CASE REPORT

Life threatening coronary artery spasm in childhood Kimura's disease

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Abstract

A 13 year old boy is described with hypereosinophilia associated with Kimura's disease, who showed repeated life threatening syncopal attacks during daily activities or at rest. Coronary arteriography demonstrated small aneurysms with irregular vessel walls of both coronary arteries, and the absence of organic stenotic lesions. Infusion of a minimal dose of ergonovine into the right coronary artery induced severe spasm of the vessel. Ventricular fibrillation recurred even after administration of nifedipine and isosorbide was started, but was completely inhibited by prednisolone.

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Keywords: coronary vasospasm; hypereosinophilia; Kimura's disease; ventricular tachyarrhythmia

Kimura's disease is a chronic disease characterised by a clinical triad of slowly enlarging subcutaneous masses with lymphoid hyperplasia in the head and neck, peripheral hypereosinophilia, and increased serum IgE concentration, often occurring in male Asian young adults.[1–3] Although the disorder's clinical course is usually benign, an unusual cardiac complication has been reported in an adult patient.[4] We present the first case of childhood Kimura's disease, in which repeated life threatening syncopal attacks occurred due to ventricular tachyarrhythmia. Severe coronary vasospasm was demonstrated on angiography after intracoronary infusion of ergonovine.

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Case report

A 13 year old, well built, Japanese boy with an unremarkable history was referred to our hospital complaining of recurrent squeezing pain in his chest over the previous five months, with each attack occurring during daily activities or at rest, predominantly in the morning, and lasting from 15 to 30 minutes. Some of the attacks were accompanied by pallor, cold sweat, and ultimate loss of consciousness with tonic convulsion. He had never smoked or drank alcohol.

On admission, his heart rate was 68 beats per minute and his blood pressure was 103/42 mm Hg. Subcutaneous nodules, about 3×4 cm in size, were examined in the left postauricular area and in the right upper arm. Auscultation of the chest showed no abnormalities.

Blood sampling showed a white blood cell count of 11 000/mm^3 with 5600/mm^3 eosinophils. Increased eosinophilopoiesis was also demonstrated in the marrow. Serum eosinophil cationic protein and eosinophil peroxidase were raised to 239 μg/l (normal value; less than 8.8) and to 170 μg/l (normal value; less than 25.2), respectively. The serum IgE level was increased to 8300 U/ml, while specific IgE antibodies against common inhalant allergens and parasitic antigens were all negative by radioallergosorbent test. Antinuclear antibody was negative.

The patient's in vitro cytokine profiles were examined using peripheral blood mononuclear cells, because an imbalance of Th1 and Th2 type helper T cells with Th2 predominance might exist in Kimura's disease.[2] When 1×10^5 cells were cultured with a mitogenic lectin, concanavaline A, for six days, the concentration of interleukin 4 (IL-4), IL-5, and interferon γ released in the medium were 10.9 (control value; mean 1.1, SD 0.7), 372.8 (mean 9.5, SD 4.1), and 19.1 (mean 73.3, SD 110.6) pmol/ml, respectively. The increased production of IL-4 and IL-5 suggests a functional shift of the patient's helper T cells from the Th1 type to the Th2 type.

A biopsy specimen from the upper arm nodule revealed lymphoid tissue with angiolymphoid proliferation and abundant eosinophilia in the paracortex. These findings confirmed the diagnosis of Kimura's disease.

Although ECG on a treadmill exercise test did not show any significant ST segment changes or arrhythmia, Holter monitoring revealed ST segment elevation coincidentally with an episode of chest pain (fig 1). A chest *x* ray showed a normal cardiac silhouette and no pulmonary infiltrates. Echocardiography revealed normal left ventricular function. Thallium 201 myocardial perfusion scintigraphy revealed slight hypoperfusion in the inferior and inferoseptal areas of the left ventricle. The patient was suspected of having variant angina and underwent cardiac catheterisation. Coronary angiography revealed small aneurysms and partially irregular vessel walls of both coronary arteries, but no organic stenotic lesions (fig 2). However, infusion of a minimal dose of ergonovine (1 μg) into the right coronary

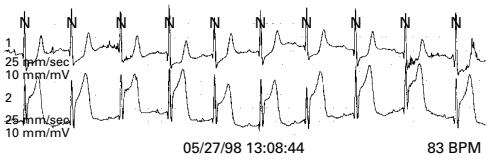

Figure 1 ECG on Holter monitoring during an episode of chest pain. ST segment elevation is clearly seen on the lower tracing.

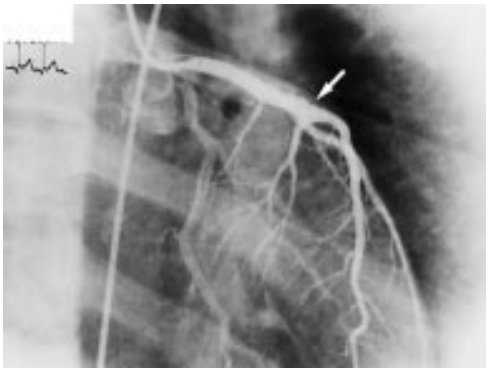

Figure 2 Left coronary arteriography revealing the absence of stenotic lesions but the presence of an irregular wall at the anterior descending branch (white arrow).

artery provoked a severe spasm of the proximal portion of the vessel, which turned like a thread. The spasm could be released by immediate intracoronary infusion of nitroglycerin without inducing myocardial infarction. We were urged to give up further catheterisation and endomyocardial biopsy.

Administration of oral nifedipine (40 mg/day) and isosorbide mononitrate (40 mg/day) was started to prevent coronary vasospasm. During the next few days, however, the patient complained of recurrent chest pain, and ultimately lost consciousness in bed. At that time, ECG demonstrated ventricular fibrillation. Emergent cardiorespiratory resuscitation was performed and the patient was revived. At the next episode of chest pain, sublingual administration of nitroglycerin was also tried, but had little effect. We then administered prednisolone with an initial dose of 1 mg/day/kg (60 mg/day). On the following day, the peripheral eosinophil count decreased to less than 200/mm^3, and the chest pain and syncopal attacks have so far not recurred.

Although the eosinophil count fluctuated between about 500 and 3000/mm^3 on tapering the dose of prednisolone, the angina was completely suppressed during the next year under medication of a low dose of prednisolone (10 mg/day) combined with ticlopidine.

Discussion

We have reported childhood Kimura's disease accompanied by life threatening events derived from coronary arterial vasospasm. Intracoronary infusion of a minimal dose of ergonovine induced severe coronary vasospasm in a child who did not have obvious atherosclerosis or thrombosis.

Angiographical studies have shown that coronary arterial spasm is associated with hypereosinophilia in several diseases, including Churg-Strauss syndrome,[5] eosinophilia myalgia syndrome,[6] adult Kimura's disease,[4] and idiopathic hypereosinophilic syndrome (HES).[7] Most cases had extremely high eosinophil counts of approximately 5000/mm^3 or more in the peripheral blood. As our patient had an increased number of eosinophils (5300/mm^3), the massive eosinophilia related to Kimura's disease might be implicated in the development of cardiac symptoms.

In contrast to the multiorgan adverse effects of HES, the course of Kimura's disease has been considered benign. In HES, various cardiovascular manifestations, such as chronic endomyocardial fibrosis, acute necrotising myocarditis, and vasculitis, have been recorded.[8 9] The present case suggests that coronary spasm is an important consequence of Kimura's disease as well as of HES.

The mechanism by which eosinophils induce coronary spasm remains unknown. A massive infiltration of eosinophils into endomyocardium and the deposition of their granular proteins, such as eosinophilic cationic protein, eosinophil derived neurotoxin, and major basic protein, have also been observed in patients with HES related myocardial injuries.[6 10 11] The eosinophil granular proteins may have toxic effects on myocardial tissue.[9 11] Although myocardial or coronary vessel histology was not determined in our case, it would be interesting to know whether inflammatory products derived from activated eosinophils may increase vascular tone or irritability.[6]

In our patient, calcium antagonist or nitroglycerin, which are commonly used for variant angina, showed little effect in coronary arterial relaxation.[7] In contrast, glucocorticoids seemed to exert strong antivasospastic effects on coronary arteries by reducing eosinophilic infiltration and suppressing the development of inflammatory mediators.[11 12] Actually, our patient did not complain of chest pain under treatment with prednisolone, even during tapering of the dose, while eosinophil count fluctuated up to 3000/mm^3. The low dose of prednisolone (10 mg/day) was enough to suppress the angina.

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