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Brief Report

Myocardial infarction in a 35-day-old infant with incomplete Kawasaki disease and chicken pox

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Abstract Kawasaki disease is an acute febrile vasculitis of infancy and early childhood. It is uncommon in early infancy, because a significant proportion of these children do not meet the classical diagnostic criteria at this age. Infants younger than 6 months with persistent fever and some of the criteria of Kawasaki disease should always raise suspicion for Kawasaki disease early to avoid delayed diagnosis with severe cardiac complications. We present a 35-day-old infant with incomplete Kawasaki disease complicated with myocardial infarction during chicken pox.

Keywords: Vasculitis; aneurysms; infection

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We report a case of Kawasaki disease in a 35-day-old infant. The course of the disease was unusual as it was complicated with early coronary artery aneurysms. During the sub-acute stage of the disease the patient manifested chicken pox and myocardial infarction.

Present history

A full-term female infant presented with fever, irritability, and poor feeding, which began a few hours before her admission. She was the fourth child of healthy non-consanguineous parents with birth weight 3200 grams and a normal perinatal course. She was receiving formula milk.

Clinical findings on admission

Body temperature was 38.5°C, pulse rate was 150 per minute, respiratory rate was 40 per minute, capillary refill was less than 2 seconds, and body weight was 4000 grams. The patient had vasomotor disturbances, irritability with a high-pitched cry, abdominal meteorism, and erythematous rash in the diaper area. Anterior fontanelle was soft and flat and muscle tone was normal.

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Laboratory work-up

Leukocytosis, anaemia (haemoglobin 7 grams per decilitre), elevated platelet count as well as C-reactive protein, procalcitonin and erythrocyte sedimentation rate were noted while albumin was low. Lumbar puncture was normal. Cultures of blood, urine, spinal fluid for bacteria, throat cultures for streptococcus, streptococcal serology, nasal secretions for adenovirus and serology for Epstein–Barr virus and measles were negative. Viral cultures and polymerase chain reaction for herpes simplex, enterovirus, Epstein–Barr virus and parvovirus were negative as well as testing for autoimmune disease or immunodeficiency. Echocardiography and ultrasonography of the brain were normal. Ultrasonography of the abdomen revealed hydrops of the gallbladder.

Clinical course

The patient was placed on double antimicrobial therapy. By the fifth day of illness the patient still had high fever (39.5°C), irritability, rash, diarrhoea,

and abdominal meteorism. Non-exudative conjunctivitis, erythematous dry lips, and periungual desquamation appeared. With the working diagnosis of Kawasaki disease, intravenous γ-globulin was given at a dose of 2 grams per kilogram in a single infusion as well as aspirin (80 milligrams per kilogram) per os. Within 24 hours the patient became less irritable, the rash faded, the oral changes, and conjunctivitis improved. Persistent fever 2 days later necessitated a second intravenous γ-globulin infusion. A second infusion was given 48 hours later and the infant became afebrile. The response to the above treatment confirmed the diagnosis of Kawasaki disease.

Echocardiography on day 12 revealed small aneurysms in the proximal segment of both left and right coronary arteries. An electrocardiogram showed a first-degree cardiac block.

During follow-up the aneurysms increased in size (left coronary artery 5.2 millimetres, right coronary artery 5 millimetres), but the patient's clinical condition remained stable. The patient was discharged on aspirin (5 milligrams per kilogram) after 37 days.

One week later she returned to receive varicella-zoster immune globulin because her brother had chicken pox. Despite the immune globulin infusion, the patient exhibited rash, which necessitated the discontinuation of aspirin for 4 days because of the fear of Reye syndrome.

A few days later, the infant was hospitalised with lethargy and poor feeding. On physical examination, she was afebrile and tachycardia was noticed. Her general condition deteriorated within hours with tachypnea, tachycardia with gallop rhythm, excessive irritability, and crackles at the basal pulmonary fields. Laboratory work-up showed elevated creatine kinase-MB, and ST-segment depression on electrocardiogram, in leads I and V1 with reverse T waves in leads V4, V5, and V6. Echocardiography revealed the known aneurysms and dilatation of the left ventricle with depressed global contractility with diffuse hypokinaesia of the lateral wall (ejection fraction 45%).

The infant was transferred to the cardiology intensive care unit and underwent catheterisation and angiography. The results of the above procedures were as follows: the right coronary artery was dominant without stenosis; the left coronary artery had a saccular aneurysm involving its bifurcation, and a stenosis was present proximal to the aneurysm (Fig 1). The anterior descending branch and the circumflex were shown through the left coronary artery. The left ventricle had impaired contractility.

All the above confirmed the diagnosis of myocardial infarction. Successful thrombolysis within the first 12 hours, with intravenous infusion of recombinant plasminogen tissue activator (Alteplase) at a dose 0.2 milligram per kilogram per hour, was performed.[1] Alteplase infusion was stopped after 24 hours and continuous intravenous infusion of heparin was commenced along with supportive therapy with inotropic agents and diuretics. The infant was discharged from intensive care unit on aspirin (5 milligrams per kilogram), warfarin, digoxin, captopril, and furosemide. The contractility of the left ventricle ameliorated, as did hypokinaesia of the lateral wall.

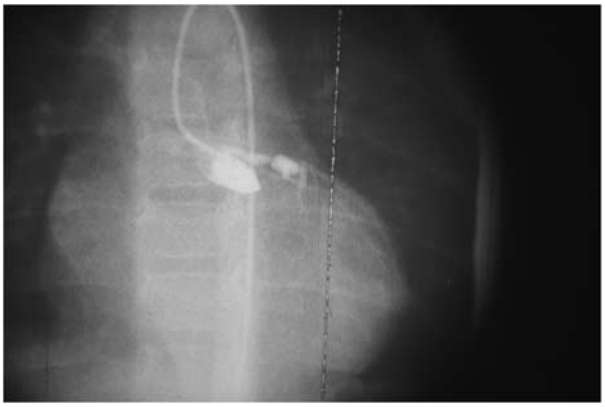

Figure 1.
Coronary angiography after thrombolysis. The left coronary artery had a saccular aneurysm involving its bifurcation, and a stenosis was present proximal to the aneurysm.

Eight months from the diagnosis the patient is in a stable clinical condition free of symptoms under treatment with aspirin and warfarin.

The last cardiac evaluation revealed improved left ventricular function, normal electrocardiogram, and decrease in the size of the aneurysms – left coronary artery 3.3 millimetres and right coronary artery 2.5 millimetres – in echochardiography. A repeat coronary angiography is scheduled.

Discussion

Kawasaki disease is an acute self-limited vasculitis of infancy and early childhood. It is the leading cause of acquired cardiac disease in childhood. Kawasaki disease is most common in Japan with an annual incidence of 150–200 per 100,000 children under 5 years of age compared with 15 per 100,000 children younger than 5 years in the United States of America.[2]

Children who are 6 months to 5 years are most susceptible. Incidence in boys is 50% greater than in girls. Coronary arteries and other medium-size muscular arteries show focal segmental destruction, with coronary artery aneurysms or ectasia developing in approximately 15–25% of patients.

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Classic diagnostic criteria for typical Kawasaki disease consist of high fever for at least 5 days with at least four of five principal manifestations such as bilateral non-exudative conjunctivitis, changes in the oropharynx, cervical lymphadenopathy, palm and sole erythaema, indurative oedema of the hands and feet, and periungual desquamation erythematous rash.[3]

Typical Kawasaki disease is also established when fever and two or three criteria are present with the coexistence of coronary aneurysms.

Incomplete Kawasaki disease refers to the clinical presentation of fever and fewer than four of the criteria. The diagnosis of incomplete Kawasaki disease is difficult because many infections and inflammatory diseases present with the same way. Incomplete Kawasaki disease is more common in infants. This age group also has a higher risk of developing coronary aneurysms.[4–6]

Fever is the characteristic finding in both classic and incomplete Kawasaki disease. Prolonged fever without evidence of infectious or immune disease should always heighten suspicion of Kawasaki disease. Other clinical findings, which are common in incomplete Kawasaki disease, are conjuctival injection, oral mucosal changes, and/or rash and anterior uveitis.[7]

The aetiology of Kawasaki disease is still unknown. The symptoms suggest a possible relationship with an infectious agent. The longer that a single infectious agent cannot be identified the more the possibility must be considered that multiple agents, leading to a common pathway, may be responsible.[8]

The "superantigen hypothesis" seems tempting, even though it remains controversial. The "superantigens" may activate the immune system in an immunologically susceptible individual.[9]

Echocardiographic and angiographic data indicate that 20–40% of untreated Kawasaki disease patients develop coronary artery abnormalities. Half of these lesions regress within 5 years. Other complications are pericarditis, endocarditis, alteration of the cardiac rhythm, peripheral thrombosis, and central nervous system disease.

Risk factors for developing complications include male sex, infants, fever for 14 days or recrudescent fever, haemoglobin lower than 10 grams per decilitre, leukocytosis, erythrocyte sedimentation rate higher than 101 millimetres per hour, elevated C-reactive protein, or erythrocyte sedimentation rate for more than 30 days, ischaemia and myocardial infarction, hypoalbuminaemia, and non-response to intravenous immune globulin infusion.[10]

Treatment

Intravenous immune globulin and aspirin should be started within the first 10 days of illness. A single dose of immune globulin (2 grams per kilogram) is the recommended therapy.

In refractory cases, a second infusion, after 48 hours, is recommended. Despite early treatment, 4% of children with Kawasaki disease develop progressive coronary lesions.

Aspirin is given in a high dose, that is, 80–100 milligrams per kilogram per day, during the acute phase. When fever resolves, it is administered in a low dose, that is, 3–5 milligrams per kilogram per day, until the platelet count and erythrocyte sedimentation rate return to normal, unless coronary artery abnormalities are detected.

Alternative therapies. A pulse of methyl prednisolone (30 milligrams per kilogram per dose) has been used to treat refractory cases. The role of steroids is debated. Other immune modulators such as competitive inhibitors of tumour necrosis factor-α, pentoxifylline, and methotrexate are being studied and further data are needed to determine the precise role of these agents in Kawasaki disease.

Children with Kawasaki disease and acute coronary syndromes may necessitate coronary artery bypass graft surgery. Heart transplantation has been occasionally used in terminal cardiac failure.

Follow-up

All patients with Kawasaki disease and coronary aneurysms still have lesions of the vascular endothelium even after the resolution of the aneurysm. Patients without aneurysms in a large proportion have inadequate coronary blood flow under stress.

Children with Kawasaki disease may experience early in their adult life an ischaemic cardiac episode and they must be cautious in strenuous exercise. A lifelong yearly follow-up is recommended.

Our patient had all the predisposing factors for developing cardiac complications – very young age, elevated erythrocyte sedimentation rate, C-reactive protein, anaemia, and refractory disease to the first immune globulin infusion. The discontinuation of aspirin for a short time period due to chicken pox as well as the activation of the immune system from the varicella-zoster virus might have an adverse effect on the evolution of acute coronary syndrome. To our knowledge, only a few bibliographic reports concerning the relationship between a viral infection and the pathogenesis of Kawasaki disease exist and these cases concern early childhood.[11–13] Our case is remarkable because of the very young age, the female sex, and the development of overt chicken pox despite the immune globulin and the varicella-zoster immune globulin infusion. We might suppose that varicella-zoster virus may trigger an immunological cascade that aggravated

the vasculitis and resulted in a myocardial infarction. In addition, thrombolysis is occasionally used in Kawasaki disease patients but is seldom reported. Our patient underwent a successful thrombolysis at this very young age.

The infant's prognosis remains uncertain due to an increased risk for recurrence of acute coronary syndrome and sudden death following an initial myocardial infarction. The risk for further cardiac complications after the myocardial infarction is high and the prospective of a coronary artery bypass graft surgery in the future is not improbable.

Incomplete Kawasaki disease should always be in the differential diagnosis of a neonate with persistent fever when the conventional work-up could not reveal the underlying cause. In the pathogenesis of Kawasaki disease, several viral pathogens, such as varicella-zoster virus, may be implicated either as triggering causes or as additional factors that could aggravate the immune response.

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