Concomitant Dengue Infection and Kawasaki Disease in an Infant: A Case Report and Literature Review

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A previously healthy 11-month-old girl presented with fever and rash for 6 days. Physical examination revealed an irritable infant with a high fever, injected conjunctivae, red cracked lips, posterior auricular lymphadenopathy, hepatomegaly, generalized erythematous maculopapular rash and petechial hemorrhage on the trunk, face and extremities. Complete blood count showed atypical lymphocytosis and thrombocytopenia. Dengue infection was initially diagnosed. The persistent fever and clinical manifestations of Kawasaki disease (KD) were observed on day 8 with high erythrocyte sedimentation rate (56 mm/hr). Treatment of KD included intravenous immunoglobulin on day 9 of the illness. Desquamation of the fingers was found on day 15 of the illness. Ectasia of left coronary artery with small aneurysmal dilatation was detected by echocardiography on day 15 of the illness. Hemagglutination-inhibition test and enzyme-linked immunosorbent assay for dengue virus eventually showed a four-fold rising. According to the literature review, this is the second reported case of dengue infection concomitant with KD. The natural course of each disease may be modified and causes some difficulties in diagnosis and management.

Keywords: Kawasaki disease, Dengue, Infant

Full text. e-Journal: http://www.medassocthai.org/journal

Despite intensive epidemiologic study, the etiology of Kawasaki disease (KD) remains unknown. However, it is believed to be caused by infectious agents. There has been previous report of dengue infection associated with KD. The authors herein report the second case of concomitant dengue infection and KD.

Case Report

A previously healthy 11-month-old girl was admitted to King Chulalongkorn Memorial Hospital, Bangkok, Thailand, on April 20, 2002 because of 6 days of fever and rash. Physical examination revealed an irritable infant with a high fever, injected bulbar conjunctivae, red cracked lips, posterior auricular lymphadenopathy (0.5 cm in diameter), hepatomegaly, generalized erythematous maculopapular (MP) rash and petechial hemorrhage on the trunk, face and extremities. Investigations showed a hematocrit (Hct) of 35.2%, a white blood cell (wbc) count of 8,700 cells/mm³ (neutrophils 18%, lymphocytes 74%, atypical lymphocytes 6%), a platelet count of 40,000/mm³, a serum sodium of 127 mEq/L and an erythrocyte sedimentation rate (ESR) of 56 mm/hr. The clinical diagnosis of dengue infection was confirmed by a positive rapid dengue immunochromatography test. On day 8 of the fever, atypical KD was diagnosed by clinical criteria including prolonged fever, MP rash, conjunctivitis, cracked lips and high ESR. Treatment with intravenous immunoglobulin (IVIG) (2 gm/kg) was given on day 9 of the fever and hypotension was observed during IVIG administration. The fever disappeared within 48 hours after IVIG treatment. Aspirin (90 mg/kg/d) was given. Ceftriaxone was prescribed due to previous positive urine culture (E. coli > 10⁴-10⁵/ml). The clean-void urine culture kept before starting the antibiotic was negative. On day 15 of the illness, desquamation of the fingers was
observed and echocardiography demonstrated a small aneurysmal dilatation (3.5 mm) of the left coronary artery. The clinical course is shown in Fig. 1. Anti-dengue IgG using hemagglutination-inhibition (HI) test and enzyme-linked immunosorbent assay (ELISA) showed a four-fold rising (HI test: < 1:20 on day 6 and 1:320 on day 17; ELISA test: dengue (DEN) IgM 26, IgG 0 Elisa units, Japanese B encephalitis (JE) IgM 4, IgG 0 Elisa units on day 6 and DEN IgM 40, IgG 28 Elisa units, JE IgM 89, IgG 28 Elisa units on day 17, respectively). Dengue virus was detected by nested polymerase chain reaction (nested PCR) on day 7. Final diagnosis included primary dengue infection and KD. Repeated echocardiography 4 months later showed normal coronary arteries. She received aspirin (3 mg/kg/day) for 6 months. She was found to be healthy at her last follow up 7 months after her illness.

Discussion

The presented patient was diagnosed as dengue infection with clinical criteria of fever, hepatomegaly, petechial rash, atypical lymphocytosis and thrombocytopenia. Serologic testing was confirmed by positive IgM of dengue rapid immunochromatography test, a four-fold rising of dengue titer using HI and ELISA test and positive nested PCR.

Atypical KD was diagnosed by prolonged fever and 3 out of 5 features, i.e. MP rash, conjunctivitis and cracked lips. High ESR, desquamation of the fingers and a coronary artery aneurysm occurring later confirmed the diagnosis of a typical case of KD.

Although prolonged fever for more than 7 days in dengue patient is possible, it is uncommon. Thus, in this situation, clinicians should search for accompanying conditions or infections.
presented patient remained febrile after day 8 and KD was eventually diagnosed.

There have been two previous reports concerning dengue virus infection and KD\(^2,3\). The first case was a 10-year-old Thai boy who presented with prolonged fever without a source of infection, and developed hypotension with evidence of plasma leakage on day 11. Fever persisted even after 3 days of resolution of plasma leakage. He developed MP rash on day 12, tachycardia and S3 gallop on day 15. KD was diagnosed on day 18 when a left main coronary artery aneurysm was detected. The diagnosis of dengue infection was confirmed by HI test. The second report was a case of 26-month-old French boy who presented with classic KD. He was one of the 13 KD patients whose sera were kept during illnesses between 1995 -1999. The serological testing using IgM antibody-capture enzyme-linked immunosorbent assay (MAC-ELISA) later tested and showed positive for dengue virus antibody. Since this report could not demonstrate clinical features of dengue infection concomitant with KD, therefore we summarized only the first and our cases that showed simultaneous presentations of the two diseases in Table 1.

Concomitant of KD and other infectious diseases has been reported such as measles, enterovirus, respiratory virus, Epstein Barr virus, *Staphylococcus aureus* and *Streptococcal pyogenes*\(^7-12\). Some reports demonstrated superantigens such as toxic shock syndrome toxin (TSST), Staphylococcal protein A (SpA) and Streptococcal pyrogenic enterotoxin B and C (SPE B and C) in KD patients\(^13-15\). These superantigens can activate an immune system detected by an increase in number of T cells expressing a specific T cell receptor (TCR V beta) region\(^16\). But it is not conclusion that KD is a supergantigen-induced disease\(^15\). Until now, no report can confirm the etiologic organism of KD. The concomitant of dengue infection and KD may be due to two possible reasons. First the association between dengue infection and KD is due to coincidence of the two diseases. Since Thailand is an endemic area of dengue virus infection and the prevalence of KD in Thailand tends to increase, concomitant of the two diseases is possible and is expected to be found more frequently in the future. Second it has been reported that dengue infection can modify immune response during acute infection\(^17\). This aberrant immune system may affect the host in susceptible to superantigen from endogenous organisms and results in clinical features of KD. However, the concomitant of KD and dengue infection can modify the clinical course of each disease and causes some difficulties in diagnosis and management.

**Acknowledgement**

The authors wish to thank Dr. Ananda Nisalak from the Armed Forces Research Institute of Medical Sciences (AFRIMS) for serological test and Dr. Wanla Kulwichit from Department of Medicine, Chulalongkorn University, Faculty of Medicine for PCR test.

**References**


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**Table 1.** Reported cases of dengue infection and KD

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex/Age</th>
<th>Type of KD</th>
<th>Grading of dengue infection</th>
<th>Coronary artery aneurysm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M/10 yr</td>
<td>Atypical</td>
<td>DHF grade III</td>
<td>LCA</td>
</tr>
<tr>
<td>2</td>
<td>F/11 mo</td>
<td>Typical</td>
<td>DHF grade III</td>
<td>LCA</td>
</tr>
</tbody>
</table>

Note: M = male, F = female, DHF = dengue hemorrhagic fever, LCA = left coronary artery

รายงานผู้ป่วยและทานวรรณограмม์: การติดเชื้อไวรัสต่อเพิ่มกับโรคคาวาซากิในผู้ป่วยเด็ก

จุฑารัตน์ เมฆณัสนิธิ, อิศยุ, พันธุ์จริญ, จิตตัณดา, ติวิษณุศาส, พระยา เลิศศิริพจน์จริญ, อุษา ทิศuations, จุล ทิศuations

ผู้ป่วยเด็กหญิงอายุ 11 เดือน ผู้ป่วยเด็กหญิงอายุ 6 ปี ผู้ป่วยมีโรคพยาบาล ตรวจพบอาการป่วยสูง หูต่อตี ตาแดง ปากแฉะแตก ต้มน้ำเหลืองหลังทุ่ง ตัวบิด มีเข็มมี maculopapular rash และคราบเลือดออกที่ลำตัว หน้า และแขน ผลการตรวจเลือดพบ การเพิ่มขึ้นของแอล्टีแมทหลงย์กี altermal lymphocyte, จำนวนแคลคิคเลือด ต่ำกว่าปกติ และ อัตราการตกของแอล์กลีเซด็นท์ (erythrocyte sedimentation rate) มากกว่า 56 มม./ชม. ได้รับการรักษาด้วย intravenous immunoglobulin ในวันที่ 9 ของโรค ออกแบบการองค์การพยาบาลและการไปโรงพยาบาลที่เหลือ ออกแบบค้นโรคไวรัสข้างเข้าในวันที่ 15 ของโรค พบการเพิ่มขึ้น 4 เท่าของระดับแดนติบอติคเตอร์ไวรัสเชื้อกีฬี hemagglutination-inhibition test จากการทานวรรณกรมรณ์พบว่า รักษาของโรคที่เป็นโรคที่ 2 ที่พยาบาลติดเชื้อไวรัส แต่งกิจ ร่วมกับโรคคาวาซากิ ซึ่งมีการค้นโรคไวรัสที่มีผลต่อไปและอาการทำให้โรควินิจฉัยได้ยาก และมีความลาดทาง การทิศuations