Dengue Hemorrhagic Fever in adolescents and young adults in the Department of Internal Medicine, Gadjah Mada University Hospital in Yogyakarta

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INTRODUCTION

Dengue fever, a well known disease in the tropical and sub-tropical parts of the world, was first described by David Beyle, a municipality surgeon in Batavia, in 1779 (Kouwenaar, 1951). A year later Benjamin Rush gave its well known colloquial name "break bone fever" (Nelson, 1964). It also has other names as five-day fever or van der Noer's fever or seven-day fever (Kouwenaar, 1951).

Hemorrhagic fever was first reported by Quinton et al. (1954), in Manila. Johnson (1954) established the causative relation of Dengue infection to Dengue hemorrhagic fever (Halstead, 1965).

The disease is caused by dengue virus, of which there are at least four, probably six types as well as chikungunya virus. Dengue Virus type 2, 3, 4, and 6, and 4 were isolated from sera of patients of Philippine H.F.; dengue virus type 1, 2, 3, 4, 5, 6, and chikungunya virus were found in Thai H.F.; and type 1, 2, 3, and 4, in Singapore H.F. (Gajdusek, 1962; Dannayya et al. 1963; Halstead, 1966).

I. Dengue virus 1, 2, 3, 4, (5, 6) = Arbovirus group B.

II. Chikungunya virus = Arbovirus group A.

Stated Sejdić et al. (1951), Dengue et al. and Merisi et al. (Kouwenaar, 1951) that Aedes aegypti and Aedes albopictus were the vectors of this disease. Vectors of importance are also Aedes polynesiensis and probably members of the Aedes scolopasis complex (WHO, 1963).

Clinically, dengue and chikungunya virus manifest itself as:

I. UNDIFFERENTIATED FEVER

This is a very mild febrile illness, frequently considered to be of respiratory origin.
II. DENGUE FEVER SYNDROME.
This includes febrile disease characterized by myalgia, arthralgia and lymphopenia, with or without rash or lymphadenopathy, but including under the following biphasic fever, severe headache, pain on moving the eyes, positive tourniquet test and a few spontaneous petechiae.

III. HEMORRHAGIC FEVER.
A. Without shock.
This includes fever, usually without prominent myalgia or arthralgia, usually becoming more severe after the first two days, positive tourniquet test, leukopenia or rash present or absent, but usually with several of all of the following: apathy, hematomas, melena, thrombocytopenia, prolonged bleeding time, elevated prothrombin time, and maturation arrest of megakaryocytes.

B. Without shock.
The pulse pressure is 20 mm Hg or less, or systolic and diastolic pressures unobtainable, with collapse of the patient. Shock may occur without the hemorrhagic manifestation described above, but with most of the following associated with serious disturbance of the hemostatic mechanism as essential criteria: hemorrhagic fever has been diagnosed; positive tourniquet test, thrombocytopenia, prolonged bleeding time and maturation arrest of megakaryocytes.

For all of the above categories, the etiology should be stated when known, or stated as unknown. (WHO, 1969)

Dengue Hemorrhagic Fever (DHF) is thought to represent a hyper紧张ity to a second or succeeding infection with dengue virus. For immune foreign adults as well as children, exposed to dengue virus during an outbreak of hemorrhagic fever have classic dengue fever or even a milder disease.

This disorder is almost exclusively a disease of children. Somchit Iarrera and (1960) found 5 cases of DHF in Thailand (Bangkok): 4 from June 1960 to June 1964, their ages ranging from 15 to 22 years; 2 were of Thai and one case of Chinese origin.

CASE REPORTS

Case 1. A 13 years old boy, Indonesian, was examined at the "AURI-Maguwo polyclinic on March 23, 1970 and consulted to the Department of Internal Medicine, Gadjah Mada University at Yogyakarta, because of 2 days fever, anaphylaxis, abdominal pain, anorexia and vomiting, diarrhea, melena and petechiae. Body temperature was 40.5°C, pulse 120/min., regular and equal. Blood pressure (BP): 10/40 Hg; positive tourniquet test; liver not palpable. Lab. exam.: Hgb., 12.2 g%, WBC 5000 EIR 6/15, diff. count: eos 9, stab., segs. 64, lymph. 27; very few platelets on slide. Slight proteinuria with leukocyturia and hematuria. Patient recovered and discharged on the 11th day after admission.

Diagnosis: Hemorrhagic Fever without shock (Dengue?). No serological test done.
Case 2. Patient was a 14 years old boy, P., Indonesian, admitted to Kalijodo Hospital in Saja on May 27, 1970 and consulted to the Department of Internal Medicine, Gadjah Mada University Hospital, Peguran Yogjakarta, because of 7 days fever and cephalgia, anorexia, nausea, vomiting, diarrhea, melaena, petechiae and ecchymoses, skin rash, glycalia and arthralgia. Bleeding on lips and gums. Patient was in a state of shock with positive tourniquet test, liver was palpable 2 fingers below the costal margin. Lab. exam: Hgb 3 g/l WBC 5200 with 25% of lymphocytes. Thrombocytes 28.000-64.000. Bleeding time longer than 90 min., clotting time was normal. 

Widal: negative. Hemagglutination Inhibition test: 

D 1 1/20 — 1/40

JBE 1/20 — 1/80.

Patient died on the 38th day after admission. 

Diagnosis: Dengue Hemorrhagic Fever with shock. 

Sequellatively proved.

Case 3. Patient was an 10 years old boy, K., Indonesian, admitted to the Department of Internal Medicine, Gadjah Mada University Hospital Peguran, Yogjakarta, on June 12, 1970, because of 4 days fever, retroorbital cephalgia, glycalia, arthralgia, anorexia, nausea, vomiting, melaena, skin rash, petechiae, ecchymoses, bleeding on lips and gums. Body temperature was 38.5° C, pulse 90/min. which was regular and equal. BP. 100/75 mg., liver not palpable and a positive tourniquet test. Lab. exam: Hgb. 12 g/l Hct. 44%, WBC 6000 with 42% of lymphocytes. Thrombocytes 100,000, prolonged bleeding time and prothrombina time was 56%.

Hct test: D 1 1/5,190 — 1/20,460

JBE 1/10,240 — 1/100,480

Diagnosis: Dengue Hemorrhagic Fever without shock.

Sequellatively proved.

Case 4. S. was a 13 years old girl, Indonesian, admitted to the Department of Internal Medicine, Gadjah Mada University Hospital, Peguran, Yogjakarta, on January 29, 1971 because of fever for 10 days, anorexia, nausea, vomiting, diarrhea, petechiae and ecchymoses. Liver was palpable and patient was in a state of shock. Lab. exam: Hgb: 10 g/l WBC 10-500 with 23% lymphocytes. Widal: negative. Bone marrow revealed an increased number of megakaryocytes 10 per low power field with synchronism between cytoplasm and nucleus, with a few plasmic around. 

Diagnosis: Hemorrhagic Fever with shock (Dengue). 

No icterological test done.

Case 5. Patient was a 25 years old female, B., Indonesian, was admitted to Kalijodo Hospital in Saja on February 5, 1971 and consulted to the Department of Internal Medicine, Gadjah Mada University Hospital, 

and discharged.
because of fever, headache, anorexia, nausea, achalasia, bone pain, some bloody vomiting and melena, petechiae, ecchymosis. Liver was not palpable and BF was normal.

H.I. test: $D_1$ 1/40

JBE 1/120

Diagnosis: Dengue Hemorrhagic Fever without shock.

Serosogically proved.

Case 6. A 22 years old male student, B.P., Indonesian, was examined at the outpatient department of the Department of Internal Medicine, Gadjah Mada University Hospital, Yogyakarta, on March 8, 1979, because of 2 weeks fever, epigastric and abdominal pain, anorexia, nausea, myalgia, arthralgia, petechiae, ecchymoses, skin rash. Liver was palpable and a normal BP and negative tourniquet test.

Lab exam.: Hgb. 13 gr%, WBC 4700 with diff. count: eos 1, stab. 2, segm 84, lymph. 12 and mono. 1%. Thrombocyte 150,000, prothrombin time 85.5%, normal bleeding time, clotting time 3 min. 17 seconds.

Bone marrow revealed an increased number of megakaryocytes 10 per low power field, with medium-cyttoplasmic dyserythropoiesis and a few platelets around.

H.I. test: $D_1$ 1/0.240

JBE 1/5.120

Diagnosis: Dengue Hemorrhagic Fever without shock.

Serosogically proved.

Besides these patients, there were another two patients aged 12 yrs, diagnosed as DHR admitted on February 7 and 11, 1979; no serological test were done on these two patients.

DISCUSSION.

The chief complaints of the 9 patients reported by Soemirti (1976) were fever (100%), petechial hemorrhage (70%) and headache (60%). Bone marrow study in 4 of his cases showed an increased number of megakaryocytes 10 or more per low power field, while other hematopoietic cells were normal in cellularity.

Dyserythropoiesis between cytoplasms and nuclei of megakaryocytes, with no or a few platelets around was found by other authors. Chromatocytes histiocytocytes phagocytizing leukocytes and or erythrocytes were reported to be significant.

Nelson et al. (1966, 1964 and 1966) found 5 characteristic phases with different pictures in the bone marrow in Dengue virus infection: the early phase (days 1-4) with hypopcellularity and almost absent megakaryocytes; while Suga Na-Nakoy (1966) found in this phase normal number megakaryocytes with younger forms in zone in all of their cases. The recovery phase (days
5–6) with hypercellularity and increased number of megakaryocytes, 10–20 per low power field with dysynchronism between cytoplasts and nucleoli and a few platelets around. Clasmatocytes, phagocytizing leucocytes and erythrocytes were also reported. The convalescence phase (after 10 days) is normocellular.

Without the relative lack of case in adults in most countries is related to immunity or age-related factors is not known. Two theories were offered to explain the pathogenesis of DHF, the disease was thought to be due to 1), virulence factors of the virus and 2), an unusual reaction in the host. Some type of hypersensitivity reaction induced by prior dengue virus infection in a host with possible inherited factors and/or nutritional state was thought to be present.

Our own cases represent DHF in adolescent and young adults of Indonesian origin, their ages ranging from 15 to 25 years, a total of 6 patients, 4 males and 2 females. 4 cases serologically proved and 2 cases clinically diagnosed. One case had a fatal end. Besides these another two cases aged 12 yrs, one male and one female were diagnosed as DHF clinically.

The bone marrow findings are in accordance with those found in the literature. The marked increased number of megakaryocytes, is significant. Clasmatocytes, phagocytizing leucocytes and erythrocytes, and megakaryocytes showing dysynchronism between cytoplasts and nucleoli are important findings in DHF.

Summary.

A short history of Dengue, the etiology of Dengue Hemorrhagic Fever and the vectors are reviewed. A classification and nomenclature for diseases suspected to be of dengue or chikungunya virus etiology, as suggested by WHO is given.

Six cases and two additional cases of Dengue Hemorrhagic Fever in adolescents and young adults are reported.

The bone marrow findings in our cases compared with those found in the literature.

The pathogenesis of Dengue Hemorrhagic Fever is reviewed in short.

Bibliography:


