edema that requires observation.

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