CASE REPORT

CONCOMITANT DENGUE HEMORRHAGIC FEVER WITH KAWASAKI DISEASE

Somkiat Sopontammarak and Pornpimol Pruekprasert

Department of Pediatrics, Faculty of Medicine, Prince of Songkla University, Songkhla, 90110 Thailand

Abstract. This is an unique case report of concomitant dengue hemorrhagic fever and Kawasaki disease, not reported previously. The unusual clinical course of persistent fever, coronary artery involvement evidenced from 2-D echocardiogram, and hydrops of the gallbladder is discussed.

Dengue infection is the most common insect-borne viral infection predominantly found in tropical and subtropical regions, and is a major public health problem in Southeast Asia. Dengue hemorrhagic fever (DHF) and dengue shock syndromes are severe forms of the disease. In DHF patients typically present with an acute febrile episode for 4-5 days. After the fever breaks the patient's condition deteriorates with plasma leakage varying in severity from mild to severe, accompanied by hypotension, shock and bleeding diathesis from thrombocytopenia. Coinfection or dual infection in DHF with chickenpox, herpes simplex, *Streptococcus pneumoniae*, melioidosis, salmonellosis, shigellosis, *Escherichia coli*, tuberculosis, and *Mycoplasma pneumoniae* have been reported, with unusual clinical manifestations (Pancharoen and Thisyakorn, 1998). Atypical Kawasaki disease (KD) with concomitant *E. coli* urinary tract infection (Levy and Koren, 1990) and *Staphylococcus aureus* toxic shock syndrome (TSS) (Gamillscheg *et al*, 1993) have been reported. This is the first report of a documented case of DHF with Kawasaki disease (KD).

A previously healthy 10-year-old boy was admitted to Prince of Songkla University Hospital with history of a high fever for 4 days without a local source of infection. On day 11 of the high fever he started developing hypotension and plasma leakage evidenced by ascites and pleural effusion with a tender and enlarged liver extending 4 cm below the right costal margin. He was transferred to the pediatric intensive care unit for close monitoring and fluid management. There was no bleeding diathesis and the highest hematocrit was 38%. The high fever persisted, but plasma leakage resolved after 3 days. A diagnosis of DHF complicated by superimposed bacterial infection was made, and antibiotics were administered. However, there were no positive cultures and no response to treatment as shown in Fig 1. High fever and tachycardia persisted; bright red lips and oral mucosa were noted. A maculopapular rash occurred on day 12 of the fever and lasted for 1 day. Abnormal cardiac findings consisting of S3 gallop rhythm and tachycardia of 140 beats/minute were observed on day 15 of the fever.

Complete blood counts at the time of presentation revealed the following data: white blood cell count 5,700/mm^3 (with 82% neutrophils, 12% lymphocytes, 6% monocytes); hemoglobin 11.8 g/dl; hematocrit 36%; platelet 227,000/ mm^3. The lowest platelet count was 109,000/ mm^3 on day 8 of the illness. Urinalysis showed protein 3+, blood 2+, negative nitrite and leukocyte esterase and normal microscopic examination. The following investigations gave normal or negative results: urea, creatinine; serum electrolytes; liver function; blood and urine cultures; serology for salmonellosis, leptospirosis, scrub typhus, murine typhus, tick typhus and melioidosis; antinuclear factor and anti dsDNA. Initial dengue hemagglutination titer on admission was 1:80, and a repeated titer 6 days later was >1: 10,240, with dengue IgM 82 IU/ml (normal < 40 IU/ml). Based on World Health Organization laboratory criteria for the diagnosis of DHF, the patient had secondary dengue infection or DHF (WHO, 1986).

Electrocardiogram on day 15 of the illness revealed first-degree heart block, sinus tachycar-

Correspondence: Somkiat Sopontammarak, Division of Pediatric Cardiology, Department of Pediatrics, Faculty of Medicine, Prince of Songkla University, Songkhla 90110, Thailand.
E-mail: ssomkeat@ratree.psu.ac.th

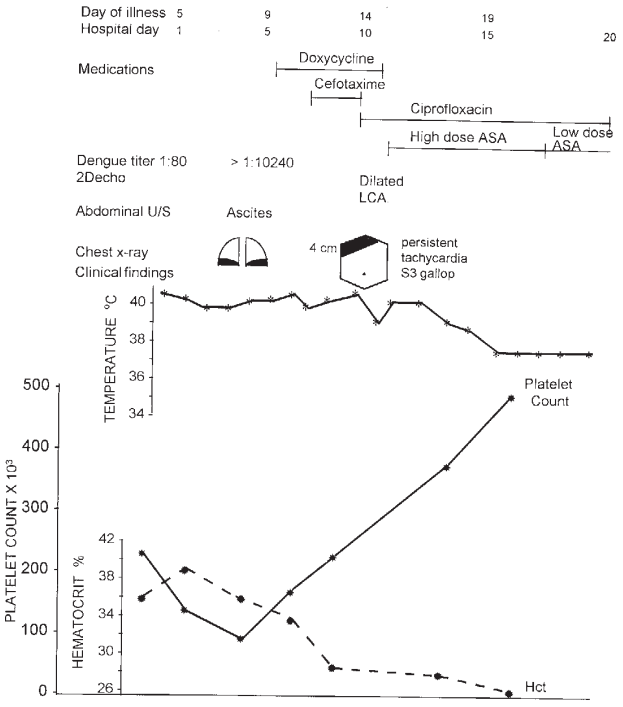

Fig 1–Clinical course during hospitalization.

dia, and nonspecific ST-T wave changes. Two-dimensional echocardiogram showed uniform dilatation of the left main coronary artery with a diameter of 5 mm and irregular intima of the artery without obvious coronary aneurysm. The right coronary artery was normal with a diameter of 3 mm. There was no pericardial effusion or mitral regurgitation, and cardiac contractility was normal. Hydrops of the gallbladder was also detected.

The diagnosis of KD was made on day 18 of the illness, and therefore intravenous immunoglobulin (IVIG) was not administered. High dose aspirin (80 mg/kg/day) was given since the platelet count had increased to 386,000/ mm^3. Defervescence occurred 48 hours later with overall improvement of the patient's general condition. The platelet count continued to rise subsequently to 485,000/mm^3 on day 20 of the illness. No desquamation of the fingertips occurred. At the time of discharge aspirin was reduced to 5 mg/kg/day. At the 3-month follow-up examination, the left coronary artery appeared smaller measuring 3 mm diameter, and no coronary aneurysm was detected. A subsequent complete blood count and electrocardiogram were normal.

The clinical and laboratory findings in this patient were consistent with the diagnoses of both DHF and KD. DHF was confirmed by specific serologic tests which revealed elevated IgM and elevated IgG greater than 128 fold (WHO, 1986), findings not observed in KD. The prolonged fever, hyperemia of the lips and oral mucosa, and a skin rash along with the coronary arteritis and hydrops of the gallbladder supported the diagnosis of KD (Saulsbury, 1995).

There are three possible explanations for the unusual findings in this patient: (1) concomitant DHF and KD, (2) DHF as an etiology for KD including coronary arteritis and hydrops of the gall bladder, or (3) atypical KD with thrombocytopenia and plasma leakage episode.

Concomitant DHF and KD is a likely possibility, not previously reported in the English literature. The overlap of both diseases could account for the lack of the typical changes in platelets (thrombocytopenia in DHF, and thrombocytosis in KD). Despite the hypotension and plasma leakage, there was no obvious hemoconcentration. Desquamation of the fingertips, a common finding in KD, was also not seen. Dengue fever may alter the course of KD and make the diagnosis of atypical KD even more difficult without using 2-D echocardiography to determine the coronary artery involvement.

Second, this patient may have had DHF with a very unusual complication of coronary arteritis and hydrops of the gallbladder, also never reported previously. Nonspecific ST and T wave EKG changes and reduced ventricular contractility have been reported in DHF (Wali *et al*, 1998). Gallbladder wall thickening has been reported in up to 32% of DHF (Satiawan *et al*, 1998), but not hydrops of the gallbladder. Ebstein-Barr virus infection has been reported as causing arteritis of the following vessels: coronary artery, bilateral common carotid and subclavian arteries, abdominal aorta and its major branches, and bilateral common iliac arteries (Muyakami *et al*, 1998). If this is a case of DHF causing coronary arteritis, dengue virus may be another potential direct or indirect cause of KD.

Third, this may be an atypical KD, with very unusual initial presentation in the form of thrombocytopenia and plasma leakage. Low platelet count (Gamillscheg *et al*, 1993; Kinney *et al*, 1992) and shock (Kinney *et al*, 1992) are very unusual in KD but pleural effusion and first-degree heart block have been reported. This hypothesis is not sup-

ported by the elevation of dengue immunoglobulin titers.

The use of aspirin following the convalescent phase of DHF is a concern because of the bleeding nature of DHF; however, the normal platelet count and monitoring for this complication justified its use. Intravenous immunoglobulin (IVIG) was not employed due to the uncertainty of the efficacy of IVIG in reducing coronary artery aneurysm complication after the 10th day of the illness.

In conclusion, the unusual course of DHF in this patient prompted us to look for an explanation. Concomitant DHF with atypical KD was considered; alternatively, dengue virus as an unusual etiology for KD was also entertained. Both considerations have not been reported.

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