A PATIENT DENGUE HEMORRHAGIC FEVER WITH SPASMS

Ulfa Kholil1, Nasronudin1,2
1 Tropical and Infectious Disease Division - Department of Internal Medicine, Dr. Soetomo General Hospital - Faculty of Medicine Universitas Airlangga, Surabaya, Indonesia.  2 Institute of Tropical Disease, Universitas Airlangga, Surabaya, Indonesia

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 southern 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

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 southern Asia.1,2

Batavia was the first city of Indonesia found Dengue Viral Infection which had been written in journal by David Bylon 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. 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 foam 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.

The physical examination of this case as followed: The patient was in good conscious (GCS 4-5-6) with tension 110/70, pulse 88×/minutes, temperature 36,8°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/mm³, trombosit 83.000/mm³, 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 laboratory examination showed: Laboratory result: Hb 11,6 g%, leukocytes 5.100 l/mm³, trombosit 83.000/mm³, 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 x-rays showed a minimal right pleura effusion cause DHF process due to extravasasion. Result of neurology division concluded a focal of secondary generalized seizure which might be caused by metabolic encephalopy (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 ampule, multivitamin 2 × 1 tablet, methylprednisilon injection 3 × 125 mg, and diazepam 1 ampule dan fentoin bolus 300 mg if spasms and dose 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 vomite 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/mm³, Diff count -1 -1 /35 /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. Assessment 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/mm³, trombosit 149.000/mm³, PCV 36.9%, LED 15-30/jam. The assessment 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 occurred with
normal noisy intestine. Laboratory showed Hb 11.7 g%, leukocytes 10.800/mm³, trombosit 201.000/mm³, PCV 36.7%. Assessment showed constant and antasida 3 × 1 tablet, 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/mm³, trombosit 317.000/mm³. 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 serotype (den-1, den-2, den-3, den-4). This viral rod-shaped, spatially termolabil, sensitive to inactivasion by dietileter and sodium dioksisoklat, stable at a temperature of 70°C. Fourth serotype the viral has been found on patients in Indonesia where den-3 serotype is the dominant and has to do with cases heavy when this incredible happenings or outbreak 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 neutralising 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 bathtub, drum chicken collects water, canned the former, etc. The data DHF have been found in every province in Indonesia where den-3 serotype is the dominant and has to do with cases heavy when this incredible happenings or outbreak of dengue viral infection.3,4,6

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

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/mm³ 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 hypoalbuminemia 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.5

| Grade   | Symptoms                                                                 |
|---------|--------------------------------------------------------------------------|
| Grade I | Suddenly fever (2-7 days)                                               |
| (lighter) | Non specific constitutional symptoms                                     |
| Grade II | Same as level I                                                          |
| (medium) | Spontan bleeding                                                         |
| Grade III | Circulation failed/sign of early shocK                                    |
| (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/mm³). The right lung of pleural effusion was improving of plasma leakage, so the diagnosed was DHF. It said that besides serotype 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 serotype 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, hiperatremia and hypoxia. A neurological disorder in form of hemiparese, tetraparese and atrophy nerve the second. 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 occurred.

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.

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.

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.

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.

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 confessed was hypothesis secondary of heterologous infection or antibody-dependent enhancement. It said that if someone sinus infection for the second time with divergent (heterologous) serotype dengue viral, it will happen cross reaction between antibodies serotype 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.

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 pathogenesis. It has been said that the complement, who switched to chemokin and mediate apoptosis causing the occurrence of leakage plasma membrane.

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.

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 coagulopatia. Dissiminated intravascular coagulation (DIC) can happen and cause bleeding great.

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.

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. Chaturvedi et al found BBB damaged during infection dengue ( den-2 ) so happen leakage protein to the brain.
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 asidosis 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.5 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.

REFERENCES

1. WHO (1996). Management of Dengue Epidemic. Report of Technical Meeting, SEARO, New Delhi, November 26–30th pp. 1–40.
2. WHO (1999). Guidelines for treatment of Dengue Fever / Dengue Hemorrhagic Fever in small hospital. WHO Regional Office for South-East Asia.
3. Soewandojo E., (2002). Tata Laksana Demam Berdarah Dengue pada orang dewasa, Seri Penyakit Tropik Infeksi, Pustaka Pelajar, hlm 417–426.
4. Hendrarwanto (1996). Dengue. Buku Ajar Ilmu Penyakit Dalam Jilid 1, edisi ketiga. Ketua editor: Sjaefolli Noer. Baiti Penerbit FKUI-Jakarta, hlm 417–426.
5. Cam BV, L Fonsmark, NB Hue, Phuong NT, A Poulsen, ED Heegard (2001). Prospective Case-Control Study of Encephalopathy in Children with Dengue Hemorrhagic Fever, Am J Trop Med Hyg, 65 (6), pp 848-851
6. Departemen Kesehatan Republik Indonesia (2004). Direktorat Jendral Pemberantasan Penyakit Menular dan Penyeihanat Lingkungan, Tata laksana Demam Berdarah Dengue di Indonesia. 2004
7. Gubler DJ (1998). Dengue and Dengue Hemorrhagic Fever. Clinical Microbiology Reviews, July, vol 11; 3 : pp 480-496
8. WHO (1997). Dengue Hemorrhagic Fever Diagnosis, Treatment Prevention, and Control. WHO, 2nd edition
9. Hendarto SK., Hadinegoro (1992). Dengue Encephalopathy, Acta Paediatr Jpn. Jun;34 (3): pp 350-357
10. George Rabeca (1992). Current Status of the Knowledge of Dengue/ DHF/DSS in Malaysia: Clinical Aspect. 5th Annual Convention of Philippine Society for Microbiology and Infectious Disease. November 28-30
11. Yeo PSD, L Pinheiro, P Tong, P L Liem, YY Sitoh (2005). Hippocampal Involvement in Dengue Fever, Singapore Med J 46 (11), pp 647-650
12. Prasonk Witayathawormwong (2004). Dengue Hemorrhagic Fever Encephalopathy/ Fatality at Petchabun Hospital: A Three-year Prospective Study (1999-2002), Dengue Bulletin Volume 28, Chapter 10.
13. Solomon T., Nguyen Minh Dung, David W Vaughan, Rachel Kneen, Le Thi Thu Thao, Boonyos R, et al (2000). Neurological Manifestation of Dengue Infection. The LANCET, 355, March 25th, pp 1053-1059
14. Supriatna, M., Setiati, T.T., Mairuhu, A.T., Koraka, P., M.R. Mac Gillavry, D.P. Brandjes, A.D. Osterhaus, J., van der Meer, E.C. van Gorp, A. Soemantri. 2007. Dengue disease severity in Indonesian children: an evaluation of the World Health Organization classification system. BMC Infect. Dis. 7:22.
15. Lei Huan-Yao, Trai-Ming Yeh, Hsio-Sheng Liu et al (2001). Immunopathogenesis of Dengue Virus Infection, J Biomed Sci 8, pp 377-388
16. Avirutnan P., Prida Malasit, Barbara Seliger, Sucharit Bhakdi and Husmann M (1998). Dengue Virus Infection of Human Endothelial cells leads to Chemokine Production, Complement Activation, and Apoptosis. Immunology, 161 : pp 6338-6346
17. Nimmannitya S., (2003). Dengue and Dengue Hemorrhagic Fever. Manson’s Tropical Disease, 21st edition, Editors: Gordon Cook and Alimuddin Zumla, ELST with Saunders, pp 765-772
18. Vasconcelos, Travassos, Coelho, et al (1998). Involvement of the Central Nervous System in Dengue Fever: Three serologically confirmed cases from Fortaleza, Ceara, Brazil, Rev. Inst. Med. Trop. S. Paulo, vol 40
19. Imbert, J.L., Guevara, P., Castaneda, J.R., Sotelo, J. Dengue Viral Infects Mouse Culture Neurons But Not Astrocytes. J. Med. Virol., 42: 28-233, 1994.
20. Lum L.C., Lam S.K., Choy Y.S., et al. Dengue Encephalitis: a True Entity? Am J Trop Med Hyg 1996. 54: 256-59.
21. Malavige GN, Fernando S, Fernando DJ and SL Seneviratne (2004). Dengue Viral Infection. Postgraduate Medical Journal ; Oct; 80 (948): pp 588-601