The Turkish Journal of Pediatrics 34: 115 - 120, 1992

KAWASAKI SYNDROME*

*Nur Olgun MD**, Hasan Özkan MD***, Hale Ören MD***
*Nesrin Erdem MD**, Necla Çevik MD*****

SUMMARY: Olgun N, Özkan H, Ören H, Erdem N, Çevik N. (Department of Pediatrics, Dokuz Eylül University Faculty of Medicine, İzmir, Turkey). Kawasaki syndrome. Turk J Pediatr 34: 115-120, 1992.

Kawasaki syndrome, also known as mucocutaneous lymph node syndrome, is an acute vasculitis of infants and young children. We describe a four-year-old girl who presented with fever, a diffuse erythematous maculopapular rash, bilateral nonpurulent bulbar conjunctivitis, dry, red, fissured lips, a tongue with a strawberry "appearance", an erythematous pharynx, indurative erythema, and edema and desquamation of the face, hands and feet. She probably developed mitral valve prolapse during the course of the disease. The diagnosis of Kawasaki syndrome was arrived at by excluding other diseases and by the presence of all the clinical criteria for Kawasaki syndrome. Since this syndrome is rarely encountered in Turkey, this case is presented and the literature regarding the syndrome is reviewed. *Key words: Kawasaki syndrome, mucocutaneous lymph node syndrome.*

Kawasaki syndrome (KD), also known as mucocutaneous lymph node syndrome, is an acute vasculitis of infants and young children. Standard diagnostic criteria for Kawasaki syndrome include A) Fever persisting for five days or longer. B) The presence of four of the five following conditions: 1) bilateral conjunctival injection; 2) change(s) in the mucous membranes of the upper respiratory tract, such as infected pharynx, injected, dry, fissured lips and protuberance of tongue papillae ("strawberry tongue"); 3) change(s) in the extremities such as edema of the hands and feet, erythema of the palms and soles, desquamation of the skin including the periungal region; 4) Polymorphous exanthema of the body trunk without vesicles; 5) cervical lymphadenopathy; c) Illness cannot be explained by any other known disease process[1].

Approximately 20 percent of children with KD develop cardiovascular sequelae, the major cause of morbidity and mortality in this disease[2]. The etiology of KD remains unknown but the infrequent person-to-person transmission, the differences in racial incidence, and the clinical findings of multi - system vasculitis suggest that it may be caused by an infective agent(s) that leads to an immune - mediated syndrome in certain genetically predisposed individuals[1].

* From the Department of Pediatrics, Dokuz Eylül University Faculty of Medicine, İzmir.
** Associate Professor of Pediatrics, Dokuz Eylül University Faculty of Medicine.
*** Research Assistant in Pediatrics, Dokuz Eylül University Faculty of Medicine.
**** Professor of Pediatrics, Dokuz Eylül University Faculty of Medicine.

Kawasaki disease occurs worldwide and affects children of all races, with Asians, particularly Japanese and Koreans, at highest risk, followed by blacks and then Caucasians who seem to be at lowest risk[1]. This syndrome, rarely encountered in Turkey, was reported in this country by Özsoylu et al[3] in 1976. We describe a four-year-old girl who fulfilled all the diagnostic criteria for KD and developed mitral valve prolapse.

Case Report

A four-year-old girl was admitted to the pediatric clinic of Dokuz Eylül University Hospital for evaluation of a 15 - day history of fever, rash, cervical adenopathy, congestion of the eyes, redness and fissuring of the lips, and swelling of the hands and feet.

Physical examination revealed a well developed child. Her weight was 18 kg and height 103 cm. She appeared irritable and acutely ill. The temperature was 40.5 °C rectally. She had a diffuse erythematous maculopapular rash covering her entire body, dry, red, fissured lips, an erythematous pharynx and a tongue with a "strawberry" appearance. She also had bilateral nonpurulent bulbar conjunctivitis and a lymph node measuring 1.5 cm in diameter in the right cervical region, Beau's lines on her fingernails, mucosal erythema of the vulva, indurative erythema, and edema and desquamation of the face, hands and feet. The remainder of the physical examination was within normal limits (Figs. 1 and 2).

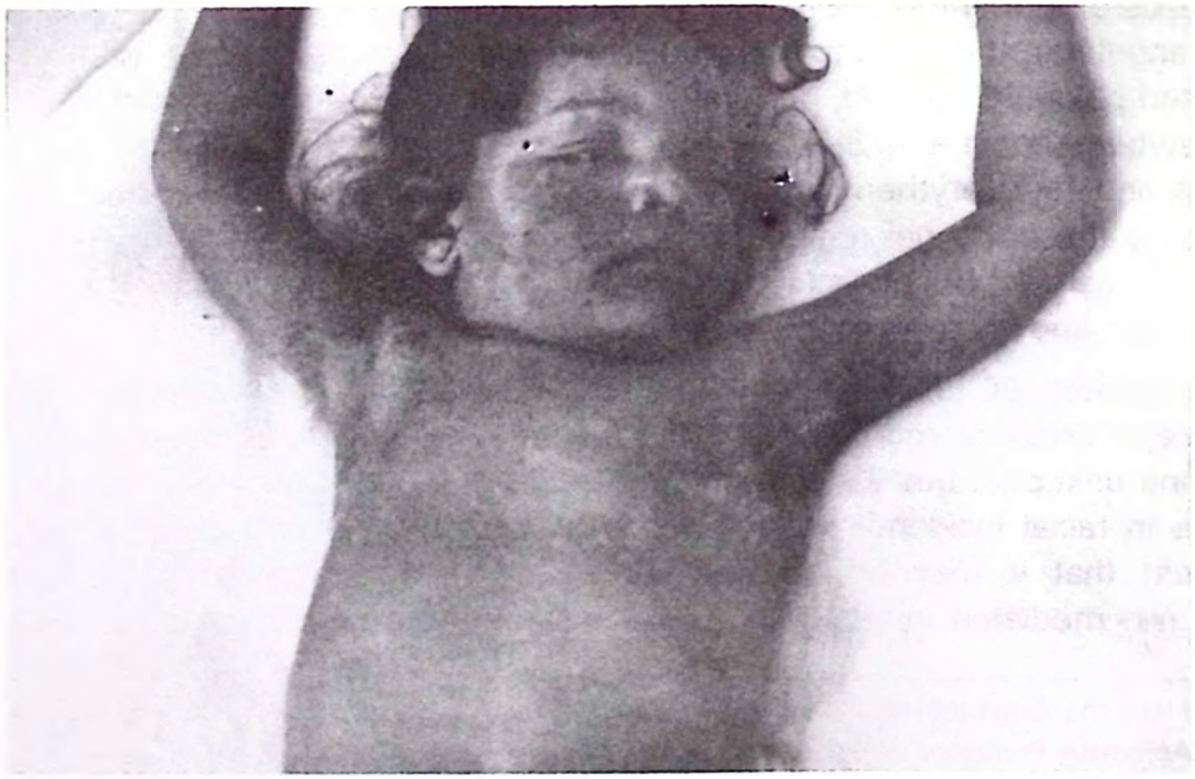

Fig 1: Diffuse erythematous maculopapular rash covering patient's entire body.

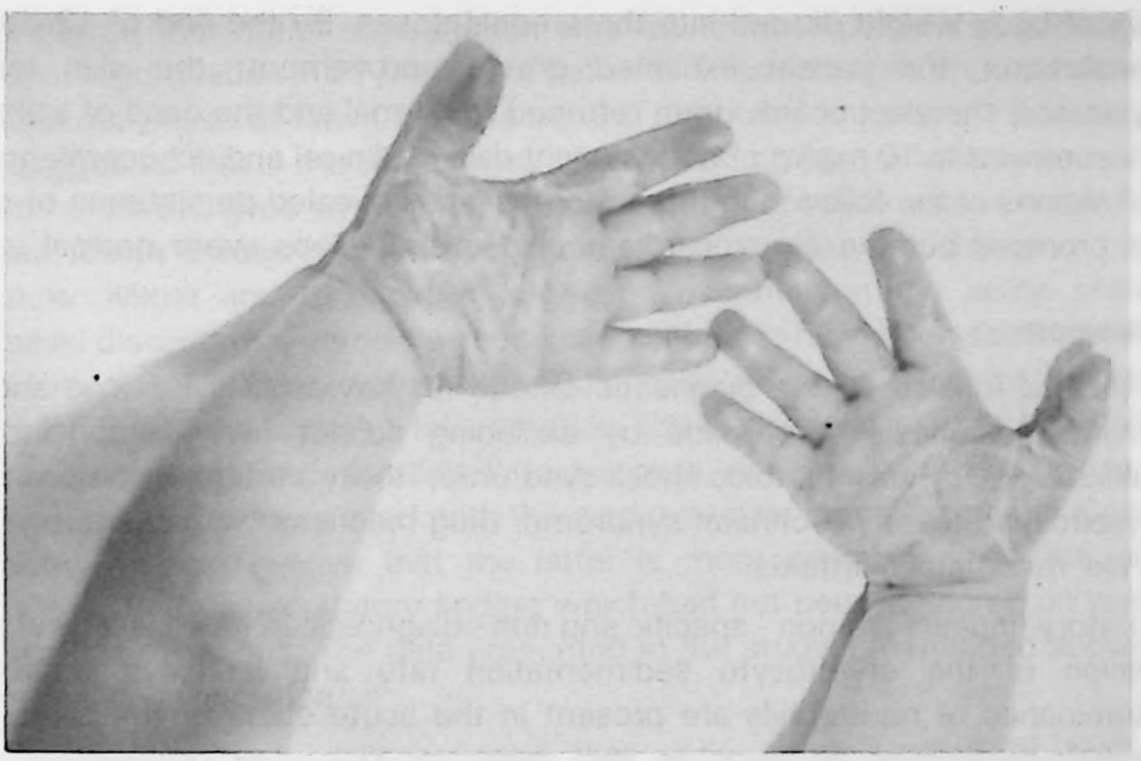

Fig. 2: Desquamation of the hands.

Initial laboratory studies revealed hemoglobin 14 g/dl and white blood cells 12,200/mm^3 with 54 % segmented neutrophils, 44 % lymphocytes and 2 % eosinophils. The platelet count was 350,000/mm^3. The erythrocyte sedimentation rate was 6 mm/hr. Urinalysis, total protein, serum electrolytes, glucose, urea, creatinine, X-ray examinations and the electrocardiogram were within normal limits. Liver function tests were normal except for a mild to moderate elevation of serum transaminases (SGOT = 81 IU/L; SGPT = 104 IU/L). The PPD test was negative. The following examinations were either normal or negative: blood, stool and nasopharynx cultures; viral serology (Epstein - Barr virus, cytomegalovirus, toxoplasma; hepatitis B and rubella); Venereal Disease Research Laboratory test for syphilis; antistreptolysin O; C-reactive protein; antinuclear antibodies; rheumatoid factor and parasitological examination of stool specimens. *E.coli* was isolated from the urine culture. The cutaneous biopsy specimen demonstrated perivascular mononuclear cell infiltration in the dermis.

During the first four days of hospitalization, the patient continued to have daily fevers of up to 40 °C, and the rash increased, despite erythromycin therapy. On the 5^{th} day, a 2/6 midsystolic murmur introduced by a click, was heard at the apex and along the left sternal border. An electrocardiogram showed sinus tachycardia and a first-degree atrioventricular block. The M - mode echocardiogram and two - dimensional studies showed posterior mitral valve prolapse. During the acute phase, salicylate therapy was administered orally in a daily dose of 100

mg/kg of body weight divided into three equal doses. By the end of 12 days of hospitalization, the patient exhibited great improvement; the skin lesions disappeared, the electrocardiogram returned to normal and the dose of salicylate was decreased to 10 mg/kg of body weight daily[7]. Clinical and echocardiographic examinations at the follow - up three months later revealed persistence of mitral valve prolapse but the electrocardiographic examinations were normal.

Discussion

Our patient fulfilled all the diagnostic criteria for Kawasaki syndrome and the differential diagnosis was made by excluding scarlet fever, staphylococcal "scalded skin" syndrome, toxic shock syndrome, Rocky Mountain spotted fever, leptospirosis, Stevens - Johnson syndrome, drug reactions, viral exanthems and juvenile rheumatoid arthritis.

Laboratory findings are non - specific and non - diagnostic in Kawasaki syndrome. Elevation of the erythrocyte sedimentation rate and leukocytosis with a predominance of neutrophils are present in the acute stage of the illness and thrombocytosis may be seen in the subacute stage. In our patient, mild leukocytosis with a predominance of neutrophils was present but the erythrocyte sedimentation rate and the thrombocyte count were normal probably because the patient had been admitted to our clinic in the third week of her illness.

Hepatic dysfunction with mild obstructive jaundice and mildly to moderately elevated levels of serum transaminases have been reported in 10 percent of children with Kawasaki syndrome[4]. Our patient also demonstrated hepatic involvement with elevated liver enzymes.

Echocardiographic and angiocardiographic data reveal that about 20 percent of patients with Kawasaki syndrome develop cardiovascular complications[1,2,5,6]. The earliest cardiac complications occur during the acute stage of the illness and include myocarditis, congestive heart failure, pericarditis with pericardial effusion, mitral and / or aortic insufficiency, arrhythmias and coronary artery aneurysm formation. Electrocardiographic changes are present in at least one - third of patients and include flattening and depression of the ST segment and T wave, decreased voltage and conduction disturbances. Over the next five weeks, these findings generally resolve, but acute coronary arteritis during the first two weeks of illness may lead to coronary artery aneurysm formation[1]. In our case, first - degree heart block and posterior mitral valve prolapse were detected at the end of the acute stage of the illness. The electrocardiogram repeated one week later showed a normal PR interval but echocardiographic examinations at the follow - up three months later revealed persistence of mitral valve prolapse which could have been attributed to papillary muscle dysfunction or valvulitis. Suzuki et

al[7], reported that mitral regurgitation was found in 47 percent of patients and tricuspid regurgitation in 53 percent of patients. These changes are often transient in the acute phase of Kawasaki disease and attributed to carditis. Fujiwara et al[8] also suggested that in the acute phase of Kawasaki disease valvular lesions due to inflammation of valves are very rare, and that most of these lesions result from a cardiac lesion involving the valvular roots, the papillary muscle and the left ventricle. Mitral and tricuspid regurgitation occurring in the acute phase of Kawasaki disease may remain as sequelae, and there have been some necropsy-based reports of severe valvulitis[9]. Additionally , despite a lack of clinical and laboratory evidence of active inflammation, the excised valves may demonstrate both acute and chronic vasculitis[10]. In our case, mitral valve prolapse may have been congenital or associated with the cardiovascular complications of Kawasaki disease. But, we believe that the latter is more probable since the patient presented a new auscultatory finding which had not been detected on previous physical examinations. The data presented in the studies mentioned above may support this association[7-10].

Recent studies have demonstrated that early administration of high-dose intravenous gammaglobulin (400 mg/kg/d for 4 days) plus aspirin (100 mg/kg/d for 14 days) will hasten the resolution of acute manifestations of the disease and reduce the prevalence of coronary artery aneurysms[1,2,11,12]. Low doses of aspirin (3-10 mg/kg/d) are then used as antiplatelet therapy until the aneurysms are resolved or the coronary arteries are demonstrated to be normal.

Our patient was admitted to our hospital in the third week of her illness and she was in the low risk group for development of coronary artery disease, therefore, high - dose aspirin therapy was initiated. Following defervescense, we reduced the dosage of the aspirin to 10 mg/kg/d and continued low - dose aspirin until the end of the convalescent period.

REFERENCES

1. Rowley AH, Gonzales-Crussi F, Shulman ST. Kawasaki syndrome. *Rev Infect Dis* 10:1, 1988.
2. Crowley DC. Cardiovascular complications of mucocutaneous lymph node syndrome. *Pediatr Clin North Am* 31:1321, 1984.
3. Özsoylu Ş, Akgün NA. Akut febril mukokutaneus lenf bezi sendromu (MLNS). *Çocuk Sağlığı ve Hastalıkları Dergisi* 19:57, 1976.
4. Melish ME. Kawasaki syndrome (the mucocutaneous lymph node syndrome). *Annu Rev Med* 33:569, 1982.
5. Kato H, Ichinose E, Yoshioka F, et al. Fate of coronary aneurysms in Kawasaki disease: serial coronary angiography and long term follow-up study. *Am J Cardiol* 49:1758, 1982.
6. Takahashi M, Mason W, Lewis AB. Regression of coronary aneurysms in patients with Kawasaki syndrome. *Circulation* 75:387, 1987.

7. Suzuki A, Kamiya T, Tsuchiya K, et al. Tricuspid and mitral regurgitation detected by color flow Doppler in the acute phase of Kawasaki disease. *Am J Cardiol* 61:386, 1988.
8. Fujiwara T, Takeuchi E, Yoshioka H, et al. Histopathological study of cardiac valvulutis in Kawasaki disease. *Proc Kinki Area Kawasaki Dis Res Jap* 6:28, 1985.
9. Fujiwara H, Hamashima Y. Pathology of the heart in Kawasaki disease. *Pediatrics* 61:100, 1978.
10. Gidding SS, Shulman ST, Ilbawi M, et al. Mucocutaneous lymph node syndrome (Kawasaki disease): delayed aortic and mitral insufficiency secondary to active valvulitis. *J Am Coll Cardiol* 7:894, 1986.
11. Bierman FZ, Gersony WM. Kawasaki disease: clinical perspective. *J Pediatr* 111:789, 1987.
12. Newburger JW, Takahashi M, Burns JC, et al. The treatment of Kawasaki syndrome with intravenous gamma globulin. *N Engl J Med* 315:341, 1986.