Kawasaki Disease in Dizygotic Twins in Turkey

To the Editor:

Kawasaki disease (KD) is an acute systemic vasculitis syndrome predominantly affecting infants and young children. It is the commonest cause of childhood acquired heart disease in developed countries. Coronary artery injury develops in 25% of untreated and 5% of treated children¹. We describe KD in dizygotic twins presenting with incomplete features resulting in coronary artery dilatation in one of the patients.

Previously healthy 7-month-old twin boys were admitted to our center with a 10-day history of fever, irritability, poor feeding, and high-pitched crying. Before referral to our hospital, amoxicillin-clavulanate was prescribed with the diagnosis of upper respiratory tract infection. However, 3 days after beginning treatment, the children were still febrile. Intramuscular ceftriaxone (1 g/day) was initiated. After 7 doses of antibiotics the patients were still feverish, so they were referred with the suspicion of meningitis/sepsis or severe viral infection. There was no history suggestive of a specific focus of infection. Their perinatal period and medical history were unremarkable except for bronchiolitis 20 days before.

On admission, the children were very irritable, their body temperature was 39°C, and oropharyngeal mucosa was erythematous. A complete sepsis examination of both patients showed leukocytosis ($21.9 \times 10^9/l$ with 68% neutrophils and $15.3 \times 10^9/l$ with 71% neutrophils), hemoglobin 11.2 g/dl and 11.8 g/dl, elevated erythrocyte sedimentation rate (90 mm and 78 mm at the end of 1 hour, respectively), raised serum C-reactive protein (78.5 mg/l and 46.2 mg/l), and normal platelet count ($179,000/mm^3$ and $149,000/mm^3$). Culture of a throat swab did not reveal any growth. Chest radiographs and abdominal ultrasonography were normal. Urine examination and culture demonstrated sterile pyuria. A lumbar puncture revealed 50 leukocytes with glucose 59 mg/dl and protein 29 mg/dl in the first patient, while his twin brother's cerebrospinal fluid (CSF) was normal. Blood and CSF cultures were sterile in both patients. During the next few days the fever continued, with strawberry-red tongues; dry, cracked, and red lips; injected bulbar conjunctivitis; and desquamation of the fingers and perianal area. KD was suspected and echocardiographic examination demonstrated ectasia of left (LCA) and right coronary arteries (RCA) with aneurysmal dilatation (maximum 4.6 mm in LCA and its branches and 5.6 mm in RCA) on the eighth day of the hospitalization in twin 1 (Figures 1 and 2) and was

Figure 1. Apical 4-space image: dilated right coronary artery and its branches. RCA: right coronary artery; RA: right atrium; RV: right ventricle; AO: aorta.

Figure 2. Apical 4-space image: dilated left coronary artery and its branches. LCA: left coronary artery; RA: right atrium; RV: right ventricle; AO: aorta.

normal in twin 2. Both children were treated with high doses of intravenous immunoglobulin (2 g/kg over 12 h) and aspirin (80 mg/kg/day for 14 days followed by 5 mg/kg/day for the next 3 months). They had a quick recovery and their fever resolved within 24 hours. Tests for antinuclear antibodies (ANA) and antibodies against dsDNA were negative. Tests for anti-smooth muscle antibodies (anti-SMA) were positive in twin 1. Repeated blood counts showed thrombocytosis. On followup, repeated echocardiography at the end of the first month revealed a decrease in coronary dilation in twin 1 and continued normal findings in twin 2.

The etiology of KD remains unknown. Shulman, *et al* hypothesized that 1 or more infectious agents may trigger pathological immune responses in individuals with certain genetic susceptibilities, resulting in clinically recognizable KD². In Japan, siblings of an index case have a 10-fold increased relative risk of KD³. The incidence is even higher in twins regardless of zygosity⁴. More than half of the second cases develop 10 days or less after the index case⁵. Our twins were admitted to hospital because of the same complaints with a 4-day interval.

A pathologic feature of KD is systemic vasculitis affecting medium-size arteries, especially the coronary arteries. Immune activation in the acute phase is an important factor in the pathogenesis of KD. The significance of humoral factors such as antiendothelial cell antibodies (AECA) or circulating immune complexes is unclear⁶. Falcini, *et al* reported that among 34 children with KD, antineutrophil cytoplasm antibodies, AECA, and anticardiolipin were present in 8%, 26%, and 30% of patients, respectively, while ANA were negative in all patients⁷. No relationship between immune findings and cardiac involvement could be identified. In another study, in 21 children with KD, ANA were detected in 9.5% while antithyroid microsomal antibodies were positive in 23.9% of patients⁸. Suzuki, *et al* showed positive immunoreactions to vascular walls of coronary arteries in 16 of 48 patients with KD⁹. Positive immunoreactivity was detected more frequently and more intensely in patients with coronary artery lesions. In our study, we detected anti-SMA in twin 1, who developed a coronary artery aneurysm, while all autoantibody tests were negative in twin 2.

Genetic predisposition and possible exposure to a common infectious agent are the proposed factors of KD in twins. Monitoring of development of autoantibodies may aid in understanding of pathogenesis of cardiovascular involvement, which is the leading cause of morbidity and mortality.

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