Non-classical Kawasaki Disease in a 2 Month Old Infant

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Kawasaki disease is an acute vasculitis of unknown etiology that has been found in all the pediatric age groups. However, most cases occur in children aged 6 months to 8 years old. The diagnosis is confirmed by the presence of fever lasting for at least 5 days and four of the following criteria, without evidence of another known disease: a) bilateral conjuctival injection, generally non-purulent; b) changes of mucous membranes in the upper respiratory tract such as injected pharynx and lips, strawberry tongue; c) polymorphous rash; d) changes in the extremities such as peripheral edema and erythema, periungual desquamation; and e) acute, usually unilateral, non-purulent cervical adenopathy [1]. Since there is no single diagnostic laboratory test, physicians use laboratory markers of inflammation (high white blood cell count, C-reactive protein, and erythrocyte sedimentation rate) to establish the diagnosis of Kawasaki disease. In some cases not all the criteria are met, and the coronary artery abnormalities develop later. The term incomplete (or atypical) Kawasaki is used for these patients [1]. Coronary artery aneurysms develop in 20–25% of untreated patients but administration of intravenous immunoglobulin within the first 10 days of fever significantly reduces this incidence [1].

We report a case of an 8 week old infant with Kawasaki disease who presented with fever followed by unilateral cervical lymphadenitis. He developed coronary dilatations despite early initiation of treatment with IVIG on day 6 of the febrile disease.

IVIG = intravenous immunoglobulin

Patient Description

An 8 week old male infant was admitted with fever lasting a few hours, without accompanying symptoms. The mother's pregnancy, delivery and past medical history were unremarkable. Physical examination on admission demonstrated an ill-appearing baby with grunting and reduced capillary refilling. Body temperature was 38.9°C, blood pressure 90/47, and oxygen saturation in room air 97%. A mild systolic murmur, graded 1–2/6, maximal over the left sternal border was heard. Several purpuric lesions, 1–3 mm in diameter, were observed on his lower extremities. The rest of the physical examination was unremarkable. Laboratory tests revealed leukocytosis, thrombocytosis, elevated C-reactive protein [Table 1], with normal urinalysis and cerebrospinal fluid analysis. At that point, erythrocyte sedimentation rate was normal, as seen sometimes in the initial phases of inflammation. Urine, blood and cerebrospinal fluid cultures were taken and found negative. The chest X-ray was normal, and an echocardiogram demonstrated a small secondum atrial septal defect. Antibiotic treatment with ampicillin and cefotaxime was initiated.

On day 2 (day of admission = day 0), a right cervical swelling appeared. Ultrasound demonstrated enlarged lymph nodes. On day 5 the swelling enlarged and became warm and erythematous. A bilateral non-purulent conjunctivitis appeared. The child became edematous with low plasma albumin levels [Table 1], most probably due to capillary leak. Urea, creatinine, electrolytes, aspartate aminotransferase and alanine aminotransferase were within the normal range. Hemoglobin dropped to 6.7 g/L, prothrombin time was 21.2 seconds (56% of control), and the activated partial thromboplastin time was 41.8 seconds. The D-dimers were 3789 ng/ml (normal 50–500 ng/ml), and a diagnosis of disseminated intravascular coagulation was made. The patient was treated with fresh frozen plasma and packed cells, and clindamycin was added because of the persistent fever. A lymph node puncture revealed no pus and a sterile culture. On day 6 a second lumbar puncture was performed, which demonstrated pleocytosis (165 cells/3 fields, 31% polymorphonuclears, 69% lymphocytes), normal glucose and protein levels, and negative culture, compatible with the

Table 1. Laboratory results in a young infant with Kawasaki disease

	Admission	Day 6	Day 13	Day 20	Discharge
WBC (kg/µl)	18.6	41.9	38.6	14.8	11.8
PMN (%)	73.6	73	44.5	9.6	8.1
Lymphocytes (%)	18.1	18	42.3	78	77.8
Hemoglobin (g/dl)	9.6	6.7	7.4	8.7	9.2
Platelets (kg/¼l)	608	228	1064	2031	1271
CRP (mg/L)	36.15	236	4.86		
ESR (mm/hr)		15	90	45	
Albumin (g/L)	41	23	25	34	36
CK (U/L)		35			

WBC = white blood cells, PMN = polymorphonuclear cells, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, CK = creatine kinase.

diagnosis of aseptic meningitis. A bone marrow aspirate demonstrated reactive colonies without evidence for malignancy. Owing to suspected incomplete Kawasaki disease, IVIG (2 g/kg) was initiated.

Due to the persistent fever, and despite the fact that the echocardiogram on day 7 showed no dilation of the coronary arteries, a second dose of IVIG (2 g/kg) was given 48 hours later. A clinical improvement was observed following that dose, and corticosteroids or anti-tumor necrosis factor medications were therefore not considered.

On day 17 the infant's body temperature normalized, and a third echocardiogram revealed a dilated (7 mm) coronary artery (left anterior descending). Treatment with aspirin (100 mg/kg/24 hours), low molecular weight heparin (enoxaparin 1 mg/kg) and a beta-blocker (propanolol 2 mg/kg/day) was initiated. A few days later periungual desquamation appeared on his hands.

On day 23 the infant was discharged in excellent general condition on a low dose of aspirin (5 mg/kg/24 hr) and propanolol (2 mg/kg/day). At a recent clinic appointment, at the age of 6 months, the infant appeared healthy and the echocardiogram indicated that the coronary dilatation had decreased to 3 mm.

Comment

Kawasaki disease is rare among infants younger than 3 months of age, and the incidence in children younger than 6 months is 3–11% [1,2]. Since incomplete Kawasaki is common among young infants, in many cases the diagnosis is made *post factum*, following the detection of coronary abnormalities. Therefore, the initiation of IVIG treatment is often also delayed, and the incidence of cardiac sequelae such as giant coronary artery aneurysms (more than 8 mm wide) and fatalities is higher [2]. A recent study demonstrated that a high proportion of general pediatricians (>50%) and infectious disease subspecialists (25%) did not consider the diagnosis of Kawasaki disease in children younger than 6 months and older than 8 years [3]. However, early initiation of IVIG can help reduce the prevalence of coronary abnormalities from 20–25% to 2–4% [1]. In our patient, coronary dilatation appeared despite prompt diagnosis and treatment on day 6, and despite the fact that a second dose of IVIG was given. However, the relatively good outcome – the child is currently well with a mild coronary dilatation – may be attributed to the early IVIG treatment.

An uncommon physical finding in this infant was the marked unilateral lymphadenitis. Among the diagnostic criteria for Kawasaki disease, unilateral cervical lymphadenopathy is the least common. It is present in approximately 50–70% of patients with the classic form of the disease, whereas each of the other four criteria (conjunctivitis, changes in the mucosa of the oropharynx, peripheral extremities edema/erythema, and rash) is found in almost 90% of cases [4,5]. Although cervical lymphadenitis is much less common than lymphadenopathy, it should be included in the clinical spectrum of Kawasaki disease. Stamos and Shulman [4] reported 11 Kawasaki patients with a median age of 5 years who had prominent lymphadenitis and an initial diagnosis of bacterial cervical lymphadenitis or deep neck infection. Hsiu-Tsun and colleagues [5] found a higher incidence of lymphadenitis in patients with the disease who were older than 5 years or younger than 5 months, including a 3 month old infant (total of 14 patients).

In conclusion, we have presented a case of an 8 week old boy with non-classical Kawasaki disease. Physicians should be aware of the existence of the disease in this age group and that unilateral lymphadenitis may be a part of the clinical presentation.

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