Case Report

A case report: how to clarify fever with thrombocytopenia due to dengue or chronic liver disease?

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ABSTRACT

Fever and thrombocytopenia mostly associated with dengue hemorrhagic fever. But on certain condition of fever with thrombocytopenia, we still seek another etiology such as chronic liver disease. How to clarify between thrombocytopenia in dengue and chronic liver disease.

Keywords: Thrombocytopenia, Dengue, Chronic liver disease

INTRODUCTION

Fever is any abnormal elevation of the body temperature above the normal range. It is a result of complex physiological response from the activation of immunologic, endocrinologic and physiological. The most common fever is associated with infectious disease.[1] Body temperature is controlled by the hypothalamus with balancing inputs from the nerves that utilize cold or warm receptors in skin. The hypothalamus also analyzing the blood temperature in the surrounding area.[2] The most common causes of febrile and thrombocytopenia is infection, and the most causes of infections are dengue.[3]

Thrombocytopenia defined as a platelet count lower than 150×10^9 /L. The etiology of thrombocytopenia can because multisystem disorder and multiple mechanisms. Sometimes it can be asymptomatic, and to identify the underlying pathogenesis can be challenging. Some of the causes of thrombocytopenia are dengue infection, HCV infection, HBV infection.[4] Main regulator of thrombocyte is thrombopoietin hormone that mainly syntheses in liver. Thrombocyte usually still in the circulation about 7 until 10 days. The pathophysiology of thrombocytopenia can be divided into two, there are increased destruction and decreased production. Decreased production can be seen in hematologic malignancies, aplastic anemia, myelodysplasia, drugs like chemotherapy, alcohol, radiation, HIV, vitamin D deficiencies, hereditary thrombocytopenia, metastatic cancer to bone marrow. Increased destruction can be seen in idiopathic thrombocytopenia purpura, drug-induced antibodies, HIV, disseminated Intravascular coagulation, sepsis, hypersplenism, etc.[5]

Dengue hemorrhagic fever is viral infection caused by dengue virus and spread by *Aedes aegypti* mosquito or *Aedes albopictus* mosquito. Thrombocytopenia is one of the criteria to diagnosing dengue hemorrhagic fever. Thrombocytopenia in dengue hemorrhagic fever because decreased production in the bone marrow and also can be caused of cross reaction of antibody and platelet that caused lysis of platelet and inhibit the aggregation of platelet. The pattern of thrombocytopenia in dengue hemorrhagic fever are the thrombocyte will decrease from the first day of fever and will show thrombocytopenia in the 4th day and still continue to decreased in the 6th day, after that the thrombocyte will be increased and will be normal in the 9th or 10th day.[6] Laboratory methods can be used to diagnose dengue, that

are isolation of the virus, nucleic acid and antibodies or antigens, or combined technique. After the virus come into the body, the virus can be checked in the bloods, serum, or plasma within 4-5 days. IgM antibodies will be first produced and will increase in the body and will be decreased after two weeks. In the second exposure of the dengue virus, the antibodies will increase rapidly. The higher level of IgG in the body can be found and persist for longer duration also can be used to check the recent or past infection by dengue.[7]

Thrombocytopenia also can be happened in the chronic liver disease. The pathophysiology associate with the hypersplenism, where the portal hypertension makes sequestration and pooling of corpuscular elements of blood such as thrombocytes, in the congested and enlarged spleen. It also can be caused of bone marrow suppression and can be caused by toxic substances like alcohol or viral infection.[8]

CASE REPORT

A female 42 years old female, who came to emergency unit, reported with a chief complaint fever for 5 days prior to admission. Medical history; she was also feels weak and with cough, there are no nausea, vomiting, headache, abdominal pain or chest pain. Patients had history of hepatitis C infection. The patient had history of hepatitis C about six years. The patient was fever (axilla temperature of 38.3), awareness is Compos Mentis, blood pressure is 110/75 mm Hg, pulse rate 78 beats/minute, respiratory rate 20 x/minute, and oxygen saturation of 98 % on room air. On Physical examination, anemic in the eyes is found. She had thrombocytopenia: platelet count 62×10^3 µL ($150-450\times10^3$ µL), low hemoglobin level 7.5 g/ dL (12-16 g/dL), low hematocrit level 26.1% (37.0-47.0 %), and low leukocytes level 2.7×10^3 µL (4.0-10.0 µL). The results of anti-SARS-CoV-2 was negative (rapid test).

The working diagnosis was observation of fever and thrombocytopenia et causa suspect dengue hemorrhagic fever, anemia, hepatitis C. The patients given natrium chloride 0.9%, dextrose 5%, aminoleban with ratio 1:1:1, esomeprazole 40 mg every 24 hours, cefoperazone 1 gram every 12 hours, lactulose 15 ml every 8 hours, curcuma one tablet every 8 hours, paracetamol 500 mg every 8 hours. The patients also given packed red cell, one pack every 24 hours.

On the 2nd day admission, she still complains cough and feel weak. The laboratory results are still thrombocytopenia (platelet 62×10^3 µL) and the chest X-ray showed normal lung and heart. The leukocytes level still low 2.87×10^3 µL, hemoglobin level also still low 7.7 g/dL, and low hematocrit level 27.4%. The patient also planned to be checked IgM dan IgG dengue, but the samples must be referred to other hospital to be checked. On the 3rd day admission, she still feels weak, but the cough and fever feel better. The laboratory results are still

thrombocytopenia (platelet 46×10^3 µL) and still decreased from the day before. The leukocytes level still low 3.30×10^3 µL, hemoglobin level increased become 9.2 g/dL, and low hematocrit level 32.5%. This day the result of IgM and IgG dengue still not finished yet. We also stop the packed red cell transfusion.

On the 4th day admission, she feels better, no fever and no cough. The result of IgM and IgG dengue are negative. The laboratory results are still thrombocytopenia (platelet 84×10^3 µL) and increased from the day before. The leukocytes level still low 3.71×10^3 µL, hemoglobin level is 9.7 g/dL, and low hematocrit level 34.5%. On the 5th day admission, she had no complaints and vital signs are normal. The laboratory results are still thrombocytopenia (platelet 77×10^3 µL). The leukocytes level still low 3.39×10^3 µL, hemoglobin level is 9.1 g/dL, and low hematocrit level 32.3%. The patient was discharged with diagnosis chronic liver disease-hepatitis C related and Anemia, thrombocytopenia (Hypersplenism): chronic liver disease. Patients also given omeprazole 20 mg twice a day, curcuma three times a day, folic acid two times a day and lactulose syrup 25 ml three times a day.

DISCUSSION

Thrombocytopenia characterized by low platelets number abnormally and one of the most common hematological disorders. 150,000 to 450,000 per microliter is the normal count of the platelets. Sometimes thrombocytopenia is the first sign of infectious disease, malignancies, autoimmune disorders, and many others.[9] Dengue is caused by Flaviviridae family which is mosquito-borne that cause wide spectrum of disease from flu-like symptoms until severe bleeding in severe dengue. The plasma leakage and organ impairment have higher risk of death if not treated well. This virus can be detected by ELISA IgM IgG antibodies and NS1 antigen.[10] The thrombocyte count of adult in dengue and dengue hemorrhagic fever is decreased from the third day of the disease to the sixth day of the disease, and getting increased again in seventh day but not until the normal range.[11]

Dengue virus can affect bone marrow progenitor cells directly or indirectly by inhibit their function to decrease the hematopoietic cells proliferative capacity. Dengue Virus also induced hypoplasia of the bone marrow in the acute phase of the disease. Dengue virus infections also make increased of platelet destruction due to apoptosis, lysis of the complement system, induced platelet consumption, and the involvement of antiplatelets antibodies.[12] This patient complain fever from five days before come to the hospital. After the laboratory tested, we found thrombocytopenia in this patient (thrombocyte total 62.000).

The patients also had history of hepatitis C infection from six years before. we assessed the patients with observation of fever + thrombocytopenia et causa suspect dengue hemorrhagic fever differential diagnose is chronic

liver disease, and hepatitis C infection. The most common etiology responsible for newly diagnosed thrombocytopenia in adult patients was found to be dengue/dengue-like fever.[13]

In our cases, the thrombocyte of the patients decreased in the next day. We checked the Ig M and Ig G anti dengue to diagnose the patients have thrombocytopenia due to DHF or due to cirrhosis. The sample must be sent to another hospital because in this hospital there were not laboratory testing for IgM dan IgG dengue. On the third day of hospitalization, the thrombocyte still decreased from 62.000 to 46.000. The pattern of the thrombocyte total still decreased like in dengue fever. The result of IgM dan IgG anti dengue is negative. Ig M dengue in the blood show the acute infection of dengue, and still can remain in blood after a month. Ig G dengue will produce in the body after two weeks of infection in primary infection and can be positive in secondary infection of dengue.[14] Chronic liver disease can make thrombocytopenia by sequestration of congestive splenomegaly, decrease level of TPO (thrombopoietin) in the circulation, and immune mediated destruction.[15] After the examination and laboratory result of this patients, we concluded the thrombocytopenia is not due to dengue but because of the chronic liver disease.

CONCLUSION

We reported a case, a female 42 years old, with history of fever from five days before came to hospital. After the laboratory examination we found the thrombocyte level is low (62.000). She also has history of hepatitis infection from six years before. The patient was previously concluded as observation fever and thrombocytopenia et causa suspect dengue hemorrhagic fever. After the laboratory examination, we found the Ig M dan Ig G dengue is negative, therefore finally she was diagnosed with thrombocytopenia due to chronic liver disease.

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