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Brief Report

Myocardial ischaemia in a child infected with influenza B

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Abstract Cardiac involvement is a rare complication of infection by the influenza B virus. It usually presents with ventricular dysfunction, arrhythmias, or both. We report a 13-year-old boy with clinical, electrocardiographic, and laboratory findings of myocardial ischaemia during an otherwise silent acute infection with influenza B. Coronary endothelial injury constituted a potential underlying mechanism, and microthrombosis was promoted by high levels of lipoprotein(a) in the serum.

Keywords: Viral infection; lipoprotein(a); myocarditis

SYMPTOMS OF UNCOMPLICATED INFECTION WITH the influenza B virus are fever, headache, myalgias, cough, and sore throat. Occasionally, it has been associated with myocarditis in adults, albeit usually mild. As far as we are aware, only one child has been described with influenza B myocarditis following a multisymptomatic illness who displayed the typical symptoms of viral myocarditis.[1] Viral myocarditis, however, has a wide spectrum of clinical signs, and may present as myocardial infarction.[2]

Case report

A previously healthy 13-year-old boy presented with a sudden onset of chest pain unrelated to exercise, dyspnoea, and pallor. The initial electrocardiogram showed elevations of the ST-segments in leads II, III, aVF, V_5 and V_6 (Fig. 1). After sublingual nitroglycerine, the pain subsided, and the patient was admitted to our unit for paediatric cardiology.

At that time, he was stable, without any discomfort or other complaints. Apart from sinus tachycardia the cardiopulmonary examination proved normal. There were no clinical signs of infection, and the body temperature was normal. White blood cells numbered 11,900 per millimetre cube, comprising 60 percent granulocytes, 27 percent lymphocytes, 8 percent monocytes, and 5 percent eosinophils. On admission, creatine phosphokinase was measured at 564 units per litre in the serum, the normal being below 270 units, and troponin T at 0.6 micrograms per litre, the normal being below 0.03 micrograms.

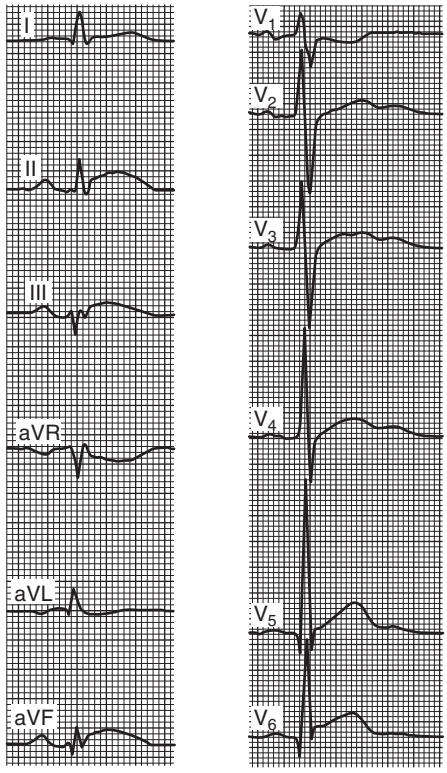

Figure 1.
The electrocardiogram on admission, with a speed of writing of 50 millimetres per second. Note the ST segment elevations in leads II, III, aVF, V_5 and V_6, indicating left ventricular myocardial infarction.

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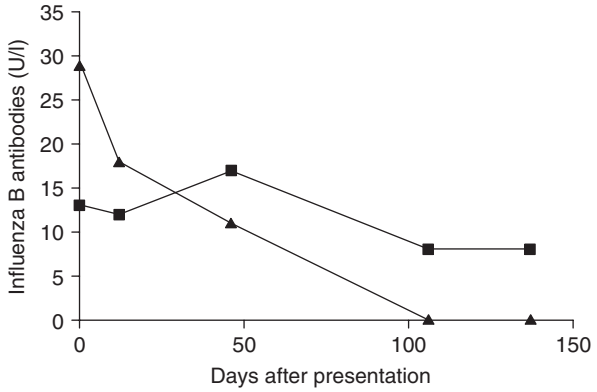

Figure 2.
IgG (■) and IgA (▲) influenza B antibody concentrations at presentation and follow-up.

These then rose to a maximum of 2,031 units and 3.0 micrograms 48 hours after the onset of symptoms, and normalized within 3 and 8 days, respectively. The muscle brain fraction of creatine phosphokinase was 10 percent. Levels of lactate dehydrogenase and aspartate aminotransferase were also transiently elevated in the serum until the fourth day after admission.

On the electrocardiogram, the T waves in leads II, III, aVF, V_5 and V_6 turned negative on the second day. After 6 weeks, repolarisation became normal. 24-hour Holter monitoring upon admission revealed sinus tachycardia with 80 beats per minute at rest and occasional isolated monomorphic premature ventricular contractions, albeit less than 20 in 24 hours. The chest X-ray was normal. On echocardiography, there was no left ventricular dysfunction or pericardial effusion. Angiocardiography demonstrated normal coronary arterial anatomy. With signs of myocarditis lacking at that time, we did not perform endomyocardial biopsy. Major clotting disorders were ruled out. Lipoprotein(a), however, a recently identified risk factor for myocardial infarction and atherothrombotic stroke in young adults, was elevated at 0.7 grams per litre, and remained elevated on several follow-up examinations.

Serologic investigations produced titers of immunoglobulins class A and class G against influenza B virus. The boy had not been vaccinated for influenza. Titer regression was diagnostic for an acute infection with influenza B (Fig. 2). Apart from the cardiac pathology, our patient had no other accompanying symptoms.

He was immobilized and anticoagulated with heparine until the markers for ischaemia in the serum had returned to normal, and the ST segments to baseline, and was discharged on the fourteenth day with an exclusion from physical exercise. Three months later, he underwent an uneventful bicycle excercise test without signs of ischaemia. A 24-hour Holter electrocardiogram was normal. At that time a single-photon emission computed tomography analysis of the heart both at rest and under physical stress revealed normal myocardial perfusion, indicating complete recovery from the myocardial ischaemia.

Discussion

Myocardial infarction is rare in childhood and adolescence. It may be a complication of congenital cardiac disease, Kawasaki disease, coronary embolization, myocarditis and chest trauma. Our patient suffered from acute myocardial ischaemia as demonstrated by a significant rise of troponin T, the muscle brain fraction of creatine phosphokinase, and lactate dehydrogenase, indicating some degree of myocytic necrosis, as well as by electrocardiography.

Elevated levels of lipoprotein(a) have been identified as a risk factor for premature myocardial infarction in young adults.[3] Showing strong structural homologies with plasminogen, this protein expresses antifibrinolytic properties both in the test tube and in experimental animals.[4] With regard to these data, a high level of the protein may have predisposed our patient to an ischaemic event in the presence of an additional trigger:

On admission, the boy had acute infection with influenza B, as confirmed by the course of the antibody titers, despite the absence of extracardiac manifestations.

Whereas myocarditis is a well-recognized phenomenon with numerous viral pathogens in children, it is exceedingly rare following infection with influenza B.[1] All published cases of influenza B myocarditis in adults and children occurred in the setting of a febrile illness with malaise and other pulmonary or gastrointestinal symptoms. To the best of our knowledge, this is the first case of monosymptomatic infection with influenza B, affecting the heart as the only organ.

Reports of viral myocarditis presenting as myocardial infarction are scarce in adults, and anecdotal in children.[5,6] Several mechanisms have been proposed. The first is arteritis of the coronary arteries and their branches. The second suggests coronary arterial thrombosis due to exposure of the basement membrane and activation of platelets. The third invokes coronary arterial spasm, while the fourth suggests coronary arterial embolism from a left ventricular thrombus.[2]

Vasculitis occasionally follows acute infection with the influenza B virus, and is assumed to be responsible for many complications, including encephalitis and bronchiolitis.[7] In the past, influenza viruses have been accused of causing endothelial injury to the heart

and the brain and of inducing hypercoagulation.[8–10] The virus may cause lysis of endothelial cells, promoting the formation of small blood clots. Perivascular infiltrations interfere with microcirculation in viral myocarditis.

We hypothesize that, in the myocardium of our patient, the infection with influenza B led to a diffuse microvascular damage, microthromboses and coronary arterial spasms, the latter being reactive to nitroglycerine. In this setting, a constitutionally high level of lipoprotein(a) rendered him susceptible to the development of myocardial ischaemia. The rise in troponin T indicated diffuse myocardial damage. Imaging studies, including echocardiography, angiography and a single-photon emission computed tomography, were not sensitive enough to detect these microinfarctions of the myocardium.

Acute cardiac ischaemia without ventricular dysfunction or significant arrhythmias has not been previously reported in association with influenza B, neither in children nor adults. Our case may serve as further evidence for the causal relationship between influenza and endothelial damage. Further histopathologic and immunologic studies are needed to address the pathogenesis of the damage to small vessels in viral myocardial disease. Procoagulative factors, such as elevated levels of lipoprotein(a), may trigger this manifestation of the disease, and must therefore be considered significant factors in the pathogenesis of viral induced myocardial ischaemia.

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