

Hospital Practice



The Many Faces of Kawasaki Syndrome

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The clinical challenge lies in recognizing cases not fully meeting the syndrome's diagnostic criteria and those that strongly resemble a variety of infectious and reactive disorders. Prompt treatment with high-dose intravenous immune globulin in combination with aspirin can significantly reduce the frequency and severity of cardiovascular complications.

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Kawasaki syndrome is an acute febrile illness associated with multiorgan vasculitis. It primarily affects infants and young children. Originally described in Japan by Tomisaku Kawasaki in 1967, it was subsequently recognized worldwide in children of every racial group. It also became apparent that the illness is not benign. Indeed, a number of children were reported to die, usually from cardiovascular complications (Figure 1). The

introduction of high-dose intravenous immune globulin (IVIG) in combination with aspirin therapy has significantly reduced the prevalence of coronary artery abnormalities. Early recognition and prompt treatment of the acute syndrome is critical. Unfortunately, the current definition of the syndrome is based on signs and symptoms that also occur in other illnesses. This can result in diagnostic dilemmas, particularly in atypical cases.

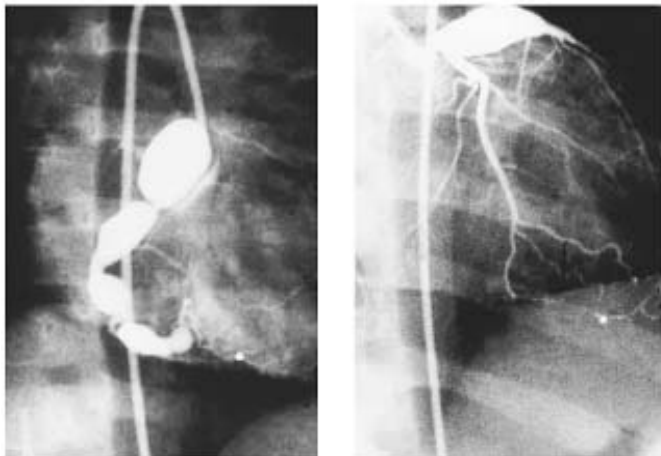


Figure 1. Coronary abnormalities are the most serious complications of Kawasaki syndrome. The angiogram of a 23-month-old child who had had the syndrome six months earlier (left) shows several large fusiform aneurysms in the right coronary artery. The angiogram of a six-year-old who had had the syndrome at 16 months of age (right) shows a giant aneurysm in the left anterior descending artery. Nearly all late deaths from Kawasaki syndrome occur in patients with giant aneurysms. (Angiograms courtesy Ziyad Hijazi, New England Medical Center, Boston)

Today, Kawasaki syndrome is most prevalent in Japan and in children of Japanese ancestry living outside Japan. In Japanese children, the incidence is highest between six and 12 months of age, with a decreasing rate during the first decade of life. The ratio of male to female cases is about 1.5 to 1. Epidemiologic

findings in the United States and Europe have been similar to those in Japan. The syndrome has been reported in all parts of the United States and Europe, occurring sporadically or as temporally limited community-wide outbreaks.

Surveillance studies suggest that in the United States approximately 3,000 patients with Kawasaki syndrome are hospitalized annually. In the United States, the prevalence is greatest among Asians, intermediate in blacks, and lowest in Caucasians. Regardless of the racial group affected, the clinical picture is similar.

Case 1

A three-year-old boy was admitted with an eight-day history of daily spiking fever, sore throat, and rash. Four days earlier, a throat culture had been obtained (which subsequently demonstrated no group A beta-hemolytic streptococcus), and amoxicillin had been prescribed. Despite antibiotic therapy, his elevated temperatures had continued (to a maximum of 103.8°F), and his parents noted swelling of the right side of his neck, with overlying erythema. He also showed increased reluctance to ambulate.

Vital signs on admission were temperature, 39.7°C; pulse, 144/min; respiratory rate, 36/min; and blood pressure, 110/70 mm Hg. Initial physical examination demonstrated an irritable child with a 3X4 cm nontender right cervical lymph node, pharyngeal injection with no exudate, and an erythematous area beginning at the base of the neck and extending onto the chest. The white blood count was 16,700/mm³ with 74% polymorphonuclear leukocytes and 15% immature band forms. A platelet count was 227,000/mm³, and the erythrocyte sedimentation rate was 127 mm/hr. During the next 24 hours, the erythema spread to involve the arms and upper legs, with accentuation in the diaper area. Bilateral conjunctival injection developed, along with abdominal distention and swelling of both hands. Examination of the cerebrospinal fluid revealed an unremarkable Gram stain, a glucose level of 54 mg/dL, a protein level of 17 mg/dL, and a white cell count of 22/mm³. Cardiac ultrasonography identified a 6-mm aneurysm in the right

anterior descending coronary artery. A rectal culture grew coagulase-positive *Staphylococcus aureus* secreting toxic shock syndrome toxin 1.

Kawasaki syndrome was diagnosed, and the patient was started on IVIG (2 gm/kg) and aspirin (100 mg/kg/day in four equal doses). Eight hours later, he was afebrile. On the fourth hospital day, he was discharged.

Classic Clinical Features

The diagnosis of acute Kawasaki syndrome should be considered in a child who has a fever lasting five days or more (without other explanation) and exhibits at least four of five clinical criteria: rash, conjunctival injection, oropharyngeal erythema, swelling and erythema of the distal extremities, and cervical lymphadenopathy (Table 1). The fever is high and prolonged, often spiking to 40°C. In the absence of anti-inflammatory therapy, daily fevers persist for one to two weeks or more.

Table 1. Diagnostic Criteria for Kawasaki Syndrome¹

Fever for five or more days without other explanation plus at least four of the following:²

Nonexudative bulbar conjunctival injection

Oropharyngeal changes (e.g., injected or fissured lips, injected pharynx, strawberry tongue)

Extremity changes (e.g., erythema of palms or soles, edema of hands or feet, periungual desquamation)

Polymorphous rash

Acute nonsuppurative cervical lymphadenopathy

¹A variety of other infectious and noninfectious disorders may present with similar findings. These should be excluded by history, physical examination, and appropriate laboratory tests.

²A diagnosis of atypical Kawasaki syndrome can be made with less than four criteria if coronary artery aneurysms are present.

Other mucocutaneous manifestations are varied, and not all patients exhibit all of them. Approximately 90% of patients experience an exanthem. The eruption favors the trunk and proximal extremities but can be generalized (Figure 2). One of the earliest findings is a perineal eruption presenting as a diffuse macular or plaque-type blanching erythema. The rash is rarely vesicular, pustular, or bullous.



Figure 2. Approximately 90% of patients with Kawasaki syndrome have an exanthem. In the child shown here, a generalized morbilliform rash appeared early in the febrile course of the illness.

Approximately 90% of patients have a nonexudative conjunctival injection. Generally it involves the bulbar conjunctiva to a greater extent than the palpebral conjunctivae. Conjunctival vessels become engorged and dilated. There is no purulent discharge or crusting of the eyelashes, as occurs in bacterial conjunctivitis. In approximately 83% of patients examined within the first weeks of illness, conjunctival injection is associated with anterior uveitis.

Oropharyngeal changes occur in almost all typical cases. The lips become dry and cherry red, and often crack, producing small hemorrhagic fissures (Figure 3). Punctate ulcerations such as those seen in herpes gingivostomatitis are not present, nor are the diffuse erosions with confluent hemorrhagic crusts that are seen in Stevens-Johnson syndrome. The tongue may have a strawberry appearance (caused by hypertrophied papillae) with hyperemia similar to that seen in streptococcal infections. A generalized erythema of the oropharynx is common.



Figure 3. Oropharyngeal changes occur in almost all typical cases of Kawasaki syndrome. The lips become dry and cherry red, and often crack, producing small hemorrhagic fissures. In addition, this boy had erythematous oral mucosa, conjunctival infection, and a generalized morbilliform rash.

Edema and redness of the hands and feet are observed in most cases (Figure 4). The hyperemic areas desquamate 10 to 18 days later, during the subacute phase of Kawasaki syndrome. The desquamation characteristically begins at the tips of the fingers and toes, and may develop into either fine peeling or a shredding of thick casts of palmar and plantar skin, similar to that seen in scarlet fever.



Figure 4. Edema and redness of the hands and feet (top) usually develops during the early phase of Kawasaki syndrome. The hyperemic areas desquamate 10 to 18 days after the onset of illness (bottom). The skin loss characteristically begins at the tips of the fingers and toes and may be either a fine peeling or a shredding of thick casts of palmar and plantar skin.

Lymphadenopathy occurs in only 50% to 75% of patients. Induration, necrosis, and ulceration at the site of a previous BCG vaccination has been described.

Among other clinical features of Kawasaki syndrome (Table 2), arthralgia and arthritis occur in approximately a third of patients and generally last about two weeks. However, joint symptoms may persist for as long as three months. During the acute phase, the arthritis usually involves the small joints. By contrast, involvement of large, weight-bearing joints usually occurs in the second and third week of illness. Tympanitis--a feature consistent with generalized mucous-membrane inflammation--is commonly present. So is urethritis (associated with sterile pyuria). Aseptic meningitis may be present, usually in association with mild mononuclear-cell pleocytosis of the cerebrospinal fluid and with normal glucose and protein. Hydrops of the gallbladder may occur with or without obstructive jaundice. Presenting features may also include diarrhea, vomiting, abdominal pain, cranial nerve palsies, or infarction of organs whose vascular supply is compromised by thrombosis.

Table 2. Associated Features of Kawasaki Syndrome

Arthralgia and arthritis

Aseptic meningitis

Cardiovascular abnormalities, including myocarditis, arterial aneurysms, pericarditis, aortic or mitral regurgitation, or ventricular arrhythmias

Diarrhea, vomiting, or abdominal pain

Hepatic dysfunction

Hydrops of the gallbladder

Peripheral gangrene

Sensorineural hearing loss

Urethritis with sterile pyuria

Uveitis

The acute phase of Kawasaki syndrome is followed by a subacute phase lasting approximately 25 days, during which the fever, rash, and lymphadenopathy resolve but irritability, anorexia, and conjunctival injection may persist. As noted, the subacute phase may include arthritis and arthralgia or desquamation of the fingers and toes. Myocardial dysfunction may also occur. Patients with cardiovascular complications may have persistent cardiac abnormalities. The convalescent phase begins when clinical signs have resolved. It continues until the erythrocyte sedimentation rate returns to normal, usually within 70 days of the onset of illness.

Occasionally, a patient experiences a clinical exacerbation involving recurrence of fever and other acute signs such as rash and conjunctival injection. This occurs most often within a few days after resolution of fever and may be associated with an increased risk of coronary artery disease.

Cardiac Findings

Myocarditis in the acute phase of Kawasaki syndrome occurs during the first week after onset of fever and is often associated with pericardial effusion. Patients rarely progress to cardiac tamponade, and the pericardial effusion generally resolves spontaneously. Congestive heart failure may occur. During the acute phase, it represents myocarditis. During the subacute stage, it is usually caused by myocardial dysfunction secondary to ischemia or infarction.

Coronary artery abnormalities occur in nearly 25% of Kawasaki syndrome patients not treated with IVIG within 10 of the onset of fever. Dilatation of the coronary arteries may be detected by echocardiography soon after onset of fever. Aneurysms of the coronary arteries may be present by the end of the first week of illness. Development of ectasia or aneurysms after three to four weeks is unusual. In rare cases, patients have aortic regurgitation or mitral regurgitation due to valvulitis, transient papillary muscle dysfunction, or myocardial infarction.

On examination, patients with cardiac involvement present with cardiac arrhythmias, gallop rhythms, or tachycardia out of proportion to their fever. Occasionally, aneurysms of the brachial, renal, or iliac arteries develop, usually in association with coronary artery abnormalities.

Case 2

A five-month-old boy presented to his pediatrician with a 15-day history of fussiness and fever to 104°F. Physical examination revealed no abnormalities. The white blood count was 16,000/mm³, with 56% polymorphonuclear leukocytes and 4% band forms. Blood culture remained sterile. Meanwhile, amoxicillin/clavulanate had been prescribed, but daily fever continued. He was seen again on day 16 of his illness. At that time, he was thought to have a stiff neck. A spinal tap showed 66 white cells, 3 red cells, normal sugar, and normal glucose. He was treated with intravenous antibiotics but remained febrile through day 25, when a faint macular rash appeared. When a mild bulbar conjunctivitis developed, the question of Kawasaki syndrome was raised. Cardiac ultrasonography showed aneurysms in two coronary arteries.

Atypical Clinical Features

Atypical or incomplete cases of Kawasaki syndrome are being recognized with increasing frequency. In patients with fever and fewer than four of the principal diagnostic features, detection of coronary artery abnormalities by two-dimensional echocardiography allows the syndrome to be diagnosed. Males under the age of six months have the greatest risk of coronary involvement, but the diagnosis should be considered in any child with prolonged fever. Such patients should undergo immediate echocardiography.

Kawasaki syndrome has a variety of clinical manifestations, some of which are characteristic but many of which are shared with other infectious and reactive disorders. The differential diagnosis includes staphylococcal or streptococcal toxic shock syndrome, rheumatic fever, scarlet fever, staphylococcal "scalded skin" syndrome, Rocky Mountain spotted fever, and leptospirosis. It also includes viral illnesses such as measles, influenza, and Epstein-Barr virus and adenovirus infections. Noninfectious diseases that must be considered include infantile polyarteritis nodosa, mercury toxicity (acrodynia), Stevens-Johnson syndrome, erythema multiforme, adverse drug reaction, and juvenile rheumatoid arthritis.

Laboratory Findings

In the first week of illness, leukocytosis with a predominance of neutrophils develops. A normocytic, normochromic anemia may also be present. Increased platelet turnover occurs, together with marked hypercoagulability, and after the first week of fever, thrombocytosis is frequently seen. Elevation of liver transaminase values, usually two- to threefold, is common, typically with a cholestatic profile of increased bilirubin and alkaline phosphatase concentrations. In up to 75% of patients, sterile pyuria due to urethritis is observed. Early in the disease, levels of acute-phase reactants such as C-reactive protein and serum- α_1 antitrypsin are elevated. These abnormalities

persist for six to 10 weeks. Although patients with Kawasaki syndrome have a polyclonal B-cell activation, their sera do not contain the usual autoantibodies associated with collagen vascular disease (i.e., no rheumatoid factor, antinuclear antibodies, or anti-DNA antibodies). The sera may demonstrate antibodies against vascular endothelial cell antigens or cardiac myosin.

Electrocardiographic changes are present in more than a third of patients with acute Kawasaki syndrome. The observed abnormalities include prolonged PR interval, left ventricular hypertrophy, abnormal Q waves, ventricular dysrhythmias, and nonspecific ST-T wave changes. Two-dimensional echocardiography has been used extensively to assess ventricular and valvular function, the anatomy of the proximal coronary arteries, and the presence of pericardial effusions. In general, it is preferable to obtain a baseline study as soon as the diagnosis is considered and a repeat study six to eight weeks later. If coronary artery abnormalities are found, more frequent follow-up studies are indicated.

Coronary arteriography is generally reserved for the patient with persistent echocardiographic abnormalities or any patient with symptoms of myocardial ischemia. It is useful for visualization of coronary artery stenoses or distal coronary artery lesions that are difficult to define by two-dimensional echocardiography.

Immunologic Patterns

There is substantial evidence suggesting that immune activation has a role in the pathogenesis of Kawasaki syndrome. Studies of tissues from children dying in the acute phase have revealed vascular inflammation and immune activation of all small- and medium-size blood vessels, particularly the coronary arteries. The initial vascular lesion is associated with endothelial cell activation, accompanied by infiltration by activated CD4 and CD8 T cells as well as monocytes and macrophages. This functional evidence is supported by findings of elevated serum levels of tumor necrosis factor (TNF)-alpha, interleukin (IL)-1, IL-6, IL-10, soluble interleukin-2 receptor, macrophage colony

stimulating factor, and soluble E-selectin. Peripheral blood mononuclear cells from patients with acute, but not convalescent, disease spontaneously produce high levels of IL-1-beta, TNF-alpha, and IL-6, which elicit proinflammatory and prothrombotic responses.

The acute phase is also associated with the appearance of circulating antibodies that are cytotoxic against vascular endothelial cells prestimulated with IL-1-beta, TNF-alpha, or gamma-interferon. Recent studies further indicate that patients have elevated anticardiac myosin autoantibodies, which may be involved in myocardial damage arising during the syndrome's acute phase. Finally, successful treatment with IVIG plus aspirin is associated with a reduction in cytokine production and endothelial cell activation. By contrast, patients treated solely with aspirin show prolonged T-cell and B-cell activation. In this regard, the magnitude and persistence of proinflammatory cytokine secretion have been reported to constitute a risk factor for development of coronary artery abnormalities. This may account for the clinical observation that patients with prolonged fever are prone to develop coronary artery abnormalities.

Potential Causes

For several reasons, including the acute, self-limited nature of Kawasaki syndrome and the frequency with which young children are affected, it is widely believed that the syndrome is caused by an infectious agent. Indeed, the clinical features and immune-cell activation of acute Kawasaki syndrome significantly overlap those of diseases such as staphylococcal toxic shock syndrome, in which bacterial toxins act as superantigens.

Staphylococcal enterotoxin B (SEB) and C (SEC), toxic shock syndrome toxin 1 (TSST-1), and streptococcal pyrogenic exotoxins are all in this category. Binding directly to conserved amino acid residues outside the antigen-binding groove on MHC class II molecules, they selectively stimulate T cells expressing specific T-cell receptor (TCR) *β*V (previously called V-beta) chains (Figure 5). Other variable elements (VJ-alpha and

VDJ-beta) of the TCR contribute much less to the recognition process. By contrast, conventionally processed peptide antigens tend to require all five variable elements of a TCR for optimal recognition and therefore stimulate a relatively low proportion of T cells.

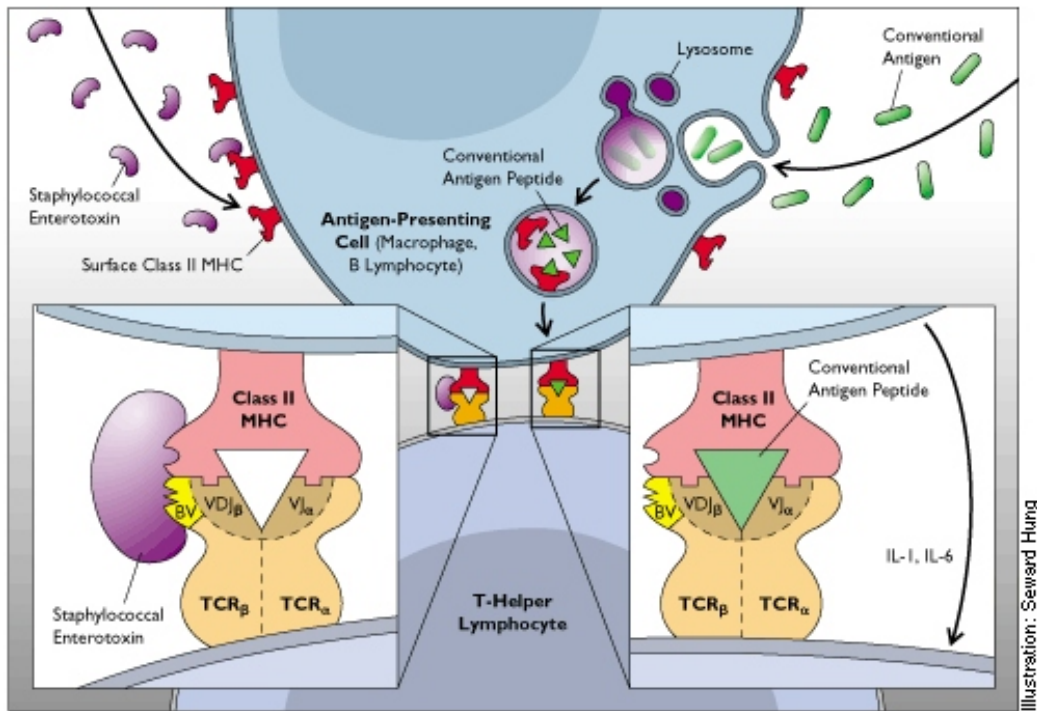


Figure 5. The immune process in acute Kawasaki syndrome is similar to that seen in diseases in which bacterial toxins act as superantigens (left). Staphylococcal enterotoxin, for example, is not internalized and broken down by the antigen-presenting cell; instead the intact superantigen binds directly to conserved amino acid residues outside the antigen-binding groove on MHC class II molecules, causing release of proinflammatory

cytokines. The toxin also selectively stimulates T cells expressing specific T-cell receptor (TCR) BV (previously called Vβ) chains. Other variable elements (VJα and VDJβ) of the TCR contribute much less to the recognition process. By contrast, conventionally processed peptide antigens (right) tend to require all five variable elements of a TCR for optimal recognition and therefore stimulate a relatively low proportion of T cells.

Illustration: Seward Hung

The capacities of microbial superantigens suggest several mechanisms by which a superantigen could trigger an immune response in acute Kawasaki syndrome. Superantigens secreted at the inflamed mucosal surface could engage HLA-DR on monocytes, macrophages, and other accessory cells to stimulate production of cytokines with potent proinflammatory properties. Superantigens could also stimulate T cells to proliferate and produce inflammatory cytokines.

To explore these possibilities, our laboratory has analyzed T lymphocytes from patients with Kawasaki syndrome, seeking evidence of selective *TCR BV* expression. Compared with healthy controls, patients in the acute phase of the syndrome demonstrated an expansion of *TCR BV2* T cells, and to a lesser extent *TCR BV8* T cells. During the convalescent phase, percentages of *TCR BV2* and *TCR BV8* T cells returned to normal. The selective expansion of *TCR BV2* was similar to the changes observed in T cells of patients with staphylococcal toxic shock syndrome. Since this initial report, there have been additional studies confirming *TCR BV2* expansion in acute Kawasaki syndrome. Other studies have failed to observe any consistent abnormality in the T-cell repertoire. These conflicting reports suggest that there is heterogeneity in the etiology of Kawasaki syndrome.

To identify the bacterial superantigens potentially involved, we have analyzed cultures in a blinded manner from the groin, axilla, rectum, and pharynx of patients in the acute phase of the syndrome, along with cultures from age-matched control patients with fever, rash, or both. All group A beta-hemolytic streptococci and coagulase-positive *S. aureus* isolates were screened for toxin production. Superantigen-producing bacteria were found in the majority of acute Kawasaki patients but only rarely in patients with other febrile illnesses. In most of the culture-positive patients, superantigen-producing *S. aureus* was isolated from pharyngeal or rectal cultures. This suggests that the primary site of bacterial colonization or infection in Kawasaki syndrome is the mucosal surface of the gastrointestinal tract. We have also isolated *S. aureus* capable of producing TSST or exfoliative toxin A superantigen from rectal cultures of patients with atypical Kawasaki syndrome. Meanwhile, there have been several reports of SEB-secreting *S. aureus*.

In brief, several staphylococcal or streptococcal toxins with superantigenic activity may trigger immune activation in acute Kawasaki syndrome. Other superantigen-producing bacteria, including *Yersinia pseudotuberculosis*, could also play such a role. In our experience, TSST appears to be the primary culprit. Similar observations have been reported in nonmenstrual toxic shock syndrome, most cases of which are associated with TSST-1-secreting *S. aureus*, although a significant proportion of cases can be associated with *S. aureus*-secreting SEB or SEC. Intriguingly, several published and unpublished cases of toxic shock syndrome have now been associated with the development of coronary artery abnormalities similar to those seen in Kawasaki syndrome. These data suggest that Kawasaki syndrome and toxic shock syndrome are overlapping entities with a common microbial trigger. The final clinical phenotype may depend on the host's age and unidentified genetic and environmental factors.

Short-Term Management

During the acute phase, management is aimed at reducing inflammation in the myocardium and coronary artery wall and at preventing coronary thrombosis. Aspirin plus high-dose IVIG are the cornerstones of therapy (Table 3). Aspirin is given in doses of 80 to 100 mg/kg of body weight per day in four divided doses, so as to achieve a serum salicylate level of 20 to 25 mg/dL. The drug is used for both its anti-inflammatory and antithrombotic effects.

Table 3. Treatment of Kawasaki Syndrome

Acute Phase

Intravenous immune globulin, 2 gm/kg as a single 10-12-hr infusion

Aspirin, 80-100 mg/kg/day in four divided doses until day 10

Convalescent Phase in Uncomplicated Cases

Aspirin, 3-5 mg/kg once a day for 6-8 weeks

Patients with Coronary Artery Disease

Aspirin, 3-5 mg/kg once a day

Dipyridamole, 1 mg/kg/day in selected patients

Anticoagulant therapy or fibrinolytic therapy or both (as needed in patients with arterial thrombosis)

Options for Patients with Chronic Myocardial Ischemia

Transluminal coronary angioplasty

Coronary artery bypass graft surgery

Cardiac transplantation

IVIg is given at a dose of 2 gm/kg as a single 10- to 12-hour infusion. Several studies have demonstrated that, in combination

with aspirin, the infusion is safe and effective in reducing the overall prevalence of coronary artery abnormalities. In particular, it prevents the formation of giant aneurysms, the most serious form of coronary abnormality caused by Kawasaki syndrome. Abnormalities of left ventricular systolic function and contractility improve rapidly with therapy. Use of a single infusion has been compared with multiple-dose IVIG regimens of approximately equivalent total dosage. In such trials, the single-dose strategy has been associated with a lower incidence of coronary abnormalities, a more rapid resolution of fever and laboratory indices of acute inflammation, a reduced duration of hospitalization, and a higher peak serum IgG level. Of note, peak adjusted serum IgG levels are lower among patients who subsequently develop coronary artery abnormalities and are inversely related to fever duration and laboratory indices of acute inflammation.

In most children, defervescence occurs within hours of IVIG administration. In afebrile children, the daily aspirin dose can be reduced, at about the 14th day of illness, to 3 to 5 mg/kg, to continue inhibition of platelet activity. Aspirin can be discontinued if no coronary abnormalities have been detected by six to eight weeks after illness onset. If coronary artery aneurysms develop and persist, aspirin therapy is continued indefinitely. Most data indicate that coronary artery abnormalities will develop in fewer than 3% of Kawasaki syndrome patients with a normal baseline echocardiogram if treatment with aspirin and IVIG is initiated within 10 days of the onset of fever.

About 15% of treated patients will experience either a persistent fever 24 to 48 hours after therapy or a recrudescence of fever after an afebrile period of 24 to 48 hours. A recent survey has found that about 10% of such patients subsequently have coronary artery abnormalities. It is generally recommended that patients who remain febrile after a first course of IVIG should be given a second course. Although this strategy has not been evaluated in a controlled trial, there is concern that persistent fever may correlate with elevated levels of proinflammatory cytokines.

At present, the use of systemic corticosteroids in the treatment of Kawasaki syndrome is controversial. The results of several studies conducted in Japan suggest that patients treated with steroids alone or in combination with aspirin have a higher

frequency of coronary aneurysms and of subsequent myocardial infarction and death. However, recent case reports of patients who remained febrile after therapy suggest a response to high-dose pulses of methylprednisolone (30 mg/kg per day for one to three days). Controlled studies are needed to determine whether intravenous methylprednisolone should be used in patients who fail to respond to IVIG.

The mechanism by which high-dose IVIG reduces the vasculitis of acute Kawasaki syndrome has yet to be established. The observation that IVIG works rapidly in reducing laboratory parameters of an acute-phase response suggests a generalized anti-inflammatory effect. IVIG has also been found to contain high concentrations of neutralizing antibodies that inhibit the T-cell response to staphylococcal superantigens. We have recently found that superantigen-stimulated T-cell activation is relatively resistant to the immunosuppressive effect of steroids. This could explain the apparent efficacy of IVIG therapy, as compared with steroid therapy, in patients with acute Kawasaki syndrome.

Certain manifestations of the syndrome are treated symptomatically. In patients with congestive heart failure, digitalis and diuretics are used as needed. In patients at risk of cardiovascular complications, some physicians add dipyridamole, at 1 mg/kg of body weight per day, to further inhibit platelet aggregation. Therapy for mucocutaneous manifestations includes emollients for desquamating skin and antihistamines for pruritus.

Long-Term Management

Patients in whom cardiovascular disease develops must be monitored closely. Stress echocardiography and coronary angiography may be indicated in patients with evidence of myocardial ischemia. For patients with obstructive changes in the coronary arteries, anticoagulant therapy may be required. For severe cardiovascular symptoms, the options include intravenous streptokinase (when a thrombus is present), balloon angioplasty, and coronary artery bypass grafting. Long-term

patency of saphenous-vein grafts has been a problem. The use of internal mammary artery grafts has been reported to give improved results.

Many patients with arterial aneurysms will show angiographic regression within six months to two years of the onset of Kawasaki syndrome. The likelihood of resolution is determined by the aneurysm's initial size. Giant aneurysms (with a maximum diameter exceeding 8 mm) carry the worst prognosis; nearly all late deaths from Kawasaki syndrome occur in this subgroup of patients. Some patients have required cardiac transplantation for severe ischemic heart disease.

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