CASE REPORT

Dengue Fever Triggering Kawasaki Disease

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Received: May 17, 2016;
Initial review: July 01, 2016;
Accepted: October 10, 2016.

Background: Several bacterial and viral infections are listed as triggering factors for Kawasaki disease; association with dengue fever is rare. **Case characteristics:** A 5-year-old girl who presented with fever that was confirmed to be dengue fever, and subsequently improved, except that the fever persisted. She fulfilled diagnostic criteria for Kawasaki disease on day 7 of fever. **Outcome:** Child responded satisfactorily to intravenous immunoglobulin administration. **Message:** Kawasaki disease should be kept as one of the probabilities in a case of dengue if fever persists beyond the expected duration.

Keywords: *Dengue virus, Lymphadenopathy, Mucosal inflammation, Rash, Thrombocytopenia.*

The exact etiology of Kawasaki disease is not known; infection is hypothesized to play a major triggering role in genetically predisposed individuals. Multiple infectious agents have been implicated, including viruses, bacteria, rickettsiae and toxins [1]. The association of Kawasaki disease with dengue fever is rare, and is a diagnostic challenge, as clinical features of the two diseases may overlap. We report a child with serologically confirmed dengue fever who subsequently developed Kawasaki disease.

Case Report

A 5-year-old girl was admitted to our hospital with high grade fever for 3 days along with vomiting and decreased oral acceptance. She had tachycardia (pulse 110/min), respiratory rate of 32/min and a normal blood pressure (90/60 mmHg). Physical examination revealed erythematous macular rashes over whole body, petechiae on extremities, and tender hepatomegaly. The hematocrit was elevated (41%), and there was associated thrombocytopenia (platelet count 67 × 10^9/L). Chest radiograph showed right-sided pleural effusion. A clinical diagnosis of Dengue fever with warning signs was made, as per WHO definition [2]. Etiology was confirmed by a positive NS1 antigen, and positive dengue IgM and IgG serology. The child was managed as per standard treatment guidelines [2]. She improved gradually over next three days. Vomiting subsided, appetite improved and vitals were maintained. There were no respiratory or abdominal symptoms. The platelets count improved to 140×10^9/L and hematocrit normalized. However, she continued to have spikes of fever, touching 39ºC or more.

On day 7 of fever, she developed extreme irritability and a diffuse polymorphic rash; examination revealed conjunctival redness, strawberry tongue, and mucositis. Two tender lymph nodes were palpable in the left anterior cervical triangle measuring approx 1.5 cm each. Tonsils were not enlarged and systemic examination was normal. She was investigated for co-existing infections including malaria, enteric fever, hepatitis, urinary tract infection, pneumonia, liver abscess and tuberculosis. Blood counts were normal and peripheral smear revealed no abnormal cells or parasites. She had negative serology for typhoid fever and viral hepatitis; SGPT was mildly raised (68 IU/L). ESR was 65 mm in the 1st hour. The chest *X*-ray was normal and tuberculin test revealed no induration after 48 hours. Cultures of blood, urine, and throat were sterile. Ultrasonography of abdomen revealed mildly enlarged liver with slight hypo-echogenicity. During the period of investigations, she continued to be irritable and had high grade fever. Additionally, she developed tender erythema of palms and soles with mild edema of hands. We suspected Kawasaki disease in view of persistent fever, extremity changes, rash, conjunctival congestion, oral mucosal involvement, and unilateral cervical lymphadenopathy, along with a negative work-up for common infections. ECG and echocardiography were normal.

We treated her with intravenous immunoglobulins (IVIG) (1 g/kg for 2 days) and high dose oral aspirin (40 mg/kg/day). Child showed significant improvement in the next 48 hours with the resolution of fever and rash. There was a marked improvement in conjunctival redness and irritability. Oral mucosa and tongue slowly regained normal texture and color. Aspirin was reduced to 5 mg/kg/day on day 14 of illness. At discharge, all signs of active inflammation had disappeared. A repeat

echocardiography at 12 weeks follow-up was also normal, and the child had no clinical evidence of any residual disease/complication.

DISCUSSION

This child presented with fever during an outbreak of dengue fever in the city. We had several reasons, besides fever, to suspect dengue fever in the index case. These included presence of characteristic rash, evidence of mucocutaneous bleeds, thrombocytopenia and capillary leak (suggested by pleural effusion). The diagnosis was established by positive dengue serology.

Recovery from dengue is characterized by symptomatic improvement (fever abets, vomiting and pain abdomen subsides, and most importantly the appetite returns), associated with improvement in platelet count. Our child had all the features of recovery except that the fever persisted. This may happen in a child having co-existing malaria, enteric fever, viral hepatitis, or urinary tract disorders. We also initially explored these diagnoses. Diagnosis of Kawasaki disease was clinical as suggested by persistence of fever and fulfilment of the other criteria such as mucosal and peripheral involvement typical of the disease. Prompt recovery following intravenous immunoglobulin also lend credit to the diagnosis.

The association of dengue fever with Kawasaki disease is rarely reported. We found only four reports of this association [3-6]. These children were aged between 26 months to 10 years. Of these, three had coronary artery involvement.Kawasaki disease in the present case may have been triggered by dengue fever. On the other hand, a chance association with dengue fever can not be excluded. Sopontamark, *et al*. [7], conducted a study on sera of 65 cases diagnosed as Kawasaki disease, collected over 4 years. Of these, 9 (18.7%) patients had proven dengue infection, on the basis of serological titers. None of these; however, had clinical manifestations of dengue fever. These findings were reported to be significant and the possibility of dengue fever as a trigger for Kawasaki disease by altering the immune response in susceptible host during the acute phase .

Despite India being endemic for dengue fever, there has been only one previous report of Kawasaki disease with dengue fever from our country [6]. We are reporting this case to enlighten our colleagues on a possible association between the two illnesses and to consider Kawasaki disease in a child with dengue fever whose fever is not responding.

Contributors: PG: conceptualized the report. The case was managed by EA, DS and PG. Literature review was carried by EA and PG. EA wrote the draft manuscript which was edited by DS and PG. All three authors have seen and approved the manuscript.
Funding: None. *Competing interests*: None stated.

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