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Case Report

A febrile thrombocytopenia is it always dengue

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ABSTRACT

Dengue is tropic infectious disease which concentrated in tropical and subtropical regions. Human immunodeficiency virus (HIV) is an infection that attacks the body's immune system. A 29-year-old female admitted to hospital with history of febrile thrombocytopenia with HIV infection on highly active anti-retroviral therapy (HAART). First, the patient was assessed with dengue hemorrhagic fever, but anti-dengue immunoglobulin G (IgG) and IgM were negative. Febrile thrombocytopenia occurs not only in dengue, but also in other conditions. Person with HIV experience a wide range of hematological abnormalities, the most prevalent of which are cytopenias, which can be anemia, leukopenia, thrombocytopenia, or a combination of these. Fever and thrombocytopenia are closely related to dengue infection, but this condition can also be caused by various factors.

Keywords: Dengue, Febrile, Thrombocytopenia, HIV, Infection

INTRODUCTION

Dengue caused by four dengue virus serotypes; DENVs 1-4, transmitted by Aedes mosquito. Dengue has become a worldwide reemerging disease and expanding globally.[1] The virus incubates for 3 to 14 days, the person may develop an acute fever with a range of nonspecific signs and symptoms.[2] Since non-structural protein 1 (NS1) is secreted from infected cells and circulates at higher levels in the blood of infected patients, it is an ideal target biomarker. IgM and IgG antibody tests are the more helpful diagnostic assays.[3] Dengue can be with warning sign, without warning sign, or sometimes can lead into severe dengue. In complete blood count (CBC), we will find leukopenia and low platelets with or without hemoconcentration.[4] HIV is an infection that attacks the body's immune system. Acquired immunodeficiency syndrome (AIDS) is the most advanced stage of the disease.[5] The main target of HIV is CD4+T cells. After a few years, severe immunodeficiency appears, and the person experience an infectious or oncological complication that is specific to them (these complications constitute AIDS).[6] World Health Organization (WHO) has established a four stages clinical classification system determined by the presence of opportunistic infections and other HIV related conditions.[7] Thrombocytopenia is commonly observed among patients infected by HIV and could be present as first sign of disease in approximately 5-15% of patient.[8] Antiretroviral therapy (ART) has been available to treat HIV infection. When administered properly, ART is very efficient in suppressing HIV replication, enhancing immune function and reducing the risk of developing AIDS.[6]

CASE REPORT

A 29-year-old female presented to the emergency room with history of fever, 3 days before admitted to hospital. The fever come and go, got better with medication but never reached the normal limit. She had episodes of nausea, non-bilious vomiting, once on first day, black-colored feces and was on her period. She had history of HIV infection on therapy with (zidovudine+lamivudine) and nevirapine twice a day each. On presentation she was conscious, oriented, febrile (38.3°C), heart rate 83/minutes, blood pressure 100/60 mmHg, and warm

peripheries. A CBC was done, showing normal leucocyte (1.5^103 ul), increased hemoglobin (14.7 g/dl) and hematocrit (42.3%), low platelets (45^103 ul). She was given fluid resuscitation by 500 cc-ringer lactate and done the post-resuscitation CBC. It showing normal leucocyte (1.37^103 ul), normal hemoglobin (13.8 g/dl) and hematocrit (40.8%), low platelets (45^103 ul). Patient was assessed by dengue hemorrhagic fever with warning sign. She had received parenteral fluids, ringer lactate 20 drip/minute, pantoprazole once a day, tranexamic acid 3 times a day, paracetamol 3 times a day, and folic acid once a day. The patient was treated for 5 days, serial CBC was performed every 12 hours to assess the hemoconcentration, platelet count and plasma leakage. On the first day of treatment, patient still complained of fever, nausea, and heavy menstrual bleeding, but bloody-feces already stopped. Furthermore, patient's temperature was always normal, but on third day of treatment, she complained itching all over her body and was given combination therapy of loratadine and cetirizine once a day. On the third day of fever, it was found that the platelet count had decreased from 45^103 ul to 38^103 ul, then on the fourth day, it decreased again to 37^103 ul, and 12 hours later it became 36^103 ul. An anti-dengue IgG and IgM was carried out and the result was negative. Patient assessed with febrile thrombocytopenia on HAART. On the fifth day of fever, the platelets had entered an increasing phase, risen to 39^103ul and 48^103 ul on the next 12 hours. On the sixth and seventh day, it became 76^103 ul and 128^103 ul respectively. Fever, nausea, and itching have improved, the patient was discharged.

Table 1: Serial CBC during the treatment.

	Febrile day 3 before loading	Febrile day 3 after loading	Febrile day 3 10 PM	Febrile day 4 6 AM	Febrile day 4 6 PM	Febrile day 5 6 AM	Febrile day 5 6 PM	Febrile day 6	Febrile day 7
Leucocyte (10^3ul)	1.55	1.37	1.26	1.59	1.09	2.02	1.45	1.95	2.62
Hemoglobin (g/dl)	14.7	13.8	13.0	13.2	13.3	13.2	13.1	13.0	13.1
Hematocrit (%)	42.3	40.8	37.8	39.0	37.9	39.5	37.5	37.7	37.8
Platelet (10^3ul)	45	45	38	37	36	39	48	76	128

DISCUSSION

There are three phases that can be seen in the setting of DENV infection: a febrile phase, a critical phase, and a recovery phase.[9] The abrupt, high-grade fever (≥38.5°C) associated with headache, vomiting, myalgia, arthralgia, and, in certain cases, a brief macular rash are the hallmarks of the febrile phase of DENV infection. Decervescence, which occurs between days 5 and 6, indicates a time during the critical phase when the temperature usually drops to about 37.5 to 38°C or lower, associated with increased capillary permeability. Leukopenia and increased hematocrit levels are frequently present with a rapid decline in platelet count can also develop up to 24 hours prior to the emergence of warning symptoms. The recovery phase involves the gradual reabsorption of extravascular fluid over 2 to 3 days start from day 7.[10]

Platelets will increase while in recovery phase.[10] Non-structural protein 1 (NS1) is an ideal target biomarker for dengue and optimal to be found on the first three day of infection. IgM and IgG antibody tests are the more helpful diagnostic assays. IgM can be detected three to five days after infection and can be found at measurable levels for several months. IgG develops later in the initial infection and quickly in the subsequent infection.[3] In this case, the patient had a fever phase, signs and symptoms of dengue infection. However, if we focus on the platelets, patients had phases of decreasing and increasing platelets faster than the onset of the normal phase. Normally, platelets start to decline during the critical phase, especially on day 5 and 6 of fever, then increase in the recovery phase, especially on day 7 onwards. However, in this case platelets decrease on day 3 and 4 of fever, and started an increasing trend on day 5 onwards. It is suspected that this febrile thrombocytopenia condition occurred not due to dengue infection. This was confirmed by the negative results of anti-dengue IgG and IgM. The patient had HIV infection and was undergoing treatment for 6 months with a combination of (zidovudine+lamivudine) and nevirapine. The use of ART can cause various side effects ranging from severe allergic reactions to mild symptoms such as fever, nausea, vomiting, headaches and abdominal pain which resemble the early symptoms of dengue, so it could be mistaken during the initial assessment.[11] HIV infects hematopoietic stem cells, which leads to the apoptosis of hematopoietic precursors, therefore, person with HIV experience a wide range of hematological abnormalities, the most prevalent of which are cytopenias, which can be anemia, leukopenia, thrombocytopenia, or a combination of these.[12] Thrombocytopenia is the second most frequent complication of HIV infection, occurring in

about 4-40% of HIV infected patients and the degree is generally mild to moderate; however, severe reduction of a platelet count <50.00 ul also occurs.[13,14] Although many drugs used for the treatment of HIV-related disorders are myelosuppressive, severe cytopenia is most often related to the use of zidovudine. However, the use of long-term combination ART or HAART has reduced the prevalence of thrombocytopenia and as time goes by, our body can adapt to the side effect and minimalize it.[12,15]

CONCLUSION

Our case highlights that, even though fever and thrombocytopenia are closely related to dengue infection, this condition can also be caused by various factors, one of that is HIV infection and even, those who currently undergoing treatment.

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