Case Reports

Kawasaki Disease—Treatment with Intravenous Immunoglobulin During the Acute Stage

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Kawasaki Disease has emerged as a major pediatric disorder in many countries and is now believed to be a leading cause of acquired heart disease(l). It has only been infrequently reported from India and, to the best of our knowledge, has never been reported to have been successfully treated with intravenous immunoglobulin during the acute stage(2-4). We report here one such child who was managed by us recently and who, at 1 year follow-up, does not appear to have developed arterial aneurysms.

Case Report

A 1½ -year-old boy first developed fever in early May 1994. He was seen by the family physician and prescribed chloroquin and paracetamol. The fever, however, continued and on day 4 of the illness he was brought to our institute. He was diagnosed to have an upper respiratory infection and given symptomatic therapy. Fever, however, persisted and on day 7 the parents noted that he had redness in the eyes and had also developed faint reddish spots over the trunk and limbs. His lips were also red and he was markedly irritable. Physical examination showed normal anthropometric parameters. He was febrile (38° C) and irritable. The pulse was 130/min, RR 30/min and BP 100/70 mm Hg. There was conjunctival injection but no eye discharge. The lips were enythematous but the tongue was normal. Palms and soles were red with a peculiar indurative edema over the finger tips and toes. There was bilateral cervical lymphadenopathy (0.5-1 cm), the nodes being firm but non-tender. Based on these clinical findings a presumptive diagnosis of Kawasaki Disease was made and the child investigated.

Hemogram showed an Hb of 10.1 g/dl, total leukocyte count of 11,000/cu mm with 69% polymorphs and 29% lymphocytes. Platelet count was markedly elevated (8.2 lakhs/cu mm) and the ESR was 52 mm in the 1st hour. His blood culture was sterile and the Widal non-reactive. ASO titer was <200 IU/ml, CRP being positive. Blood biochemistry showed normal serum electrolytes and renal and liver functions. There was no albumin in the urine and microscopy did not reveal any casts. X-ray chest was normal and there was no cardiomegaly. Mantoux test was non-reactive. The ECG was normal. Echocardiography was done during the second week of illness and it showed normal left ventricular function with no evidence of any dilatation or aneurysms of

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coronary arteries. There was no evidence of any pericardial effusion. By this time (day 12) the child had developed characteristic desquamation of skin on fingers and toes - a finding virtually pathognomonic of Kawasaki Disease in this clinical setting *(Fig.* 2).

Intravenous immunoglobin (400 mg/ kg/day x 5 days) along with high dose aspirin (100 mg/kg/day) was started on day 9 of the illness. The child became afebrile by day 4 and was discharged after 8 days of hospitalization on low dose aspirin (5 mg/ kg/day). On follow-up 2 weeks later the platelet count had dropped to 1.6 lakhs/cu mm and the ESR was 20 mm in 1st hour. Repeat echocardiography done 1 year after the initial illness was also normal, there being no evidence of coronary aneurysms. Aspirin was discontinued after 12 months. On clinical examination there was no evidence of peripheral arterial aneurysms.

Discussion

Kawasaki Disease was first described by Tomisaku Kawasaki of the Japan Red Cross Hospital in Tokyo in 1967 when he reported 50 children with an acute febrile illness and certain peculiar skin manifestations(5). This was followed by

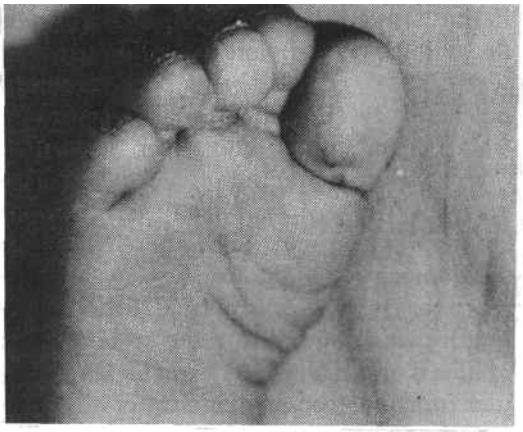

Fig. 1. Showing desquamation of skin over toes.

similar reports from the United States(6). The major significance of this disease relates to the fact that 20-30% of these patients, if left untreated during the acute phase, go on to develop coronary artery abnormalities with consequential ischemia, infarction or death (l,7,8). Kawasaki Disease has now become a leading cause of acquired heart disease in children in many countries (l).

The diagnosis of Kawasaki Disease is made on the basis of certain clinical findings *(Table I),* there being no specific confirmatory laboratory tests. Our case fulfils the clinical criteria required to make a diagnosis of Kawasaki Disease. It must be noted that all criteria need not be present in all the children. For example, adenopathy is present in only 50% of the children and each of the other criteria is found in approximately 90% of patients with classic Kawasaki Disease(l).

A large number of other less specific clinical features may be present *(e.g.,* arthritis/ arthralgia, hepatic dysfunction, aseptic meningitis and pneumonitis (l). Though none of the laboratory features is diagnostic, most children with Kawasaki Disease would have polymorphonuclear leukocytosis, a raised erythrocyte sedimentation rate and elevations of other acute phase reactants *(e.g.,* C-reactive protein, alpha-1 anti-trypsin). Thrombocytosis is also characteristic(1).

The incidence of Kawasaki Disease is highest in Japan but it has been reported from virtually all parts of the world. The first case from India was reported in 1977(2). At that time, however, no specific therapy was known for this disorder. Nitsure *et al.(3)* used intravenous irnmunoglobulin (IVIG) in a child from Pune, but by that time he had already developed coronary and peripheral artery aneurysms. Seshadri *et al.* have reported a 14 years old boy with typical features of Kawasaki Disease but the authors have not

commented on the use of IVIG(4). Our case, therefore, is probably the first child in India who was treated with IVIG during the acute phase of the illness.

The conventional treatment of this disease involves use of IVIG for 4-5 days(l,7). Recently, however, single dose IVIG (1-2 g/kg) (9,10) has also been used successfully for management of this condition, although experience with this regime is still limited(10). The precise mechanism of action of IVIG is not understood. However it has been hypothesized that it blocks the Fc receptors on macrophages and down regulates cytokine production and action (l,7,9). The morphological correlates of these actions pertain to a cessation of the progression of the vasculitis from the stage of peri-arteritis to pan-arteritis. IVIG should be used as early as possible once the diagnosis is made, but can be used with benefit even later on in the course of the illness if aneurysms have not developed.

Aspirin is used in high doses initially because of its anti-inflammatory effect. It is recommended that this dose may be decreased once the child becomes afebrile and the low anti-thrombotic dose (3-5 mg/ kg/day) be continued for 6-8 weeks(l,7). Aspirin alone, however, does not decrease the frequency of development of arterial aneurysms. Use of corticosteroids is not recommended.

Pediatricians should be more aware of this condition because if it is diagnosed early and specific treatment given, the long term cardiac complications can be avoided. Kawasaki. Disease should be considered in the differential diagnosis of acute febrile illnesses in children where the duration of fever is more than 5 days. It cannot be over-emphasized that the diagnosis of this condition is essentially clinical and is based on the diagnostic criteria listed for this purpose *{Table I).* The aim of this communication is to sensitize pediatricians in India to the existence of this condition and the benefits that accrue from early specific therapy.

TABLE I- *Diagnostic Criteria for Kawasaki Disease (l).*

A. Fever lasting for atleast 5 days.

B. Presence of four of the following five conditions:
   1. Bilateral conjunctival injection
   2. Changes of the mucosae of the oropharhyx, including injected pharynx, injected and/or fissured lips, strawberry tongue.
   3. Changes of the peripheral extremities, such as edema and/or erythema of hands and/or feet, desquamation usually beginning periungually.
   4. Rash, primarily truncal; polymorphous but nonvesicular
   5. Cervical lymphadenopathy.

C. Illness not explained by other known disease process.

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