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Literature Review

A PATIENT DENGUE HEMORRHAGIC FEVER WITH SPASMS

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ABSTRACT

Indonesia is one of the countries with the high endemic of Dengue viral infection followed by Thailand, Myanmar, India and Srilanka. For more 10-15 years, Dengue Viral Infection/DHF has become a cause of patient who should be hospitalized and was the first cause of death children in south easthern Asia.[1,2] Batavia was the first city of Indonesia found Dengue Viral infection which had been written in journal by David Bylon in the 1779. Encephalopathy of dengue (ED) is one unusually complication of dengue viral infection which had been characterized by aberration the arrangement of nerves central (CNS). This paper want to describe of a young teenage with suffer from DHF and seizure. Beside it, pleural effusion and cerebral edema had been found. Seizure most likely due to dengue encephalopathy associated with cerebral edema and was supported by positive IgG and IgM anti dengue. Corticosteroid was given to improve cerebral edema. By good management as long as admission, she was discharged from hospital with a good condition.

Key words: dengue viral infection, encephalopathy endemic, pleural effusion, IgM anti dengue test, IgG anti dengue test

ABSTRAK

Tercatat negara-negara endemis tinggi kasus DD/DBD adalah Indonesia diikuti oleh Thailand dan Myanmar, endemis sedang adalah India dan Sri Lanka. Selama lebih 10-15 tahun terakhir, DD/DBD telah menjadi penyebab terbanyak indikasi opname dan menduduki peringkat pertama penyebab kematian anak-anak di Asia tenggara.[1,2] Di Indonesia, demam dengue endemik dilaporkan pertama kali di Batavia oleh David Bylon pada tahun 1779. Ensefalopati dengue (ED) adalah salah satu komplikasi tidak lazim dari infeksi viral dengue yang ditandai dengan kelainan susunan saraf pusat (SSP). Dilaporkan seorang anak remaja dengan DBD tingkat I dan kejang. Bukti yang mendukung kebocoran plasma sebagai ciri dari DBD adalah efusi pleura dan edema logis. Kejang diduga akibat dari demam berdarah ensefalopati berkaitan dengan edema otak dan diperkuat oleh IgG positif dan IgM anti demam berdarah, Kortikosteroid diberikan untuk meningkatkan edema otak. Dengan manajemen yang selama masuk, maka akan keluar dengan keadaan baik.

Kata kunci : infeksi viral dengue, endemik encepalopati, efusi pleura, uji anti dengue IgM, uji anti dengue IgG

INTRODUCTION

Today, dengue viral infection has been the main health problems. An estimated 2.5 billion people than 100 countries at risk exposed infection. Reported a 10 million cases dengue fever and 500,000 dengue hemorrhagic fever was dengue shock syndrome with mortality 5% occurring every year. Indonesia is one of the high endemic countries followed by Thailand and Myanmar, India and Srilanka. For more 10-15 years, dengue fever/dengue hemorrhagic fever has become a cause most indication hospitalized and was the first rank cause of death children in southeastern Asia.[1,2]

Batavia was the first city of Indonesia found Dengue Viral Infection which had been written in journal by David Babylon on 1779. On the next years, on 1968, DHF had been found in Surabaya and followed by other city such as Jakarta, Medan, and so on. In Indonesia adult cases trend to increase, since the 1993-1998 mostly of DHF case (60%) occurring at age group 5-14 years, then in 1997 and 1998 shift to age more than 15 years.[3,4]

Encephalopathy of dengue (ED) is one of unusual complication dengue viral infection which had been characterized by aberration the arrangement of nerves central (CNS). Diagnosis encephalopathy had been identified after marker of diagnosis DHF with accompanied manifestation CNS had been found. Actually ED is a rare but more recently increased every year. At the intensive care child hospital - Ho Chi Minh had reported that rate of occurrence ED about 0.5% of the DHF by mortality of 22%; while at the child devision of RS Cipto Mangunkusumo - Jakarta obtained incident ED of 6.2% of the DHF that had been hospitalized. With encephalopathy, these cases were unusually occurred as a complication of prolonged shock with bleeding, but can also be occurred in DHF not be accompanied by shock.[5,6] This paper would like to show on experience of a doctor which had found a DHF patient with spasms manifestation, and had been predicted as that this one had releated with primer disease, of DHF.

CASE

A patient Nn R, 15 years old, address Balon-Cepu came to IRD RSUD Dr. Soetomo with firstly complain of spasms.

The history of this case as followed: A patient got spasms since in Cepu Hospital or 5 hours before hospitalized. When she showed spasms attach she did not conscious two eyes of her foamed an appearance with hand and feet get stiff, no frothy mouth or bitten tongue, spasms occured about 5 minutes, then the patient conscious, She was bought to Surabaya by ambulance. She showed a clinical manifest of spasms

On the 7th day of fever she showed a better temperature than the days before especially on the first day of fever suddenly showed a high temperature, headache, nausea, painful muscle and joints. The temperature was becoming decrease after get a medicine but the temperature showed increase again especially on the 5th day, then she send to Cepu hospital and was hospitalized for 2 days with diagnoses DHF with low trombosit. There was no nose bleeding, gum bleeding or manifestation of other bleeding. When there was no abnormality of intestine moving. On the last disease history there was no spasms history when the patient had been suffered from DHF in 2 years old and hospitalized in Cepu hospital until recovered and discharged in better health condition.

The physical examination of this case as followed: The patient was in good conscious (GCS 4-5-6) with tension 110/70, pulse 108×/minutes (low), breath 22×/minutes, and temperature 37,4°C. There was no anemia, icteric, cyanosis or dyspneu. Did not found enlargement of the heart, normal heart sound and there is no murmur. Vesikular breath sound, there was no ronchie and wheezing. Move equipment in normal limit with result of Rumpel Leede test showed a positive.

The laboratory examination showed: Laboratory result: Hb 11,6 g%, leukocytes 5.100 l/mm^3, trombosit 83.000/mm^3, PCV 33%, GDA 90 mg/dl, SGOT 87 U/L, BUN 5 mg/dl, SC 0,53 mg/dl, K 3,78 meq/L, Na 145 meq/L. Thorax x-ray showed a minimal right pleura effusion. Result of head CT- scan showed cerebral edema.

The division of the lung xrays showed a minimal right pleura effusion cause DHF process due to extravasasion. Result of neurology division concludedas a focal of secondary generalized seizure which might be caused by metabolic ensefalopaty (anoxiq of the brain can cause cerebral edema).

There for the conclusion of the assesment she suffer from DHF with brain edema. Diagnosis planning showed DL series (total trombosit evaluation), IgM and IgG anti dengue, pleura fluid analisys (if trombosit > 100.000). The treatment had been done by given infus ringer acetat 2000 cc/24 hours, diet TKTP 1900 calori, paracetamol 3 × 500 mg, ranitidine 2 × 1 ampoule, multivitamin 2 × 1 tablet, methylprednisolon injection 3 × 125 mg, and diazepam 1 ampoule dan fenitoin bolus 300 mg if spasms and dosis maintenance 3 × 100 mg.

On the next period, the doctor in charge observed the clinical manifestation as followed: On the second day in Dr. Soetomo hospital there was no fever (in the 8th day) and the complaint of headache was decrease, painful of muscle and joint got better. Nausea and vomit were still exist. There was no manifestation of bleeding and didn't show a spasms. Tension 110/50 mmHg, pulse 92×/minutes, RR 20×/minutes, and temperature 37°C. Examination of head, neck, breast, abdomen, and member's motion in normal limit. Laboratory: Hb 12.2 g%, leukocytes 4.200/mm^3, Diff count - / - / 3 / 55 / 39 / 3 , PCV 35.8% , Trombosit 33.000/mm3, albumin 3.4 mg/dl, total protein 6.2 mg/dl, SGOT 67 U/L, SGPT 72 U/L, and also Ig M and IgG anti dengue showed positive result. Physiologic coagulasion showed that PPT 12,1(C=13,9), KPPT 25,7. Assesment showed DHF with brain edema. Therapy: Infus ringer acetat 2000 cc and HES 500 cc/ 24 hours, methylprednisolon 3 × 125 mg (the 2nd day), Fenitoin maintenance 3 × 100 mg.

On the third day in Dr. Soetomo hospital the clinical manifestation of this case as following: There was no fever found and complaining of chemical manifestation was becoming decrease. There was no spasms and bleeding. Tension 110/70 mmHg, pulse 88×/minutes, RR 20×/minutes, temperature 37°C. Laboratory result showed Hb 12.6 g%, Leukocytes 5.500/mm^3, trombosit 149.000/mm^3, PCV 36.9%, LED 15-30/jam. The assesment showed as a case of DHF with brain edema. The treatment was to continue given methylprednisolon 3 × 125 mg until 3 days and together with other drug

On the fourth day in Dr. Soetomo hospital hospital the clinical manifestation of this case as following: The patient could not defaecates for 3 days, but no fever, bleeding, or spasms. Tension 110/70 mmHg, pulse 64×/mnt, RR 18×/mnt, temperature 36,8°C. Meteorism occured with

normal noisy intestine. Laboratory showed Hb 11,7 g%, luekocytes 10.800/mm^3, trombosit 201.000/mm3, PCV 36.7%. Assesment showed constant and antasida 3 ×1 tablespoon, ranitidine 2 × 1 ampoule, multivitamin 2 ×1 tablet had been given, the condition of care more better.

On the fifth day in Dr. Soetomo hospital the clinical manifestation of this case as following: There was no complain. General condition is good. Stabil sign vital. Hb 12 g%, leukocytes 8.720.000/mm^3, trombosit 317.000/mm^3. Repeated breast x-ray showed no pleura effusion and the patient permitted to go home after the doctor control and the result better health.

DISCUSSION

Dengue viral is infection a single stranded RNA that was the family of flaviviridae and consists of 4 serotipe (den-1, den-2, den-3, den-4).This viral rod-shaped, spatially termolabil, sensitive to inactivasion by dietileter and sodium dioksikolat, stable at a temperature of 70°C. Fourth serotipe the viral has been found on patients in Indonesia where den-3 serotipe is the dominant and has to do with cases heavy when this incredible happenings or outbrench of dengue viral infection.[3,4,6]

The length of the genome of dengue viral about the planning. The virions mature have three protein structure (core, associated membrane, envelope), and 7 (NS1, NS2a, NS2b, NS3, NS4a, NS4b, and NS5). Principal biological function of these viruses associated with the envelope. It said that these proteins to bind with a receptor on a cell host and allowing the past. The envelope this is also related with the hemaglutinasion to erythrocytes, inducing an antibody netralising and who were protective immune response.

Principal of dengue vector in Indonesia is the Aedes aegypti, and Aedes albopictus, aedes albopictus. The nest of vector is found in clearly water and as in the bathtube, drum chicken collectors water, canned the former, etc. The data DHF have been found in every province in indonesia and 200 city has been reported outbreak of Dengue Viral Infection.[6]

There are many clinical spectrum of Dengue Infection forms. The differences of degree severity of clinical manifestation of DHF case it might be due to underlying pathophysiology of disease.[6,7]

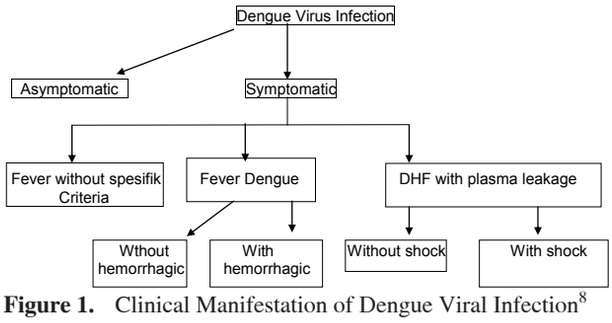

Figure 1. Clinical Manifestation of Dengue Viral Infection[8]

Clinical Criteria:
1. Fever (suddenly high temperature for 2–7 days)
2. Manifestation of bleeding (Tourniquet test which is positive, petekie, purpura, ekimosis, epistaksis, gum bleeding, hematemesis or melena, hematuria)
3. Enlargement of liver
4. Shock, with high pulse and low and decrease tension, hypotension, foot and hand moist skin, with restless case.

Laboratory Criteria
1. Trombocytopenia (total trombosit 100.000/mm^3 or less)
2. Hemoconcentration (decrease hematokrit 20% or more)

The diagnosis of DHF in this case based on the two clinical criteria and supported by thrombocytopenia and hemoconcentration. The presence an effusion of pleura and or hipoalbuminemia can strengthen the diagnosis.[6] DHF diagnosis should be identified by laboratory test of IgM and IgG anti dengue or ELISA method of dengue based on the severity of dengue viral infection.[8]

Table 1. The Severity of Dengue Viral Infection[8]

Grade	Symptoms
Grade I (lighter)	Suddenly fever (2-7 days) Non specific constitunal symptoms Bleeding manifestation on only if positive in tourniquet test
Grade II (medium)	Same as level I Spontan bleeding
Grade III	Circulation failed/sign of early schock (pulse fast and low, tension decrease (20 mmHg or less), hypotension, cyanosis around mouth, skin cold and moist
Grade IV	Shock (tension and pulse can not feel)

This patient showed symptoms of muscular pains and manifestation bleeding form of a positive Rumple Leede, and obtained thrombocytopenia (83.000/mm^3). The right lung of pleural effusion was improving of plasma leakage, so the diagnosed was DHF. It said that besides serotipe and virulence viral; other factors that influence the clinical manifestation DHF was age, sex, immune status and the background host. Guzman *et al* said that a severity hospitalized cases DHF/DSS the highest were found in group of babies and elderly, if these cases got secondary infection due serotipe den-2 it could cause a risk of mortality 15 times in children than adults. DHF had been reported more severity of women malnutrition

Retrospective Research of 152 DHT cases that hospitalized in RSCM-Jakarta. Acquired image clinical most prominent form of hyperpyrexia, change of consciousness and convulsions. Examination laboratory showed, there were increased serum transaminase, hiponatremia and hypoxia. A neurological disorder in form of hemiparese, tetraparese and atrophy nervus the second.[9] This event were followed by Malaysia, reported the manifestation symptoms of weakness instrument motion and decline sensory on either side and bleeding the brain. There were also manifestation neurological form as stiff of the neck and seizure general in children supposedly caused by increased pressure intrakranial. The act of lumbar puncture (LP) have been done to exclusion possibility meningitis or ensephalitis. The result showed the all of the cases recovered perfect and leave no bad symptoms occured.[10]

In Singapore ever reported a sufferers dengue virus infection with a complication CNS disorder with manifestation of amnesia; obtained the result PCR and serologis a positive and results MRI brain disorder showing the hippocampus.[11]

In Thailand reported incidents encephalopathy related DHF about 34 the case of 1.465 cases DHF that hospitalized at the pediatrics RS Petchabun for 3 years (2.3%). Acquired 30 cases fall into encephalopathy during the shock 4 in while in the healing. Factors the risk for the encephalopathy among other: shock conflict, bleeding gastroduodenal that profuse, impaired function severe heart and granting liquid excessive.[12]

In south Vietnam the studies against 378 sufferers suspected infection exposed to the CNS; infection acquired incident CNS just because dengue viral as many as 4.2%. Of the ED the 7 people exposed infection primary and 13 people exposed secondary infection. Acquired isolation virus (PCR positive) on 10 sufferers while 3 patients of indicates the presence of antibodies in liquid his mind. Manifestation main CNS disorder of patients was in form of impairment of consciousness and convulsions.[13]

Research of case-control and prospective study on the intensive pediatrics hospital in Ho Chi Minh showed that the patients ED got an increase a liver enzyme and bilirubin with a significant result and one case produce PCR-RNA virus DEN-3 from a liquid the brain, 14 cases showed a positive result of IgM anti DHF and the majority MRI showed edema of the brain.[5]

Patient with manifestation CNS disorder in form of spasm. She does not obtain bleeding gastroduodenal, disorder electrolyte, shock and granting liquid glasses. Results CT-scan of head showed an barin edema.

Immunopathogenesis DHF and DSS still controversial. The first theory which was professed was hypothesis secondary of heterologous infection or antibody-dependent enhancement.[14] It said that if someone sinus infection for the second time with divergent (heterologous) serotipe dengue viral, it will happen cross reaction between antibodies serotipe viral from infection with the viral formerly without neutralization through the process so that the viral could enter the monocytes. The number of monocytes and t-cell infected was increase, it was describing increasing of antigens, frequency dengue viral - t cells and activation and proliferation t memory. T cells also produces sitokins as IFN-γ, IL-2 dan TNFα and also lysis of monocytes that infected dengue viral. The complement will be enabled by complex antigen-antibody by sitokins so that the discharge occurs c3a and c5a, which directly affect the permeability vascular. The synergistic effect of IFN-γ, TNF-α and complement who switched to would cause the occurrence of plasma leakage from the endothelial cells.[6,7,15]

Dengue hemorrhagic fever can be stimulated a transcription and to secretions RANTES and IL-8, the establishment of an antibody hemorrhagic fever and the establishment of the complement non-lysis complex. Dengue viral infection in endothelial cells in vitro can cause the occurrence of pothogenesis. It has been said that the complement, who switched to chemokin and mediate apoptosis causing the occurrence of leakage plasma membrane.[16]

A second hypothesis that the dengue virus could change genetic as resulting from pressure during a replication of the viral in human body and mosquitoes. A phenotype in a genome is a replication of the viral and could cause the viremia, increase and it is potential to cause virulence of the plague. It says that there the manifestations, and the DSS is probably caused by a variant of dengue viral that has a different degree virulence. The epidemic in southeast Asia support this hypothesis. It was reported that the risks may - in Thailand DSS regarding the DEN-2. Philippine DEN-3 role in the outbreak in Indonesia den-3 a type virus existing related with severe cases presently occurring outbrench of dengue virus infection.[6,15]

Typical patofisiologi of dengue fever is the leakage of plasma and disorder hemostasis. The data prove the existence of a leak plasma namely the increase in the hematokrit, an effusion of the pleural and ascites, hipoproteinemia and decrease in volume plasma. Lost plasma that weight can cause the occurrence of shock hypovolemia and death. Hemostasis an abnormality that occurs because by 3 the main factor of change namely: vascular, thrombocytopenia, and coagulopati. Dissaminated intravascular coagulation (DIC) can happen and cause bleeding great.[7,17]

Pathogenesis the occurrence of encephalopathy hemorrhagic fever was still not clear. Some research in Indonesia Thailand and other Asian countries get that an abnormality of the CNS occurs in DHF prolonged with or without the occurrence of shock. The hemorrhage brain is not caused directly by a virus that may be pierced Blood Brain Barrier (BBB). Gathered evidence in the form of the virus den-3 isolation from a liquid the brain on 4 cases, from 6 the remaining positive result PCR.[18]

Imbert et al, 1994. stated that dengue viral which have the ability to infect broad neurons mice in vitro, viruses like has a specific receptor on the surface of neurons.[19] Chaturvedi et al found BBB damaged during infection dengue (den-2) so happen leakage protein to the brain.

Gubler et al suspected the genetic variation or due to changes in biological virus and also strains some viral.[18]

Lum LC et al, 1996 reported that many factors who caused the encephalopathy among other: impaired function heart, disorder electrolyte, edema cerebri (caused by changes permeability vascular so extravasation a liquid); hipoperfusi (resulting from disruption circulation) and encephalitis week.[20] In some patients encephalitis this obtained isolation virus from a liquid the brain.[21]

Abnormality CNS on DF/DHF formerly thought due to nodular that causes penetrated BBB. The cognitive deficit is more because encephalopathy than encephalitis. Although the MRI by contrast show bbb who was whole, but partly expert confident that encephalitis caused by invasion virus directly to the brain through BBB, while other writers postulates that due to the occurrence of encephalitis process imunopatologis.[11]

Due to an immune response that rises rapidly, difficult to get the isolation virus den a positive on blood sufferers. All the case indicating the presence of antibodies with titer high when examined. So clinical manifestation sufferers and the levels hi antibodies against flavivius, IgM anti dengue a positive and neutralization a positive test had been considered that the virus as a cause.[21]Based on patient who was 2 years old had gotten DHF, so it was really possible as the secondary heterologous infection. The ultimate principle management DBD aims to replace the liquid plasma during a period of leakage active in 24-48 the first hour because at that period would cause the occurrence of shock, anoxia, acidosis, and death. Antipyretic can be given during phase of heat, avoid the use of aspirin. The critical period happen when a transition from phase of heat into free heat that can be started on the third day. A liquid used as a substitute for plasma shall spatially isotonic having the content of the electrolyte similar to plasma.[3,6,17]

On ED consciousness patient decreased to become on somnolen, it could accompanied by seizure. ED can happen to DBD/SSD. When patients shock,it will be found impairment of consciousness, and to ensure the ED shock to be overcome first. The act of lumbar punction (LP) done when shock has handled awareness but still declining (careful when platelets <50,000). On ED could be found elevated levels of transaminase (SGOT/SGPT), PPT & KPTT elongated, their blood sugar decline alkalosis on analysis gas blood, and hiponatremia.[6]

ED is one of complication DHF, its treatment more complicated. Several points that should undertaken in management ED[3]:

1. Replacement no liquid given in doses full, but fairly given 4/3 to 4 5/dose to prevent or make it worse edema brain during phase recovery shock
2. Wearing a liquid crystalloids ringer acetic to avoid metabolism lactate in liver, when accompanied by impaired liver
3. A corticosteroid administered to reduce edema the brain, but is contra indication on DSS with hemorrhage massive.

On encephalopathy likely edema the brain and alkalosis, therefore when shock has handled, liquid replaced with a liquid containing no hco3- and the amount of fluid must be reduced. Prevent increased pressure an extern cranial by reducing the amount of fluid (when necessary with a diuretic), correction asidois and disorders electrolytes. Try not giving drugs that not needed to reduce the burden detoxification medicine in heart. Transfusion of blood fresh or components can be given over indications proper.[6]

Main therapy with this replacement liquid to crystalloid and had given colloidal. Ringer acetat was chosen because obtained increase transaminase, given 2 quarts in and colloidal (HES) 500 cc within 24 hours. methyl prednisolon 3 × 125 mg was given for 3 days, associated with edema cerebri. There was no shock; disorder diuresis, disorder electrolyte and lengthening faal hemostasis.

A patient DBD could be discharged after to meet the criteria of clinical improvement, no fever for 24 hours), (without antipyretic cannot be found distress the breath (because effusion of the pleura or acidosis), hematocrit stable, the number of platelets tending to rise (> 50.000), three days after shock handled, and has been improving appetite.[6] The patient was discharged after fulfill the criteria of those mentioned above. When a repeat photograph thoracic legs already does not obtain again an image of an effusion of plura.

SUMMARY

It has been reported a young teenage with DHF followed by seizure. Evidences that supporting plasma leakage as hallmark of DHF are pleural effusion and cerebral edema. Seizure most likely due to dengue encephalopathy associated with cerebral edema and strengthen by positive IgG and IgM anti dengue. Corticosteroid was given to improve cerebral edema. By good management as long as admission, she was discharged from hospital with good condition.

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