Original Article

Dengue Infection in Pediatric Patients with Thalassemia: Aggravation of Anemia

Ampaiwan Chuansumrit[1], Rungrote Natesirinilkul[2], Bunchoo Pongtanakul[3], Kanchana Tangnararatchakit[1], Nongnuch Sirachainan[1], Adisak Tantiworavit[4], Pimlak Charoenkwan[2] and Sutee Yoksan[5]

[1]Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok; [2]Department of Pediatrics, Faculty of Medicine, Chiang Mai University Hospital, Chiang Mai University, Chiang Mai; [3]Department of Pediatrics, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok; [4] Department of Medicine, Faculty of Medicine, Chiang Mai University Hospital, Chiang Mai University, Chiang Mai; [5]Center for Vaccine Development, Institute of Molecular Biosciences, Mahidol University, NakornPathom

Abstract

Objectives: *To study the clinical manifestations and outcomes of treatment in thalassemia patients with dengue infection.* ***Methods:*** *A total of 95 acute febrile illness episodes among 88 thalassemia patients (male, 48; female, 40) from three university hospitals between 1997 and 2013, were retrospectively studied. Their median age was 11.6 years (range 2.0 to 19.9). The types of thalassemia included β-thal major (n = 8), β-thal/HbE (n = 32), AE Bart's disease (n = 6), Hb H disease (n = 38), β-thal/HbS (n = 1), unspecified thalassemia disease (n = 1) and homozygous Hb Constant Spring (n = 2). Twenty-four patients were transfusion-dependent while the remaining patients were non-transfusion-dependent. Splenectomy was performed in 9 patients.* ***Results:*** *Eighty-two episodes were diagnosed with dengue infection (DF 22, DHF 60: grade I 23, II 20, III 13 and IV 4 cases) while 13 episodes were diagnosed with other self-limiting viral infections. The majority of patients presented anemia due to acute hemolysis and hemoglobinuria leading to low hematocrit and requiring packed red cell transfusion. They had elevated levels of AST and ALT resulting from hepatic involvement. Eight of 82 dengue infection cases were complicated with IAHS (n = 1); seizure (n = 3) caused by hyponatremia, encephalitis and encephalopathy; and severe liver impairment (n = 4) causing hepatic encephalopathy in 3 cases. The prompt hospitalization of the indicated patients using a multidisciplinary approach to monitor and provide adequate fluid and packed red cell replacement therapy and effective bleeding control yielded an excellent outcome with 100% survival rate.* ***Conclusion:*** *The early recognition, early diagnosis of dengue infection and appropriate packed red cell transfusion are essential for a favorable outcome.*

Keywords : ● *Thalassemia* ● *Dengue* ● *DF* ● *DHF*

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Requests for reprints should be addressed to Prof. Ampaiwan Chuansumrit, Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Rama VI Road, Bangkok 10400, Thailand. E-mail: ampaiwan.jua@mahidol.ac.th

Introduction

The global distribution of the dengue virus has been established mainly by humans to every corner of the world.[1] People in endemic areas especially pediatric patients are at high risk to be infected. Dengue virus is transmitted by the *Aedes* mosquitoes such as *Aedes aegypti* and *Aedes albopictus*. The four distinct serotypes are classified as dengue 1 to 4. Infection with any of the four serotypes causes similar clinical symptoms that may vary from asymptomatic to symptomatic in mild form, called dengue fever (DF) which has no plasma leakage and the more severe form of dengue hemorrhagic fever (DHF) with plasma leakage according to the World Health Organization (WHO) criteria in 1997.[2]

Thalassemia is an inherited hemolytic anemia caused by mutations of globin genes resulting in decreased or absent production of globin chains, the major components of the hemoglobin. The prevalence of thalassemia diseases in Thailand is rather high, approaching 1% of the population, while 40% of population comprises carriers of thalassemia and hemoglobinopathies.[3] Pediatric patients with thalassemia diseases infected by dengue virus unusually present anemia instead of hemoconcentration. This study presents the clinical course of dengue infection in patients with thalassemia diseases.

Subjects and Methods

A total of 95 acute febrile illness episodes among 88 patients from three university hospitals, namely, Ramathibodi Hospital (n = 48), Chiang Mai University Hospital (n = 20) and Siriraj Hospital (n = 20) between 1997 and 2013, were retrospectively studied. The study was approved by each Faculty Ethics Committee and written informed consent was obtained from parents. Sixty-eight patients had been previously reported[4-6] and 20 patients were added. The detailed information of clinical manifestations, laboratory findings, management and outcome was collected from the medical records of the hospitals and the Division of Pediatric Hematology.

All patients were closely followed up at out-patient clinics during the febrile stage until 24 hours of defervescence. History-taking, physical examination of the vital signs, cardiovascular, respiratory, abdomen and neurological systems, tourniquet test and complete blood counts were performed daily. The patients with the following warning symptoms and signs were hospitalized[7] : severe abdominal pain, severe nausea and vomiting, poor appetite, thirst, irritability, restlessness, sleepiness, behavioral change, cold clammy skin, clinical deterioration, oliguria, any bleeding episodes apart from petechiae and ecchymosis and abnormal laboratory findings either of hematocrit > 42% or rising to > 10-15% from normal baseline for age and sex, or platelets < 100 x 10^9/L.

Patients received supportive treatment, airway management, fluid and electrolyte therapy, and antibiotics administration when appropriate, based on their clinical and laboratory findings. Patients with epistaxis received anterior nasal packing with gel foam. For patients with serious hematemesis, a small nasogastric tube was gently inserted to assess and drain blood from the stomach. Gastric lavage with cold water was not conducted. Patients also received ranitidine or omeprazole. Patients with hypermenorrhea received intravenous conjugated estrogen (premarin) at a dose of 25 mg/kg every 6 hours for 24-48 hours.

Laboratory testing

Complete blood counts were analyzed within 4 hours after blood collection using a Cell Dyne Ruby hematology analyzer. Biochemistry and liver function were performed using standard methods. Urinalysis was performed using urine reagent strips for urinalysis (Teco, Diagnostics, the Netherlands). Acute hemolysis was diagnosed by an abrupt drop of the hematocrit combined with increased fragmented red blood cells on the peripheral blood smear and increased indirect bilirubin. Hemoglobinuria was defined by positive test for the blood of urine reagent strips combined with negative for red blood cell in the urine sediment. Every

patient with hemoglobinuria was screened for the glucose-6-phosphate dehydrogenase (G 6-PD) deficiency by screening test of a fluorescence spot test and visualized under ultraviolet light (R&D Diagnostics) during acute hemoglobinuria and steady state upon follow-up.

Diagnostic criteria

The three stages[2] of dengue infection are named febrile, toxic and convalescent. The febrile stage lasts 2 to 7 days followed by an abrupt fall to normal or subnormal temperatures during the toxic stage lasting 24 to 48 hours and finally, a rapid recovery during the convalescent stage. The clinical manifestations of DF include a mild or high febrile syndrome of abrupt onset, headache and pain behind the eyes, muscle, bone or joint pain, nausea, vomiting and rash. Apart from petechiae, bleeding manifestations are not common. Patients with DHF have similar signs and symptoms followed by plasma leakage. Typical cases of DHF are characterized by four major clinical manifestations defined by the WHO[2]: (i) sustained high fever for 2-7 days, (ii) a hemorrhagic tendency, such as a positive tourniquet test, petechiae or clinical bleeding, (iii) thrombocytopenia (platelet $\leq 100 \times 10^9$/L) and (iv) evidence of plasma leakage caused by increased vascular permeability manifested by hemoconcentraion (a > 20% increase in hematocrit) or pleural effusion. In this study, a right lateral decubitus chest radiograph was taken the day after defervescence in patients without evidence of hemoconcentration.

The severity of DHF is categorized in four grades according to the WHO criteria in 1997.[2] Grade I presents without overt bleeding but a positive tourniquet test; grade II, with clinical bleeding diathesis such as epistaxis, and ecchymosis; grade III, circulatory failure manifested by a rapid, weak pulse and narrowing pulse pressure (< 20 mmHg) or hypotension with cold clammy skin and restlessness; and grade IV, profound shock in which pulse and blood pressure are not detected. In 2009, the WHO established another criteria to classify dengue infection as dengue without warning signs, dengue with warning signs and severe dengue with severe plasma leakage, severe hemorrhage and severe organ impairment.[8] The association of severity in these two criteria[9] is shown in Table 1.

Confirmation of dengue infection

Dengue virus infection was confirmed by virus isolation of mosquito inoculation or the presence of dengue specific IgM and IgG antibodies determined by capture enzyme-linked immunosorbent assay (ELISA) in acute and convalescent sera (Vaccine Development Center, Thailand). Primary infection was defined by a ratio of IgM to IgG of > 1.8 while the remaining patients were defined as having secondary infection. Alternatively, serological testing in both acute and convalescent sera by hemagglutination inhibition test to dengue serotypes 1, 2, 3 and 4 was performed. Primary infection was defined by the acute dengue titer of less than 1:1,280 and four fold rising of antibody titer to only one dengue serotype while the acute dengue titer over 1:1,280 or four fold rising of antibody titer to all four dengue serotypes was defined as having secondary infection.

Blood component therapy

Blood component therapy was used when necessary depending on the clinical manifestations assessed by the investigators. These indications included: packed red cells (PRC) for volume replacement in patients with acute hemolysis and massive bleeding, fresh frozen plasma (FFP) for massive bleeding due to coagulopathy and volume replacement in cases with hemoconcentration, unstable blood pressure or rapid pulse unresponsive to crystalloid fluid replacement. Cryoprecipitate was used to replace fibrinogen and platelet concentrate, in either single- or multiple-donors, and was used to maintain a platelet count $\geq 100 \times 10^9$/L for patients with thrombocytopenia exhibiting bleeding manifestations except for petechiae and ecchymosis.

Statistical analysis

Chi-square and Fisher's exact tests were used for

discrete data, where appropriate. The Mann-Whitney *U* and Wilcoxon signed-rank tests were used for continuous data. A *p-value* of < 0.05 was considered statistically significant.

Results

The study investigated 95 episodes of acute febrile illnesses among 88 patients (male, 48; female, 40) whose ages ranged from 2.0 to 19.9 years with a median age of 11.6 years as shown in Table 1. Seven cases had two subsequent episodes of acute febrile illnesses. The types of thalassemia and the diagnosis of dengue virus infection are shown in Table 2. Twenty-four of 88 patients were transfusion-dependent while the remaining patients were non-transfusion-dependent. Splenectomy was performed in 9 patients including β-thal major (n = 1), β-thal/Hb E (n = 6), Hb H disease with Hb Constant Spring (n = 1) and unspecified thalassemia disease (n = 1). Eighty-two episodes were diagnosed with dengue while 13 episodes were diagnosed with other self-limiting viral infections designated as other febrile illnesses (OFIs). All patients required medical care on the second to third day of fever and were hospitalized according to admission criteria.

For the clinical manifestations and laboratory findings, the median duration of total fever in patients with OFIs was 5 days (range 3 to 8 days), which was significantly shorter than those with dengue infection (DF: median 6 days, range 4 to 10 days; and DHF: median 6 days, range 3 to 11 days) with a *p-value* of 0.002.

Table 1 Diagnosis of dengue infection among the studied patients

WHO 1997	WHO 2009	Number of episode	Male	Female	Median age (range)
Dengue fever	Dengue without warning sign of plasma leakage	22	9	13	11.8 (3.5-19.9)
DHF grade I	Dengue with warning sign of plasma leakage but no bleeding	23	15	8	13.5 (2.8-18.1)
DHF grade II	Dengue with warning sign of plasma leakage and bleeding	20	9	11	11.0 (4.9-18.0)
DHF grade III	Severe dengue with threatened shock	13	8	5	10.5 (2.0-16.6)
DHF grade IV	Severe dengue with profound shock	4	3	1	11.8 (9.6-13.7)
Other febrile illnesses	-	13	7	6	9.9 (3.8-16.9)
Total	**-**	**95**	**51**	**44**	**11.6 (2.0-19.9)**

Table 2 Thalassemia patients with dengue infection

Type of thalassemia	Total	DF	DHF Grade I	DHF Grade II	DHF Grade III	DHF Grade IV	OFIs
β-thalassemia major	8	3	2	3	0	0	0
β-thalassemia/Hb E disease	35	7	7	7	9	2	3
AE Bart's disease ± Hb Constant Spring	6	3	1	0	1	0	1
Hb H disease ± Hb Constant Spring or Pakse	42	8	12	9	3	1	9
β-thalassemia / Hb S	1	0	0	1	0	0	0
Unspecified thalassemia disease	1	0	0	0	0	1	0
Homozygous Hb Constant Spring ± Hb E	2	1	1	0	0	0	0
Total	**95**	**22**	**23**	**20**	**13**	**4**	**13**

Anemia was mainly from the acute hemolysis process starting from the early febrile stage. Hemoglobinuria was found in 18 of 95 episodes (20.5%) including AE Bart's disease with and without Hb Constant Spring (n = 2), Hb H disease with and without Hb Constant Spring (n = 14), β-thal/Hb E (n = 1) and homozygous Hb Constant Spring (n = 1). Patients had DF (n = 6); DHF (n = 10) including grade I, 6; II, 1; III, 3; and OFIs (n = 2). The G 6-PD screening test during acute hemoglobinuria and steady state on the follow-up were normal. The levels of hematocrit were low in all patients but patients with DHF had the lowest hematocrit level although without significance. Also, the reduction of the hematocrit was highest in patients with DHF compared with those with DF and OFIs but without significant difference. Consequently, patients with DF, DHF and OFIs possessed the similar requirement of packed red cell transfusion. In addition, a higher number of patients with DHF exhibited bleeding manifestations compared with those with DF and OFIs as shown in Table 3. Accordingly, the platelet counts in patients with dengue infection (DF and DHF) were significantly lower than those with OFIs ($p = 0.001$). In addition, patients with DHF had a significantly lower platelet count than those with DF ($p < 0.0001$). Similar findings were observed in serum alanine transaminase (ALT) and aspartate transaminase (AST) levels due to hepatic involvement. Most patients with dengue infection either DF or DHF had high abnormal levels of ALT and AST than those with OFIs with *p-values* of 0.01 and 0.008, respectively.

Eight of 82 dengue cases exhibited complications. All were diagnosed with DHF (grade I, 1 case; grade II, 1 case; grade III, 3 cases; and grade IV, 3 cases). One patient (case 1) had infection associated hemophagocytic syndrome (IAHS). He had progressive pancytopenia and the bone marrow aspiration on day 5 of fever revealed increased reactive histiocytes with hemophagocytic activity. He was responsive to intravenous immunoglobulin administration and packed red cell transfusions, so the pancytopenia gradually resolved. Three patients (cases 2, 3, and 4) had generalized tonic clonic seizures on days 5 and 4 of fever, and one day after defervescence, respectively. The final diagnosis was hyponatremia inducing seizure, encephalitis and encephalopathy, respectively since only one patient (case 3) had positive result of dengue nonstructural protein antigen 1 (NS1) in her cerebrospinal fluid. Four patients (cases 5, 6, 7, and 8) had severe liver impairment with AST or ALT level higher than 1,000 units/L. Three of them exhibited hepatic encephalopathy. These patients received intensive management in the ICU with ventilator support, central line insertion, inotrope administration, fluid and electrolyte therapy, and adequate blood component support as shown in Tables 4 and 5. All patients survived without morbidity. Ultimately, the duration of hospitalization in patients with dengue infection (DF: median 5 days, range 2 to 8 days; and DHF: median 6 days, range 2 to 18 days) was significantly longer than those with OFIs (median 4 days, range 2 to 4 days) with a *p-value* of 0.047.

Table 3 Bleeding manifestations in thalassemia patients with dengue infection

	Dengue fever (n = 22)	**Dengue hemorrhagic fever (n = 60)**	**Other febrile illnesses (n = 13)**
Petechiae	1	9 (31.0%)	0
Ecchymosis	0	2 (6.9%)	0
Gastrointestinal bleeding	0	4 (13.8%)	0
Epistaxis	1	11 (37.9%)	1
Hypermenorrhea	1	2 (6.9%)	0
Gum & teeth bleeding	0	1 (3.5%)	0

Table 4 Laboratory findings in thalassemia patients with dengue infection

	Dengue fever (n = 22)	Dengue hemorrhagic fever (n = 60)	Other febrile illnesses (n = 13)
Baseline hematocrit (%)			
Median	26.8	27.0	32.0
Range	23.9-31.3	24.0-30.0	28.2-33.0
Lowest hematocrit (%)			
Median	20.8	19.0	23.0
Range	12.4-31.0	9.6-35.0	15.6-27.5
Reduction of hematocrit (%)			
Median	22.3	25.0	14.1
Range	9.5-34.4	14.3-40.0	8.1-31.8
Lowest platelet (x 10^9/L)			
Median	81	50	148
Range	48.0-401.0	12.0-189.0	40.0-421.0
White cell count (x 10^9/L)			
Median	2.4	2.9	6.5
Range	0.8-12.6	1.4-9.1	1.6-20.3
AST (U/L)			
Median	258	373	100
Range	72-552	42-5344	35-162
Abnormal test (case)	6/6	34/34	4/5
ALT (U/L)			
Median	92	93.5	28
Range	33-185	12-2041	20-65
Abnormal test (case)	5/6	30/34	2/5

Table 5 Blood component therapy in thalassemia patients with dengue infection

	Dengue fever (n = 22)	Dengue hemorrhagic fever (n = 60)	Other febrile illnesses (n = 13)
Packed red cells	16 (72.7%)	51 (85.0%)	8 (61.5%)
Fresh frozen plasma	0	7 (11.6%)	0
Platelet concentrate	0	7 (11.6%)	0
Cryoprecipitate	0	2 (3.3%)	0

To confirm dengue infection, dengue virus isolation was carried out in 27 cases revealing positive results in 8 cases: serotype 1 (3 cases, one each for DHF grades I, II, and III), serotype 2 (5 cases: DF, 1 cases; DHF grade I, 2 cases; grade II, 1 case and grade III, 1 case). The remaining subjects had negative results including 6 cases with OFIs, 7 cases with DF and 6 cases with DHF. Complete dengue specific antibody test results were available in 71 episodes. Primary dengue infection was found in 20 cases (28.2%) including DF, 6 cases and DHF, 14 cases while secondary dengue infection was found in 51 cases (71.8%) including DF, 12 cases and DHF, 39 cases.

Table 6 Clinical manifestations and management for 8 patients with complications

Patient no.	Sex	Age	Type of thalassemia	Severity of DHF	Baseline Hct (%)	Minimum Hct (%)	Maximum Plt (x 10^9/μL)	Maximum AST/ALT (unit/L)	Bleeding/Complication	Treatment	Hospitalization (days)	Serology to dengue
1*	M	9.0	Hb H with HbCS	III	35	12	72	nd	- Progressive pancytopenia - IAHS on day 5 of fever	- IVIg - PRC x 3 (600 mL)	8	primary
2*	F	13.0	Hb H with HbCS	IV	25	15	71	nd	- Generalized tonic clonic seizures on day 5 of fever, serum sodium 122 mEq/L	- Correct hyponatremia - PRC x 4 (1,000 mL) - FFP x 2 (800 mL)	10	secondary
3*	F	10.5	Hb H with HbCS	III	32	13.6	51	711/232	- Shock - Petechiae, hemoglobinuria - Confusion & generalized tonic clonic seizures on day 7 of fever, CSF 2 monocytes & positive dengue IgM - Adrenal insufficiency - Raised BUN/Cr (2.9/1.6 mg/dL)	- Central line insertion - Endotracheal intubation with ventilator support - Inotrope administration - PRC x 8 (1,345 mL) - FFP x 3 (1,190 mL)	22	secondary
4	M	16.0	β-thal / Hb E on regular transfusions and deferiprone 90 mg/kg/d, serum ferritin 1,272 ng/mL	I	25.7	21.8	41	265/98	- One day after defeverescence developed headache and generalized tonic clonic seizures CSF few RBC, no WBC - Adrenal insufficiency	- PRC x 1 (500 mL) - Plt x 1 (10 units)	18	secondary
5	M	11.9	β-thal / Hb E on regular transfusions and desferrioxamine 28 mg/kg/d for 7 days/wk, serum ferritin 2,072 ng/mL	IV	28	20	28	4,267 / 2,041	- Upper GI bleeding - Liver failure - Hepatic encephalopathy - Shock	- Central line insertion - Endotracheal intubation with ventilator support - Inotrope administration with ventilator support - PRC x 3 (750 mL) - FFP x 3 (900 mL) - Cryoppt x 3 (10 units) - Plt x 7 (47 units) - Partial exchange	13	primary
6*	M	15.4	AE Bart's disease	III	29.1	18.3	90	1,738 / 542	- Hemoglobinuria - Raised BUN/Cr (40/1.9 mg/dL)	- PRC x 2 (500 mL)	7	secondary
7*	M	10.5	β-thal / Hb E	IV	27.6	28.8	25	5,344 / 1,846	- Upper GI bleeding - Liver failure - Hepatic encephalopathy - Shock	- PRC x 3 (750 mL) - FFP x 1 (200 mL) - Plt x 1 (6 units)	11	secondary
8*	M	13.7	β-thal / Hb E postsplenectomy	IV	20.4	17.7	82	1,378 / 1,108	- S pneumonia sepsis - Raised BUN/Cr (58/1.3 mg/dL) - Liver failure - Hepatic encephalopathy - Shock	- PRC x 2 (500 mL) - FFP x 2 (400 mL)	15	primary

* Non-transfusion-dependent thalassemia; nd, no data; IVIg, intravenous immunoglobulin; CSF, cerebrospinal fluid; plt, platelet concentrate; cryoppt, cryoprecipitate

Discussion

Patients with thalassemia diseases manifest an unusual presentation of dengue virus infection. They presented anemia with low hematocrit levels instead of hemoconcentration found in patients without underlying diseases. Importantly, the clinical signs and symptoms during febrile stage cannot distinguish dengue infection from other febrile illnesses. Patients with thalassemia diseases with any acute febrile illness risk acute hemolysis manifested as pallor and hemoglobinuria especially patients with alpha thalassemia disease such as hemoglobin H disease. Even one patient with homozygous hemoglobin Constant Spring in the current study exhibited hemoglobinuria. Serious complication was previously reported in G 6-PD deficiency patients with DHF[10], however, all patients with hemoglobiuria had negative G 6-PD screening test during hemoglobinuria and steady state during the follow-up in the current study. The heterozygous state of G 6-PD deficiency among female patients could be misclassified as normal. As a consequence, they were at risk for anemia and required packed red cell transfusion to maintain adequate intravascular volume. Also, they were prone to severe liver impairment since they might have had underlying liver impairment from transfusion and non-transfusion induced iron overload[11,12] or hepatitis infection.[13] They were prone to complicated dengue infection requiring close monitoring and prompt intervention to yield a favorable outcome. The current study enrolled thalassemia patients from three university hospitals. They were treated by pediatric hematology specialists and other related specialists in the comprehensive centers. As a result, the outcomes were excellent. All patients including complicated cases survived without morbidity. Apart from hematologists, the complete support of physicians, nurses and paramedical personnel in various aspects of intensive care, cardiology, pulmonary medicine, nephrology, gastroenterology, infectious disease and blood bank was the key to success.[14]

Moreover, all patients required medical care from the initial febrile stage and were hospitalized to closely monitor alteration of their clinical manifestations. In addition, early recognition of dengue infection during the febrile stage by medical personnel was another important factor. The confirmation of dengue infection relies on serological testing on acute and convalescent sera.[2] At bedside, the diagnosis of dengue infection is based on the clinical signs and symptoms as well as the daily complete blood count for the evidence of plasma leakage of pleural effusion, hemoconcentration and thrombocytopenia. Virus isolation can be performed in an advanced laboratory setting only and takes a few days to obtain the results. Also, dengue virus identification by the polymerase chain reaction technique is both time-consuming and costly. Patients with thalassemia had a higher positive rate for dengue virus isolation (8/21 = 38.1%) compared with patients without underlying disease (86/401 = 21.4%) as previously reported[5] but without significant difference. The recent determination of dengue nonstructural protein 1 antigen in the serum or urine[15,16] by ELISA and strip tests is a helpful and reasonably priced test. The cost per test is approximately 300 baht. However, patients with positive test can manifest DF or DHF and patients with negative results cannot be excluded from dengue infection, commonly positive in the early febrile stage. Moreover, the commercially available dengue IgM test will be positive in the late febrile stage or on day 4 to 5 of fever. It will be mostly positive in patients with primary dengue response (high IgM and low IgG) while those with secondary dengue response will have negative IgM results (low IgM and high IgG). Patients with thalassemia had a lower secondary response (51/71 = 71.8%), reflecting a less competent immune response compared with those without underlying disease (666/750 = 88.8%) as previously reported[5] but without significant difference. Immune status including phagocytic activity, cell mediated immune response, humoral antibody and complement system in pediatric thalassenmia patients did not differ from the general population and no difference was found between splenectomized and non-splenectomized

thalassemia patients.[17-19] However, the innate immune response of thalassemia patients to the dengue virus infection has not been established yet. Further intensive study is warranted.

In addition, a predictor of dengue shock syndrome (DHF grades III and IV) during the febrile stage of elevated soluble thrombomodulin over 10 ng/ml is not available in routine practice.[20] Therefore, the close monitoring of patients with acute febrile illnesses for dengue infection is essential for a favorable outcome. Proper management of acute hemolysis is absolutely necessary. Finally, management for complicated cases by multidisciplinary approach is crucial. The team should be notified in advance to provide care to those patients with multiple organ involvement.

Conclusion

Patients with thalassemia risk anemia rather than hemoconcentration during the febrile stage of acute febrile illnesses. They need appropriate packed red cell transfusion. They should be closely monitored for complications that manifest requiring a multidisciplinary approach in the comprehensive center. Patients with suspected complications should be appropriately referred to the comprehensive center with complete intervention facilities.

Conflict of interest statement

The authors state they have no interests that might be perceived as posing a conflict or bias.

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การติดเชื้อไวรัสเดงกีในผู้ป่วยเด็กโรคธาลัสซีเมีย: ภาวะซีดมากขึ้น

อำไพวรรณ จวนสัมฤทธิ์[1] รุ่งโรจน์ เนตรศิรินิลกุล[2] บุญชู พงศ์ธนากุล[3] กาญจนา ตั้งนรารัชชกิจ[1] นงนุช สิระชัยนันท์[1] อดิศักดิ์ ตันติวรวิทย์[4] พิมพ์ลักษณ์ เจริญขวัญ[2] และ สุธี ยกส้าน[5]

[1]ภาควิชากุมารเวชศาสตร์ คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี [2]ภาควิชากุมารเวชศาสตร์ คณะแพทยศาสตร์มหาวิทยาลัยเชียงใหม่
[3]ภาควิชากุมารเวชศาสตร์ คณะแพทยศาสตร์ศิริราชพยาบาล [4]ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์มหาวิทยาลัยเชียงใหม่
[5]โครงการวิจัยและพัฒนาวัคซีน มหาวิทยาลัยมหิดล

วัตถุประสงค์ *ศึกษาอาการแสดงและผลการรักษาในผู้ป่วยโรคธาลัสซีเมียที่ติดเชื้อไวรัสเดงกี* ***วิธีการ*** *ศึกษาภาวะไข้เฉียบพลันย้อนหลัง 95 ครั้งในผู้ป่วยโรคธาลัสซีเมีย 88 ราย (ชาย 48 ราย หญิง 40 ราย) จากโรงพยาบาลมหาวิทยาลัย 3 แห่ง ระหว่าง พ.ศ. 2540 ถึง 2556 อายุมัธยฐาน 11.6 ปี (พิสัย 2.0 ถึง 19.9) เป็นผู้ป่วยโรคเบต้าธาลัสซีเมียเมเจอร์ 8 ราย เบต้าธาลัสซีเมีย/ฮีโมโกลบิน อี 32 ราย เออีบาร์ท 6 ราย ฮีโมโกลบิน เอช 38 ราย เบต้าธาลัสซีเมีย/ฮีโมโกลบินเอส 1 ราย ไม่ทราบชนิดโรคธาลัสซีเมีย 1 ราย และ โฮโมไซกัสฮีโมโกลบินคอนแสตนท์สปริง 2 ราย ผู้ป่วย 24 รายได้รับเลือดทดแทนอย่างสม่ำเสมอแต่ผู้ป่วยที่เหลือไม่ต้องรับเลือดทดแทน และ 9 รายได้รับการตัดม้าม* ***ผลการศึกษา*** *ให้การวินิจฉัยโรคติดเชื้อไวรัสเดงกี 82 ครั้ง (ไข้เดงกี 22 ราย ไข้เลือดออก 60 รายแยกเป็นเกรด I 23, II 20, III 13 และ IV 4) และติดเชื้ออื่นที่ไม่ใช่ไวรัสเดงกี 13 ครั้ง ผู้ป่วยส่วนใหญ่มีภาวะซีดเนื่องจากภาวะเม็ดเลือดแดงแตกอย่างเฉียบพลันร่วมกับปัสสาวะสีโค้ก (hemoglobinuria) ทำให้ผู้ป่วยมีระดับฮีมาโตคริทต่ำและต้องได้รับเม็ดเลือดแดงทดแทน ผู้ป่วยยังมีระดับ AST และ ALT ที่สูงขึ้น พบภาวะแทรกซ้อนในผู้ป่วย 8 รายได้แก่ IAHS 1 ราย; ชัก 3 รายเนื่องจาก hyponatremia, encephalitis และ encephalopathy; การทำงานของตับบกพร่องอย่างมาก 4 รายทำให้เกิดภาวะ hepatic encephalopathy 3 ราย ดังนั้นการรับผู้ป่วยที่มีข้อบ่งชี้ไว้รักษาในโรงพยาบาล การติดตามดูแลรักษาผู้ป่วยด้วยทีมผู้เชี่ยวชาญจากสหสาขาวิชา การให้สารน้ำและเลือดอย่างเพียงพอ ร่วมกับการควบคุมอาการเลือดออกอย่างมีประสิทธิภาพ ทำให้มีผลการรักษาที่ดี ผู้ป่วยรอดชีวิตทุกราย* ***สรุป*** *การวินิจฉัยภาวะติดเชื้อไวรัสเดงกีโดยเร็วและถูกต้อง ร่วมกับการให้เลือดทดแทนอย่างเหมาะสมมีความสำคัญต่อผลการรักษาที่ดี*

Keywords : ● *Thalassemia* ● *Dengue* ● *DF* ● *DHF*
วารสารโลหิตวิทยาและเวชศาสตร์บริการโลหิต 2558;25:209-19.