



CASE STUDY

AN ELDERLY FEMALE WITH PULMONARY OEDEMA MANIFESTATION OF DENGUE HAEMORRHAGIC FEVER: A CASE REPORT

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ABSTRACT

Dengue Haemorrhagic Fever (DHF) is an arthropod borne viral disease. The main vector of the disease are the *Aedes* mosquitoes. Indonesia as one of the tropical nations in South Asia falls into one of the countries in which DHF is an endemic. The notable clinical symptoms are fever usually 40°C with a saddleback or biphasic pattern in 6% of DHF cases¹, pain in body, muscles, retroorbital and joints, nausea and vomiting. Fluid accumulation, due to plasma leakage, may occur in the abdominal cavities, pleural space, and even the lungs². The rise of non-communicable diseases like diabetes mellitus has impacted the clinical progression of DHF by increasing the risk of developing into dengue shock syndrome and atypical clinical manifestation of dengue plasma leakage and bleeding disorder³. This case report will discuss one of these atypical clinical manifestations of DHF. The case is an elderly female presenting in the emergency room with a dengue fever, Diabetes mellitus type 2, cardiomegaly and during inpatient care developed a pulmonary Oedema. Patient experienced prolonged fever and on the 7th day of care develops a pulmonary oedema, the patient is then moved to the intensive care unit, and with proper treatment and monitoring was able to recover from the disease

Keywords: Dengue Haemorrhagic Fever, Elderly, Diabetes Mellitus type 2, Pulmonary Oedema

АБСТРАКТ

Геморрагическая лихорадка Денге (ГЛД) - это вирусное заболевание, переносимое членистоногими. Основным переносчиком заболевания являются комары рода *Aedes*. Индонезия как одна из тропических стран Южной Азии относится к числу стран, в которых ЦГВ является эндемичным заболеванием. Характерными клиническими симптомами являются лихорадка обычно 40°C с седловидным или двухфазным характером в 6% случаев ЦМВ¹, боли в теле, мышцах, ретроорбитальной области и суставах, тошнота и рвота. Скопление жидкости, обусловленное утечкой плазмы, может происходить в брюшной полости, плевральном пространстве и даже в легких². Рост числа неинфекционных заболеваний, таких как сахарный диабет, повлиял на клиническое течение ДГП, увеличив риск развития синдрома шока денге и атипичных клинических проявлений денге - утечки плазмы и кровотечения³. В данном отчете рассматривается одно из таких нетипичных клинических проявлений ЦМВ. В данном случае речь идет о пожилой женщине, поступившей в приемный покой с лихорадкой денге, сахарным диабетом 2-го типа, кардиомегалией, а во время пребывания в стационаре у нее развился отек легких. У пациентки наблюдалась длительная лихорадка, и на 7-й день лечения развился отек легких, после чего пациентка была переведена в отделение интенсивной терапии, и при надлежащем лечении и наблюдении удалось добиться выздоровления.

Ключевые слова: Геморрагическая лихорадка Денге, пожилые люди, сахарный диабет 2-го типа, отек легких

INTRODUCTION

Dengue Haemorrhagic Fever (DHF) is an arthropod borne viral disease. The main vector of the disease are the *Aedes* mosquitoes. Dengue virus has 4 serotypes (DENV 1-4) with all these serotypes being able to cause DHF. South America, south Asia, and Australia have shown to be the hotspot of DHF. Indonesia as one of the tropical nations in South Asia falls into one of the countries in which DHF is an endemic. According to the data taken from the National Dengue Surveillance registry of the Indonesian ministry of health shown that incidence rate of dengue has increased from just 0.05 cases per 100,000 person-years in 1968 to 77.96 cases per 100,000 person-years in 2016. This increased in incidence rate is also accompanied by declining in Case Fatality Rate (CFR) from 20% in the late 1960's to 0.79% in 2016.

The notable clinical symptoms are fever usually 40°C with a saddleback or biphasic pattern in 6% of DHF cases, pain in body, muscles, retroorbital and joints, nausea and vomiting. Minor haemorrhagic manifestation includes epistaxis, purpura, malaise, ecchymosis, petechiae, epistaxis, haematuria, bleeding gums, aches or pain, or a positive tourniquet test result². Fluid accumulation, due to plasma leakage, may occur in the abdominal cavities, pleural space, and even the lungs². A critical phase of DHF is when the temperature suddenly drops to 37.5 C to 38 C or less on days three through seven. This phase is marked by increasing haematocrit, declining platelet count. An increase in plasma leakage also occurs during this phase and could lead to shock, organ dysfunction, disseminated intravascular coagulation, or hemorrhage¹. The rise of non-communicable disease like diabetes mellitus has also impacted the clinical progression of DHF by increasing the risk of developing into dengue shock syndrome and atypical clinical manifestation of dengue plasma leakage and bleeding disorder³. This case report will discuss one of these atypical clinical manifestations of DHF. We would like to present the case of a 63-year-old female presenting in the emergency room with a

dengue fever, Diabetes mellitus type 2, cardiomegaly and during inpatient care developed a pulmonary Oedema.

CASE

Mrs W is a 63-year-old female, she came to the emergency room with a chief complaint of fever with the onset of 3 days. The patient also complaint aching all over her body and an abdominal discomfort that cause poor appetite. The patient has a history of diabetes type 2 and a cardiomegaly. The patient routinely consumes 2 mg of glimepiride for the diabetes but has not taken any medication for the cardiomegaly. On physical examination the patient weigh 90 kg and there were generally no abnormalities except for an epigastric pain and a pitting oedema in both ankles, and on laboratory examination an increase in segment neutrophil to 81 % and a high random glucose of 334 mg/dl were present, the platelet was 205.000 /microliter blood, Haemoglobin 14.7 mg/dl, leucocyte 7.500/ microliter blood, haematocrit 44%. A Chest radiograph revealed a cardiomegaly. An ECG shown a normal sinus rhythm. The patient initially was assessed with observation of 3rd day of fever, diabetes type 2, and cardiomegaly and received the treatment of normal saline infusion 1500 ml per day, aspart insulin 3x9 unit, insulin glargine 9 unit at night, bisoprolol 1x2.5 mg, furosemide injection 1x20 mg, omeprazole injection 1x40 mg, ceftriaxone 2x1 gram, diabetes mellitus diet 1500 calories. The patient then was moved to the inpatient ward.

The patient experienced a sudden dyspnoea on the sixth day of care. Upon physical examination rales were present on the base of both lungs, the vital sign was: BP 120/90 mmHg, heart rate 98 BPM, respiratory rate: 25 times/ minutes. Temperature: 37.2 Celsius, oxygen(O₂) saturation: 92 % with nasal canula on 2 litre per minutes oxygen. The patient was moved to the High Care Unit (HCU). A complete blood count was examined again and showed that the patient's platelet had dropped to 64.000, haematocrit 38 %. The patient was tested for IgG and IgM dengue with a positive result. A blood gas analysis showed

compensated respiratory alkalosis. An elevated blood sugar level of 258 mg/dl was also present. A repeated chest x-ray had shown a bilateral pleural effusion and a perihilar haziness. The diagnosis was then updated to acute pulmonary oedema, dengue haemorrhagic fever, hyperglycaemia in diabetes mellitus type 2, cardiomegaly. The patient received additional treatment of O₂ via Non-Rebreathing Mask with the rate 10 litre per minute, injection of furosemide 2x40 mg, insulin regiment were increased, aspart 3x10 unit with the monitoring of blood sugar level per 12 hours. On the 14th day of the treatment the patient was stable with the vital sign of blood pressure 140/80 mmHg, heart rate 98 BPM, respiratory rate 20 times/ minutes, temperature of 36.5^ocelsius, and oxygen

saturation of 98% with room air, platelet count of 107.000 / microliter blood, and blood sugar lever of 180 mg/ dl The patient was then discharge from the hospital.



Figure 1. the chest x-ray of Mrs. W, (left) on the 1st day of care, (right) on the 7th day of care. A perihilar haziness and bilateral fluid effusion are seen in the 7th day of care

Table 1. Laboratory examination of the patient

parameter	Normal Value	1 st day	5 th day	7 th day			
				06.00	18.00	06.00	18.00
WBC (K/ul)	5-10	7.5		12.6	13	-	-
Haematocrit (%)	37-47	44		40	38	-	-
Platelet (K/ul)	150-400	205		82	74	-	-
Hb (g/dl)	12-16	14.7		14.1	13.4	-	-
Random Glucose (mg/dl)	70-150	334	111	68	102	180	102
Creatinine (mg/dl)	0.6-1.2	-	0.72	-	-	-	-
Ureum (mg/dl)	15-40	-	17	-	-	-	-

Table 2. Electrolyte examination of the patient

Day of care	Normal Value	8 th day	9 th day
Natrium (mmol/l)	135-153	127	139
Potassium (mmol/l)	3.5-5.3	4.4	3.6
Chloride (mmol/l)	96-110	96	100

Table 3. Immunoserology examination of the patient

Day of care	Normal Value	6 th day
IgM Dengue	Negative	Positive
IgG Dengue	Negative	Positive

DISCUSSION

Dengue Haemorrhagic Fever (DHF) occurred when *Aedes* mosquitoes transmit the dengue virus through dermal injection¹. After dermal injection dengue virus will infects the immature Langerhans cell and keratinocyte. These cells then travel to the lymph nodes, in which monocytes and macrophages will be recruited and thus amplifying the infection and the virus spread of the dengue virus through the lymphatic system. Dissemination of the virus through the lymphatic system will propagate the virus infection furthering target the leukocyte and mononuclear cells circulating in the blood⁵. The incubation period of dengue virus is 3-14 days and after the incubation period clinical symptoms will manifest. World Health Organization has created the criteria to diagnose DHF as follows: fever or history of fever lasting 2–7 days, haemorrhagic phenomenon, thrombocytopenia (platelet count < 100,000), and evidence of plasma leakage due to increased vascular permeability⁶. Laboratory test such as NS1, a specific viral protein secreted by infected cell during the onset of the symptoms throughout the 9th day and a serologic test of IgM dengue after the 3rd day of infection or IgG at the later phase of disease are helpful in diagnosing DHF⁷. Fluid resuscitation and symptomatic drugs remain the mainstay treatment for DHF. Blood products transfusion such as Fresh Frozen Plasma (FFP) is only indicated in patient with massive haemorrhage and low platelet count although no guideline gives a clear threshold for a low platelet count⁸.

Mrs.W case is a unique case of DHF as it was accompanied by diabetes mellitus, cardiomegaly, and an acute pulmonary oedema. We believe that each of these conditions is intertwined. Dengue in elderly patient has an atypical manifestation. The patient present in the emergency department with only fever, body ache, and the laboratory examination did not show a tendency toward dengue. This atypical dengue manifestation is likely cause by age-related decline in immune function, predominantly affecting cell-

mediated and humoral immunity resulting in impaired cytokine response altering disease presentation⁹. Another study shown that bleeding manifestation is also fewer in elderly patient compared to adult patient. This atypical manifestation makes it harder to diagnose dengue since it will not fit the diagnosis criteria base on WHO 2009 guideline. Elderly patients are also at risk at developing severe dengue because (1) impair immune function such as impaired monocyte response to a oxidative stress in dengue infection, (2) increase probability of acquiring secondary dengue due to age, (3) the increase in acquiring chronic disease and other comorbidity such as diabetes mellitus, heart failure, obesity, sarcopenia, etc¹⁰. A study conducted by Singh et al shown that a person with diabetes who contracted DHF will have a higher C-reactive protein (CRP) and Endocan levels. An increase in CRP and endocan could trigger an increase in vascular permeability and thus could worsen the complication of plasma leakage in DHF. Increased blood glucose and poor glycaemic control are also present in diabetes patients with DHF and thus warrant extensive glucose monitoring and intensive glucose control, preferably by insulin injection³.

Pulmonary manifestations such as pleural effusion, acute lung oedema, and pulmonary haemorrhage are rare in DHF. A chest radiograph of DHF patients with pulmonary manifestation usually shows a bilateral pleural effusion and a ground glass opacity is much rarer¹¹. Plasma leakage remains the accepted aetiology of the pulmonary manifestation^{12,11}. This might explain why the patient experience a sudden shortness of breath since DHF patients that is accompanied with diabetes mellitus will be at risk for a more severe plasma leakage due to increase in inflammation. Other possibilities as how could an acute pulmonary oedema occurred in our patient is that it was caused by a combination of heart pump failure and the increased vascular permeability due to DHF and Diabetes. As we mention in the beginning of this report the early physical examination

showed the patient has a bilateral pitting ankle oedema and a chest radiograph of cardiomegaly, these findings are suggestive with a heart failure¹³, however due to limitations in our hospital an echocardiography was not done. The initial fluid treatment of 1500 ml/ day was given because the patient was having an abdominal discomfort that cause poor appetite and fever, both of which put the patient at risk of dehydration. The possibilities of heart failure combined with an DHF and DM likely caused an increased vascular permeability in the pulmonary vasculature and caused fluid to extravasate into the lung interstitial and caused an acute pulmonary oedema¹⁴. Diuretic such as furosemide remains the mainstay of treatment of patient with fluid overload in dengue¹⁵ since it may remove fluid overload and thus preventing ARDS and the need for mechanical ventilation. The administration of diuretics not necessarily warranted the cessation of IV fluid administration, rather it is given at a slower rate and a fluid balance, the measurement of fluid intake and the measurement of fluid output, must be monitored¹⁶.

CONCLUSION

Elderly patient with DHF and with comorbid such as diabetes and cardiovascular diseases are at risk of developing severe DHF complications. Atypical symptoms such as prolonged fever, absent of thrombocytopenia at admission due to decline of immune system warranted an intensive monitoring of clinical, radiology examination, and laboratory examination to diagnose, treat the DHF accordingly and to avoid the complications of DHF. A prompt immunoserology examinations such as NS-1 testing or IgG and IgM dengue are useful in diagnosing DHF early in elderly patient with comorbid. Another important aspect for the best clinical outcome for elderly DHF patient with comorbid disease is that comorbid disease must also be controlled during the treatment course.

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DECLARATIONS

Author contribution. The authors confirm their contribution to the paper as follows: introduction and abstract: 3rd Author, case: 1st. Author; discussion: 2nd author; draft manuscript preparation: 1st. Author. 3rd . Author. All authors reviewed the results and approved the final version of the manuscript.

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