An Acute Thrombus Formation in the Left Coronary Artery of an Atypical Kawasaki Patient

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Received: 24 Dec. 2017; Accepted: 18 Feb. 2018

Abstract- Kawasaki disease (KD) is a self-limited syndrome with serious heart complications, mostly seen in children of age 5-month to 4-year-old. KD needs to be diagnosed soon to start IVIG within 10 days of starting symptoms to lower heart complications to 5 folds. Our case, a 2-year-old boy presented with prolonged fever and pharyngeal erythema. In early evaluation, erythrocyte sedimentation rate (ESR) was elevated, and after that, Color Doppler echocardiography with suspicion for KD was performed and showed aneurysm and thrombosis formation in the left coronary artery (LCA). Hence, intravenous immunoglobulin (IVIG) was started for the patient concurrent with daily check of troponin I level. In this case report, we present remarkable echocardiographic findings of a patient with the delay in diagnosis of KD demonstrating an aneurysm and acute thrombus formation in LCA.

Key words: Atypical Kawasaki disease, Coronary thrombosis, IVIG

Acta Med Iran 2018;56(5):351-354.

Keywords: Kawasaki disease; Fever; Thrombosis formation; Heart aneurysm

Introduction

Kawasaki disease (KD) is a high-risk disease of the heart according to American heart association (1). The predominant age of acute phase of KD is 5 months to 4 years, but there are cases of the acute disease in adulthood as well (2,3). Although this is a self-limited syndrome, meaning the fever and rash will disappear simultaneously without any treatment, most guidelines believe that the golden time for treatment is only 10 days in order to reduce serious risks of heart sequels like aneurysm formation of coronary artery, coronary artery calcification and thrombotic occlusion which may appear years later after the acute phase, and leading to arrhythmia, MI and sudden death (4,5). Coronary artery aneurysm is the resultant of pancarditis due to the increase of pro-inflammatory cytokines. The most important inflammatory cells are neutrophils, and the key involved cytokine is Interleukin 6 (IL-6), which causes many of the clinical features and laboratory findings of KD including coronary artery sequels (6,7). Hence, a decrease in IL6 and other cytokines causing endothelial inflammation will be seen, if within 10 days from the onset of the symptoms IVIG is started which results in 5 fold decrease in the risk of aneurysm and thrombosis formation (4,8). Other treatments in refractory cases who don't respond to IVIG are high-dose pulse methylprednisolone, cyclophosphamide, methotrexate, ulinastatin, cyclosporine A and plasmapheresis (6). Diagnosis of KD is clinical and based on the following criteria; fever which lasts at least for 5 days and the presence of 4 out of these 5 clinical features: 1) any signs of erythema, edema or desquamation in extremities; 2) polymorphous exanthema; 3) bilateral bulbar conjunctivitis without exudates; 4) mucosal or lip changes, including strawberry tongue, pharyngeal erythema or lip crackling; 5) cervical lymphadenopathy usually unilateral. In a typical case of KD, based on these criteria the diagnosis of KD can be made on fourth day of the illness. However, sometimes KD presents an atypical form which is harder to diagnose, and the clinician has to make the diagnosis based on other signs or laboratory findings (9) which are brought in table 1.

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Table 1. Typical laboratory features of Kawasaki disease

Test/feature	Value/result
Leukocytosis	>15,000
Normocytic normochromic anemia	
Thrombocytosis	>450,000
CRP	elevated
ESR	>40 mm/h
ALT	elevated
AST	elevated
GGT	elevated
Ferritin	elevated
Albumin	<3 g/dL
Sterile pyuria	Negative urine culture >10 leukocytes/field in urine analysis
Sodium	decreased

GGT=(gamma glutamyl transpeptidase), ALT=(alanine transaminase), AST=(aspartate transaminase), CRP=(C-reactive protein)

Case Report

A 2-year-old boy was referred to the emergency room with prolonged fever and pharyngeal erythema. ESR level was checked which was elevated, so he was admitted, and echocardiographic studies were performed, reporting a large aneurysm and a thrombosis in the LCA (Figure 1). Patient's fever started 1 month prior to the admission, which was associated with diarrhea. After the onset of fever, tonic-clonic generalized seizure occurred and the patient was hospitalized that time with the diagnosis of simple febrile convulsion for the first time, and discharged with phenobarbital and cefixime prescribed. During his first admission, ESR was reported 11. After discharge, the fever didn't go away and no considerable response to prescribed antipyretic or other antibiotic drugs was observed. After 30 days another ESR test was taken, showing an ESR of 52 hence the patient was admitted and echocardiographic images showed an aneurysm and a large thrombosis in the LCA. At the time of presentation, he did not have any complaints of mucosal or skin changes. In physical examination, he was ill and febrile (temperature 39° C of auxiliary). Also, his heart rate was 150 beats/min, blood pressure was 90/50 mmHg, and respiratory rate was 24 breaths/minute. Head and neck examination showed unilateral cervical lymphadenopathy and mild pharyngeal erythema, but other mucocutaneous findings of KD was not observed. Other examinations were all normal. The patient was admitted in pediatric ICU and received the first dose of IVIG (2 g/kg), anti-thrombotic therapy with heparin (Loading dose of 100 units/kg IV infusion and then 15 units/kg/hr IV as initial maintenance dose) and cardiopulmonary monitoring. An EKG was performed which was normal; his chest X-ray was normal as well. Daily troponin I level was continuously being checked for ruling out myocardial infarction (MI). Blood tests revealed white blood cells 10,000 counts/mm³ (52% neutrophils and 41% lymphocytes), hemoglobin 9.7 g/dl, and platelet 229 counts/mm³. Liver enzymes and liver function tests were normal. Daily troponin I was negative every day during hospitalization. The lab results are depicted in table 2.

Table 2. Laboratory findings of the patient

Test	Result
WBC	10000/mm3
HB	9.7 mg/dl
PLT	229000/mm3
ESR	36
CRP	2+
AST	26 IU/L
ALT	15 IU/L
Albumin	3.9 g/dl
PT	13 S
PTT	37
Total protein	6.4 g/dl
CPK	106 U/L
Troponin I	<0.1 ng/dl

In the fifth day of admission, warfarin (0.1 mg/kg PO QD) was added to heparin, and he received the second dose of IVIG because fever continued after the first dose of IVIG. Echocardiography was performed at the second day of admission, the fourth day of admission and the time of discharge and it still showed LCA aneurysm and the thrombus. Another EKG was taken which was normal, and the patient was discharged with prescription of warfarin (0.1 mg/kg PO QD) and aspirin (5 mg/Kg PO QD), and also he was referred to cardiology clinic in order to follow-up. At the time of discharge, ESR level was 19. 8 weeks after the initial echocardiogram, another one was repeated and displayed the aneurysm and thrombus, but the thrombus was smaller and in echocardiography of 6 months later the thrombus was gone (Figure 2).

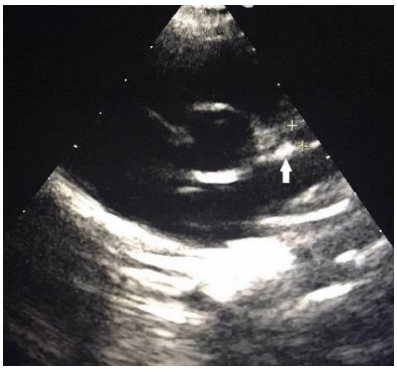

Figure 1. The patient's left coronary artery with thrombosis (arrow shows thrombus)

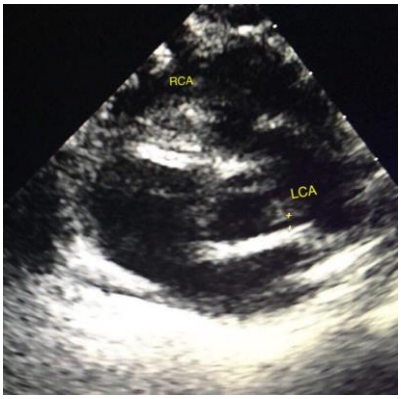

Figure 2. The patient's left coronary artery, six months later

Discussion

The case we present is an incomplete form of KD meaning that finding of coronary artery abnormalities confirmed the diagnosis. Among diagnostic criteria for KD our patient had fever, cervical lymphadenopathy, and erythema of pharynx. In 1993 another case of atypical KD affecting a 7-month-old baby was reported with the presentation of fever, exanthema and pharyngeal erythema that went through an acute thrombus formation in the left circumflex coronary artery and died in the ninth day of the illness. The baby also had a febrile convulsion episode like our patient, but he met toxic shock syndrome criteria as well, which made the diagnosis even harder and he had a worse general condition due to respiratory failure and shock symptoms (10). Another report of thrombus formation was found in a 4.5-month-old baby in 2000. Despite the patient was under antithrombotic therapy (high dose aspirin and dipyridamole from the 7th day of fever), 3 months after the onset of acute illness, a thrombus was found in a giant aneurysm located in the left anterior descending (LAD) coronary artery. Although commencement of treatment in this patient was sooner than ours, and our patient's thrombus formation was more acute, he seemed to respond to antithrombotic therapy better. However, similar to our case their patient seemed to be an atypical form of KD (11). In the report of Heaton *et al*., two cases of diagnosed atypical Kawasaki died as a result of MI in spite of receiving IVIG within the first 10 days of the acute phase of illness and neither developing thrombus formation (12). Virtually similar to our case, De Rosa *et al*., have reported a 7-year-old child, whom the diagnosis of KD was confirmed 15 days after the onset of fever and a thrombus was seen in his LAD which was 2mm long. He received one dose of IVIG and antithrombotic therapy without any ischemic cardiac complications (7). An extensive dilatation of coronary arteries and acute thrombus formation in the LAD of a 7-month-old baby following prolonged fever was reported in 2013. This was another atypical form of KD who was resistant to treatment and received 3 doses of IVIG, steroids and infliximab, but fever recurred. The size of the thrombus was reduced by receiving abciximab. Besides, the KD in this patient was complicated by pericarditis (13). Almost 3 weeks after the onset of fever in a 3-month-old baby, performing an echocardiography following a cardiac arrest, the diagnosis of KD was confirmed according to the report of Jone *et al*., The patient had a giant right CA aneurysm with small thrombus, and multiple coronary artery aneurysms in his LAD with the ejection fraction of 41%. He received tissue plasminogen activator (tPA) both intracoronary and IV, abciximab, enoxaparin, aspirin, and clopidogrel. 2 weeks later his EF was 63%. It was a delayed diagnosis in comparison to our case, but

our case didn't receive tPA and abciximab therapy and his response toward just heparin, warfarin, and aspirin was amenable (14). The first case report of thrombus formation in the coronary sinus following KD was recounted by Song *et al*., in a 3-month-old baby. In this incomplete KD which presented with prolonged fever associated with upper respiratory tract infection, IVIG was started on day 10 after the onset of fever which was the first day of hospitalization as well, and his first echocardiography was reported to be normal. On the 15th day of hospitalization, coronary artery aneurysms were seen and on day 29, echocardiography displayed coronary sinus dilatation with a thrombus. Treatment with heparin was started and similar to our case a good response was observed, since on day 34 the thrombus was disappeared (15). To sum up, in our case there was an obvious delay in the diagnosis of KD that can be explained because of atypical presentation of the patient. It is also worth-mentioning that thrombus formation was the common finding in all these atypical cases and this supports the idea that atypical form of KD is a possible risk factor of aneurysm and thrombus formation but it needs further evaluation. Other possible risk factors of coronary artery aneurysm are persistent fever, infants younger than 1-year-old and children older than 9-year-old and late diagnosis (16,17). There are other challenges ahead in order to well-diagnose KD, including lack of specific diagnostic tests. So it is highly recommended to have in mind that any patient of these ages presented with a prolonged fever should be investigated for KD in order to start early therapeutic approaches and avoid delay in diagnosis and subsequent loss of patients due to MI and other life-threatening complications.

Acknowledgments

The authors thank the patient's parents for allowing the case to be published.

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