Case Report

Atypical Kawasaki Disease Presenting with Symptoms from the Genitourinary System: An Autopsy Report

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Summary

Symptoms from the genitourinary system are unusual in Kawasaki disease (KD). Renal involvement is even rarer and it is confirmed by biopsy when the person is alive. We describe the case of an 11-year-old boy admitted to the hospital complaining about prolonged fever (5 days) and hematuria. His urinalysis showed also pyuria, proteinuria and urinary renal tubular epithelial cells concentrations. During the next days, the patient presented limb edema. After almost 2 weeks of hospitalization the patient was transferred to the intensive care unit because of melena and intense abdominal pain. Upon admission, the patient collapsed and died. The diagnosis of KD was established during autopsy. The macroscopical and histopathological examination of the heart showed increased dimensions and weight and multiple thrombi in the coronary arteries with intramural dense polymorphonuclear inflammatory infiltration and necrosis. Histological examination of the kidneys revealed normal glomerulus, mild expansion of mesangial matrix, interstitial infiltration with lymphocytes, plasmatocytes and eosinophiles, normal vessels and normal immunofluorescence.

Introduction

Kawasaki disease (KD) is an acute self-limited vasculitis of infancy and early childhood of unknown etiology. The diagnosis of KD is purely clinical based on specific diagnostic criteria. Atypical KD in which patients have fewer than four of the five clinical features is being increasingly reported [1]. Clinical diagnosis for these patients is sometimes difficult. We report the case of an 11-year-old boy that was admitted complaining about prolonged fever and hematuria. The diagnosis was not established up until the death of the child. The autopsy revealed multiple thromboses of the coronary arteries and lesions of necrotic vasculitis due to KD.

Case

An 11-year-old boy was admitted to the hospital complaining about prolonged fever (5 days) and hematuria. During physical examination, the patient appeared ill with a temperature of 38.2°C, heart rate of 120 beats min^{-1}, and a blood pressure 138/56 mmHg. A mild respiratory distress was observed. The rest of the physical examination did not present any remarkable result. Initial laboratory testing indicated white blood cell count 10 800 μl^{-1}, platelet count 255 000 μl^{-1}, hematocrit 40%, hemoglobin 12.9 g dl^{-1}, blood urea nitrogen 122 mg dl^{-1}, uric acid 10.5 mg dl^{-1}, strongly positive C-reactive protein and direct Coombs reaction positive. The levels of serum complement 3 were low. Antistreptolysin O test was positive. His urinalysis showed pyuria, hematuria, proteinuria and urinary renal tubular epithelial cells concentrations. Chest radiographs on the day of admission were normal.

During the next days, the patient presented limb edema. By hospitalization day 4, the boy presented tachypnoea and asthmatic episodes. By hospitalization day 10 cardiac ultrasonography revealed a slight increase of the pericardial fluid.

After almost 2 weeks of hospitalization the patient presented melena and intense abdominal pain and subsequently he was transferred to the intensive care unit. Upon admission, the patient collapsed and cardiopulmonary resuscitation was performed for 45 min without yielding any result.

The patient was referred to our Department for autopsy on the following day. The skin and conjunctiva had a yellowish color and a limited mild

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doi:10.1093/tropej/fmn065 Advance Access Published on 31 July 2008

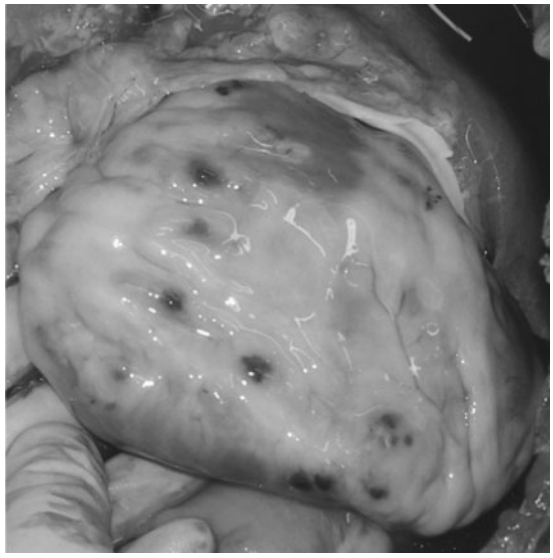

FIG. 1. Heart of increased dimensions and weight (310 g), presenting multiple thrombi in the coronary arteries with intramural dense polymorphonuclear inflammatory infiltration and necrosis.

exanthema on the lower extremities was observed. The macroscopical and histopathological examination of the heart showed increased dimensions and weight (310 g), intermediate edema and multiple thrombi in the coronary arteries (Fig. 1) with intramural dense polymorphonuclear inflammatory infiltration and necrosis. The lungs were congested with a mild mixed type inflammatory infiltration of the alveoli by macrophages. In the liver, a diffuse inflammatory reaction was present. The choledochal cyst presented signs of active cholecystitis while in the neighboring fat tissue, thrombosis and necrotic vasculitis were observed inside small and large lumen arteries. Histological examination of the kidneys revealed normal glomerulus, mild expansion of mesangial matrix, interstitial infiltration with lymphocytes, plasmatocytes and eosinophiles, normal vessels and normal immunofluorescence.

The death of the 11-year-old boy was attributed to coronary thrombosis as a consequence of KD.

Discussion

The diagnosis of KD is mainly clinical. It requires the recognition of five from six of the following symptoms: prolonged fever of unknown etiology, and moreover unresponsive to antibiotics, conjunctivitis, mainly of both eyes; erythema of oral mucosa and pharynx, strawberry tongue; diffuse inflammation of both hands and often feet; polymorphous desquamative rash; acute non-purulent cervical adenopathy [2].

The situation is even more complicated in cases of atypical KD. In our case, (i) the age was not the typical, (ii) except from the fever, none of the above mentioned criteria for KD was recorded and (iii) symptoms from the genitourinary system (hematuria of glomerular origin, aseptic pyuria and proteinuria) prevailed.

Symptoms from the genitourinary system are unusual in KD. Renal involvement is even rarer and it is confirmed by biopsy when the person is alive. Interstitial infiltrate [3], patchy zones of cytoplasmic vacuoles, necrosis and apoptotic bodies [4] have been described. In our case, the post-mortem histological results showed normal glomeruli and diffuse interstitial infiltration by lymphocytes, plasmatocytes and granulocytes.

The acute abdominal pain is also a rare complication of the KD. Mesenteric vasculitis in KD has been reported, but in most cases it remains asymptomatic. Abdominal complications are unusual and are associated with ischemic bowel stricture [5]. In our case, the complications caused by mesenteric ischemia were presented 2 weeks after the initial onset of the disease.

The lungs were also affected and presented interstitial inflammation, which justifies the reported asthmatic episodes and dyspnoea. Pleural effusion was also observed during the autopsy. Lung involvement in KD is uncommon. Lung changes are due to interstitial pneumonitis, lower respiratory tract inflammation and pulmonary arteritis [6]. The pulmonary involvement in KD may be due to increased vascular permeability as occurs in other vasculitides.

The most striking findings came from the heart with multiple necrotic lesions on the coronary arteries wall and multiple thrombi in their lumen. Autopsies have shown that the majority of deaths from KD are due to complications of coronary artery thrombosis or rupture of the coronary artery aneurysms [7]. About 20% of untreated KD patients develop coronary artery abnormalities, including diffuse dilatation and aneurysm formation. These findings emphasize the need for a very high index of suspicion to make the diagnosis.

As above mentioned, the diagnosis of KD is mainly clinical. However, the above case remained without diagnosis because the clinical picture was not the typical of KD, unusual symptoms, such as those from the genitourinary system, prevailed. Moreover, incidence for KD in Europe is quite low, comparing with countries in Asia, Japan and America [8].

The quite low incidence in Europe (and in Greece), probably means that there is a low level of suspicion and even cases presenting typical signs and symptoms of KD escape. Furthermore, not all children with KD develop the complete picture before coronary involvement is recognized. All the above cases are treated as 'Pyrexia of Unknown Origin' extending into

weeks. A high level of suspicion is needed by Greek pediatricians in order to recognize in time the patients with KD, treat accordingly and prevent sad complications from the cardiovascular system, or even the death of the child.

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