Dengue Infection with Unusual Manifestations: A Case Report

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Abstract

Since 1978, there has been an increasing number of reported cases of dengue infection with unusual manifestations and most of them had dengue shock syndrome. We report here one patient who had dengue hemorrhagic fever grade II with liver failure and hepatic encephalopathy and very high elevation of liver enzymes. She made a complete recovery after conservative therapy. She is the fourth case of reported dengue hemorrhagic fever grade II who had unusual manifestation.

Key word : Dengue Hemorrhagic Fever, Unusual Manifestations, Liver Failure

SIRIVICHAYAKUL C, et al
J Med Assoc Thai 2000; 83: 325-329

Dengue infection is a principal mosquito borne viral infection and is one of the major public health problems in Southeast Asia primarily in children. The dengue virus may cause asymptomatic infection, undifferentiated fever, dengue fever (DF), or dengue hemorrhagic fever (DHF)[1].

In general, vital organs are not primarily involved in dengue infection. Signs and symptoms of vital organ involvement are usually secondary to shock and hemorrhage. However, since 1978, there have been many reported cases of dengue infection with unusual manifestations, most of which had central nervous system involvement and/or hepatic involvement and they had a very high case mortality when compared to the average case mortality rate in dengue shock syndrome, DHF and DF which were only 7.6 per cent, 0.2 per cent and 0.04 per cent respectively (data in Thai patients from 1989 to 1998 according to the Ministry of Public Health). Early recognition and appropriate management of dengue infection with unusual manifestations may be important in reducing the case mortality rate. We report here a patient who had DHF grade II with liver failure and hepatic encephalopathy and very high levels of liver enzymes.

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CASE REPORT

A 12-year-old Thai girl from an orphanage in Bangkok came to the Hospital for Tropical Diseases on October 27th, 1997, with chief complaints of fever, nausea and vomiting for three days. Physical examination revealed a slightly ill girl with only mild injected pharynx and tonsils. Her body weight was 33 kilograms and there was no other abnormal finding. Due to a concurrent outbreak of DHF in the orphanage, the patient was admitted because DHF was highly suspected. On the 2nd day of admission (4th day of illness), she still had a high fever, vomiting, and began to have thrombocytopenia. Maintenance intravenous fluid was started because she had frequent vomiting and could not eat or drink. The illness continued through the 3rd and 4th days of admission with uneventful events. The only changes in these two days were enlarged liver and decreased platelet count (Table 1).

On the 5th day of admission, in addition to fever, anorexia, nausea, and vomiting, the patient became drowsy and was sometimes confused (hepatic encephalopathy grade II according to Rogers and Rogers)[2] but there were no symptoms or signs of shock. Jaundice and dark urine were additional signs. Laboratory investigations are shown in Table 1. Coagulogram revealed slight prolonged prothrombin time and partial thromboplastin time (about 2 times the normal values). Urinalysis was normal except for the presence of bile in the urine. Blood ammonia and G6-PD level was not measured. The patient was diagnosed as having DHF grade II with acute hepatic failure and hepatic encephalopathy. She was treated symptomatically with intravenous crystalloid fluid and glucose, vitamin K, restricted dietary protein, and oral sucralfate to pre-vent gastrointestinal hemorrhage.

On the 6th day of admission, the patient vomited a small amount of coffee ground vomitus and passed one melenic stool. Her vital signs were still stable but hematocrit dropped to 26 per cent. Two units of packed red blood cells and one unit of fresh frozen plasma were transfused. Other clinical findings did not significantly differ from the previous day as well as on the 7th to 9th day except returning of coagulogram to normal value and increasing of platelet count to more than 100000/ mm^3 on the 7th day. The patient began to regain consciousness and appetite on the 10th day of admission. Her liver function gradually returned to normal within one month. She was discharged with complete recovery.

Table 1. Clinical and laboratory findings in the patient according to date of admission.

Clinical & laboratory findings	Date of admission							
	1	2	3	4	5	6	7	8
Body temperature (°C) (highest/lowest)	40.2/37.8	39.0/37.8	38.5/37.0	37.8/37.0	38.0/36.9	38.3/37.0	38.0/37.0	37.8/36.7
Blood pressure (mmHg)	110/70	110/60	100/60	100/60	100/60	110/60	110/70	110/80
Consciousness*	normal	normal	normal	normal	grade II	grade II	grade II	grade II
Liver size**	0	0	3	3	4	4	4	3
Hematocrit (%)	38	39	38	40	34	26	30***	33
Platelet count (x10^9/l)	103	81	45	45	54	65	114	125
Direct bilirubin (mg/dl)	-	-	-	-	3.1	5.8	13.2	14.2
Indirect bilirubin (mg/dl)	-	-	-	-	8.2	7.9	13.8	10.9
AST (u/l)	-	-	-	-	16340	13340	2770	700
ALT (u/l)	-	-	-	-	10780	9460	5420	2525
Cholesterol (mg/dl)	-	-	-	-	45	-	57	70
Albumin (g/dl)	-	-	-	-	3.3	2.9	3.3	2.5
Blood urea nitrogen (mg/dl)	-	-	-	-	8.8	11.2	13.4	14.0
Creatinine (mg/dl)	-	-	-	-	0.6	0.6	0.4	0.2

AST = serum aspartate aminotransferase
ALT = serum alanine aminotransferase
* = grading according to Rogers and Rogers[2]
** = centimeter below right costal margin
*** = after blood transfusion

The diagnosis of secondary dengue infection was confirmed serologically by enzyme linked immunosorbent assay[3] which showed undetectable antibody to dengue virus on the first day of admission but 71 units of IgM and 185 units of IgG seven days later. Other possible infections, including hepatitis A and B, leptospirosis, enteric fever and scrub typhus were excluded by serological tests. Hepatic failure due to drug toxicity was unlikely because only acetaminophen and domperidone in therapeutic doses were given dose by dose to the patient by nurses since the beginning of illness.

DISCUSSION

Since 1978, there have been 51 cases of clinically and serologically confirmed dengue infection with unusual manifestations reported in nine reports[4-12]. These may be only a tip of the iceberg since many cases were not reported or had inadequate data[13-16]. Among 51 reported cases, thirty-six cases were reported from Thailand, nine cases from Malaysia, four cases from Indonesia, one case from Jamaica and one case from Puerto Rico. There were 24(47.1%) males and 27(52.9%) females, their age ranged from 2-months to 51 years old, 37 cases (72.5%) were less than 8 years old and only 3 adults were reported (18, 21 and 51 years old from Malaysia, Jamaica and Puerto Rico respectively). Thirty-nine cases (76.5%) were diagnosed as DHF and only 12 cases were diagnosed as DF. Among the DHF cases, 15 cases (38.5%) were grade IV, 21 cases (53.8%) were grade III, and only three cases (7.7%) were grade II DHF. Significant unusual manifestations are summarized in Table 2. Nineteen out of 51 cases died (37.3%). Patients who had convulsions seemed to have a higher mortality (Table 3) and patients with DHF grade IV had markedly higher mortality than those with DHF grade II and III (Table 4), but grading of consciousness[2] did not seem to correlate with mortality. Exchange transfusion was performed in three cases and all survived. Autopsy was done in 12 out of 19 cases (63.2%) who died and disclosed liver damage in all cases which ranged from fatty change, centrolobular degeneration, focal hemorrhage, focal necrosis, to severe necrosis. However, in three surviving cases in whom liver biopsy was done, fatty change was the only finding in all cases.

Hepatic abnormality is believed to be mainly caused by ischemia because almost all of the patients had shock before hepatic manifestations occurred[17]. Moreover, three of the reviewed cases who had DF and elevation of liver enzyme had unusual hemorrhage which could cause ischemia and finally liver damage. The pathologic findings of coagulative necrosis of the liver also suggested ischemia as the cause of hepatic abnormality[18]. However, two of the reviewed cases who had DHF grade II had liver failure. Although one case had underlying thalassemia, the other had no underlying abnormality. This data in addition to detectable dengue antigen in hepatocyte[19] suggests that the dengue virus may have a direct effect on liver cells. Drugs toxicity, especially acetaminophen, can also be a cause of hepatic failure but there was no firm evidence[20]. Our reported case had DHF grade II

Table 2. Reported unusual manifestations in dengue infection.

Unusual manifestations	No. of cases/total cases reported			
	DF	%	DHF	%
Jaundice	0/12	0	15/39	38.5
Elevation of liver enzyme	4/5	80	13/13	100
Reye's syndrome	1/12	8.3	4/39	10.26
Convulsion	6/12	50	13/39	33.3
Alteration of consciousness	10/12	83.3	32/39	82.1
Spasticity	2/12	16.7	2/39	5.1

Table 3. Comparison of mortality in patients with and without convulsion.

	Survived	Died	Mortality (%)
Had convulsion	8	11	57.9
No convulsion	24	8	25

Table 4. Comparison of mortality among patients who had DF and different grading of DHF with unusual clinical manifestations.

	DF	DHF grade II	DHF grade III	DHF grade IV	Total
Total	12	3	21	15	51
Died	4	0	6	9	19
Survived	8	3	15	6	32
Case mortality rate (%)	33.3	0	28.6	60	37.3

and liver failure with the highest elevation of liver enzymes among cases ever reported. Her liver damage can not be explained by circulatory failure, so, it supports that ischemia may not be the sole cause of liver damage.

The central nervous system may be involved by multiple factors. Hepatic encephalopathy is the most commonly mentioned cause because many cases had concurrence of hepatic and neurologic manifestations. The findings that many patients who survived encephalopathy had complete recovery and most patients had normal cerebrospinal fluid findings suggest that the encephalopathy is only a functional change. Reye's or Reye-like syndrome[21] is also an important factor causing neurologic manifestations since there have been at least five reported cases who had embarrassments of liver function, raised blood ammonia, and alteration in consciousness. Intracranial hemorrhage is the other cause of neurologic manifestation. There were many reported autopsy cases showing intracranial hemorrhage which ranged from mild to severe bleeding[7,18] and it may be the important cause of persistent neurologic abnormality in surviving cases. Direct central nervous system infection by dengue virus itself has been suggested[14] and there is increasing evidence supporting this hypothesis[12]. Other metabolic causes such as hypoglycemia or hyponatremia should also be excluded in every patient who have changes in consciousness. Our reported case had neurologic manifestations which were most likely due to hepatic encephalopathy because her consciousness improved shortly after improvement of hepatic function shown by normal coagulogram.

Exchange transfusion seems to be helpful in lowering mortality in dengue infection with unusual manifestations[22]. However, because of the small sample size, further study is warranted before making any conclusion of the efficacy of exchange transfusion. In patients who have only mild metabolic disorders and no shock, as in our case, exchange transfusion may be not necessary. But in severe cases who have shock complicated by multiple metabolic embarrassments, exchange transfusion may be indicated. However, we suggest that the most important management of DHF is to prevent shock because the case mortality rate is markedly increased in patients with more severe dengue shock syndrome and unusual manifestations (Table 4).

(Received for publication on June 10, 1998)

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โรคติดเชื้อไวรัสเด็งกี่ที่มีอาการผิดแปลกไปจากปกติ : รายงานผู้ป่วย 1 ราย

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ตั้งแต่ปี พ.ศ. 2521 มีรายงานผู้ป่วยติดเชื้อไวรัสเด็งกี่ซึ่งมีอาการผิดแปลกไปจากปกติจำนวนมากขึ้นเรื่อย ๆ ผู้เขียนได้รายงานผู้ป่วยไข้เลือดออก 1 ราย ซึ่งมีความรุนแรงเพียงระดับ 2 แต่พบว่ามีอาการตับวายร่วมกับอาการทางสมอง และพบว่าระดับเอ็นซัยม์ตับสูงมาก ผู้ป่วยหายเป็นปกติหลังให้การรักษาตามอาการ ผู้ป่วยรายนี้นับเป็นรายที่ 4 ของรายงานผู้ป่วยไข้เลือดออก ซึ่งมีความรุนแรงระดับ 2 แต่พบมีอาการผิดแปลกไปจากปกติ

คำสำคัญ : ไข้เลือดออก, อาการผิดแปลกไปจากปกติ, ตับวาย

ชูเกียรติ ศิริวิชยกุล และคณะ
จดหมายเหตุทางแพทย์ ฯ 2000; 83: 325-329

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