

Nosocomial Sepsis Concomitant with Kawasaki Disease: A Case Report

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ABSTRACT

Kawasaki disease is an acute febrile systemic vasculitis presenting with unknown etiology. Coronary artery ectasia or aneurysms may develop in 15% to 25% of untreated children and may lead to sudden death or ischemic heart disease later in life. Thus, early diagnosis and treatment with intravenous immunoglobulin and acetylsalicylic acid as soon as possible are important. Patients who have persistent or recurrent fever more than 24 hours after completion of the initial treatment should also be assessed for other causes of fever including intercurrent infection, and the diagnosis of refractory Kawasaki disease should be reevaluated.

INTRODUCTION

The Kawasaki disease is a type of vasculitis which was first defined in Japan in 1967 and is characterized by fever, rash, bilateral non-exudative congestion of the conjunctiva, cervical lymphadenitis, swelling and erythema of hands and feet. It is the second most common vasculitis in childhood after Henoch-Schönlein vasculitis and the most common acquired heart disease in developed countries. Its aetiology and pathogenesis have not been unraveled yet.^[1] To prevent cardiac complications, it is necessary to make diagnose in the acute phase and to start intravenous immunoglobulin (IVIG) treatment together with high dose acetylsalicylic acid (ASA). The most important complications are ectasia or aneurysms of the coronary arteries. Despite the single-dose IVIG, 20% of the patients, however, may develop persistent or recurrent fever. Thus, they need a second dose of IVIG. Some studies report that corticosteroids and immunosuppressive treatments can

be administered to patients who do not respond to varied doses of IVIG.^[2]

Nosocomial infections are an important problem in hospitals with large intensive care units and where invasive procedures or major surgeries are carried out. Among all nosocomial infections, nosocomial sepsis is a significant contributor. Every year 35 million people are hospitalized, and 2.5 million people develop nosocomial infections in the United States of America. Of this group, 250.000 people have nosocomial sepsis, and 62.500 of them die consequently.^[3]

Here, we presented a case that was diagnosed with nosocomial sepsis while he was on the treatment of Kawasaki disease.

CASE REPORT

A 2-year-old boy who had a fever that persisted for seven days, body rash, weakness and less appetite than before,

first presented to a medical clinic. He had been diagnosed with upper respiratory infection and antibiotics, antipyretics had been started. Despite this, the complaints remained and he presented to another hospital. On his physical examination hyperaemia of the conjunctiva, 2x2 cm lymphadenopathy on right cervical area, hyperaemia of peroral area and oropharynx, maculopapular rash were present. His complete blood count (CBC) showed a white blood cell (WBC) count of 18300/mm³, with 12810/mm³ neutrophils, 1300/mm³ lymphocytes, 430/mm³ monocytes. The platelet count was 395000/mm³ and C-reactive protein (CRP) was 85 mg/dl. The rest of his laboratory findings were normal. With these symptoms and findings, the patient was diagnosed with Kawasaki disease. IVIG and ASA treatment started with 2 gr/kg of 12h infusion and 80 mg/kg/day four doses per day, respectively. Echocardiography (echo) was performed twice and both of them were evaluated as normal. After the regression of his fever, the patient was discharged on the 10th day of his hospitalization with 5 mg/kg/day ASA treatment. Two days later, the patient was admitted to our emergency unit with fever and erythema of his eyes. The only significant entry in his medical history was his premature birth at 32 weeks. His physical examination revealed; weight: 10 kg (<3 percentile), height: 84 cm (10–25 percentile) fever: 38.9°C, pulse: 120/min, respiratory rate: 15/min, blood pressure: 100/50 mmHg. He had bilateral conjunctivitis and a white strawberry tongue. On his right cervical area, painless, mobile, 0.5x0.5 cm lymphadenopathy was present and his cardiovascular examination showed a 2/6 systolic murmur. The rest of his examination was normal. His laboratory data showed as follows: hemoglobin: 9.6 gr/dl, WBC: 16970/mm³, hematocrit: 28%, platelets: 346000/mm³. The peripheral blood smear showed 75% neutrophils, 25% lymphocyte. CRP was 85 mg/dl and the sedimentation rate was 89 mm/h. The other biochemical data were normal. According to these results, refractory Kawasaki disease was diagnosed and pediatric cardiology was consulted. An echo was performed and it showed coronary artery ectasia. Advised by pediatric cardiology, the second infusion of IVIG (2 gr/kg/single dose) was applied and the dose of ASA was regulated as 100 mg/kg/day. After this, second dose of IVIG, his fever regressed within 48 hours. After being followed up without any fever for another two days, he developed a resistant fever again. Fever source could not be found to explain the resistant fever in his physical examination. Laboratory data showed; hemoglobin: 8.6 gr/dl, WBC: 6240/mm³, neutrophils: 4560/mm³, hematocrit: 25%, platelets: 186000/mm³ CRP: 18 mg/dl, procalcitonin: 7.95 ng/ml. Pediatric rheumatology was consulted for the etiology of his fever. Rheumatologic diseases were ruled out and bone marrow aspiration was advised because of hemophagocytic syndrome (HLH). Therefore, pediatric hematology was consulted to rule out HLH and the other causes of fever. A bone marrow smear was performed, but there were no pathologic findings on it. A new blood test showed ferritin: 179 ng/ml fibrinogen: 523 mg/dl very-low-density lipoprotein (VLDL): 15.8 mg/dl triglyceride: 79 mg/dl. The laboratory data and the bone

marrow smear did not demonstrate the criteria of HLH. After this, due to his persistent fever, pediatric cardiology consultation was made again. It was advised that the patient should be evaluated for non-responder IVIG treatment-refractory Kawasaki disease and high dose steroid treatment should be started. Before starting this steroid treatment, as a differential diagnosis, nosocomial sepsis was considered because of his long term hospitalization. Blood culture was taken and a piperacillin-tazobactam (100 mg/kg/day, 3 doses) treatment was started. On the 24th hour after taking the blood culture, gram-negative bacillus signal was reported. On the 48th hour of the antibiotic therapy, the fever regressed. *Klebsiella pneumoniae* (extended-spectrum beta lactamase-piperacillin-tazobactam susceptible) isolation was reported. With the patient's fever regressed, pediatric cardiology was consulted again. The repeated echo showed that the ectasia of the coronary arteries was still continuing and the rest was still the same. In the first week of his high dose ASA treatment, his sedimentation level was found normal and ASA treatment was regulated as 5 mg/kg/day. Antibiotic therapy continued till the 10th day, and he was discharged on the 14th day of his hospitalization. Twenty days after his discharge, an echo was performed again and the regression of his coronary artery ectasia was seen. Finally, the last echo, which was performed at the 6th month, was normal, and the ASA treatment was discontinued.

DISCUSSION

To make a diagnosis of Kawasaki disease, at least five of the following symptoms are required: fever, changes of the peripheral part of the extremities, polymorph exanthema, bilateral conjunctival congestion, changes of oropharyngeal mucosa and cervical lymphadenopathy. 'Japanese Diagnostic Guidelines' accepts that in addition to four of these six major findings, establishing of coronary artery changings with echo or angiography is sufficient to diagnose Kawasaki disease.^[3,4] Kawasaki disease has three clinical periods as follows: subacute, acute and convalescent. The acute period which is characterized by fever and the other clinical findings of the disease lasts 1–2 weeks. The subacute period starts with regression of the fever and the other clinical findings and lasts till the 4th week. This period is also very important due to its increased risk of coronary artery aneurysms related to thrombocytosis and sudden death. The convalescent period (6th–8th week) is the period when all clinical findings regress and the sedimentation rate returns to normal. Coronary artery involvement in Kawasaki disease may cause myocardial ischemia, rarely infarct, rupture of aneurism and even death in 20–30% of the cases that are not treated with IVIG during the acute period. With the administration of high dose IVIG and ASA, the risk of the involvement of coronary arteries decreases to 2–3%.^[5,6] Furthermore, between the 3rd and 14th day of the IVIG treatment, persistent or recurrent fever is defined as refractory Kawasaki disease. Treatment options of the cases of refractory Kawasaki disease after IVIG include pulse steroid, abciximab (glycoprotein

IIb/IIIa inhibitor) and plasma exchange.^[7] In our case, 12 days after the first IVIG dose, the fever increased again and the second dose of IVIG was administered because refractory Kawasaki disease was considered. In his follow up, the ectasia of the proximal parts of the coronary arteries was seen. Following the 4th day of the second dose of IVIG, the regressed fever presented itself again. At first, we thought that it was a non-responder IVIG treatment-refractory Kawasaki disease. However, a nosocomial infection, which may appear after 48–72 hours of hospitalization, was also among our differential diagnoses.^[3] High procalcitonin levels of the patient in this period and no explicable source of fever, pointed in the direction of nosocomial sepsis. Thus, the nosocomial sepsis was considered as preliminary diagnosis and antibiotic therapy was started. The regression of the fever after antibiotic therapy and the isolation of *Klebsiella pneumoniae* (extended-spectrum beta lactamase-piperacillin-tazobactam susceptible) in the blood culture confirmed our diagnosis. Refractory Kawasaki disease and non-responder IVIG treatment-refractory Kawasaki disease should be considered after ruling out of the other causes of the fever. On our patient, the other causes of the fever were investigated and nosocomial sepsis was regarded before starting the steroid treatment.

In conclusion, when recurrent or refractory fever is present in patients who received appropriate treatment for Kawasaki disease, firstly, refractory Kawasaki disease should be ruled out. Subsequently, the other causes of fever, including sepsis, should be kept in mind in cases with long term hospitalization due to the Kawasaki disease because nosocomial sepsis is very common among these patients.

Informed Consent

Written informed consent was obtained from the parents of the patient for the publication of the case report and the accompanying images.

Peer-review

Internally peer-reviewed.

Authorship Contributions

Concept: E.A., L.Ş.K.; Design: E.A., N.D.; Supervision: N.D., M.K.; Materials: E.A., L.Ş.K., B.C.; Data: E.A., L.Ş.K.; Analysis: N.D., M.K.; Literature search: E.A., L.Ş.K., B.C.; Writing: E.A., L.Ş.K., B.C.; Critical revision: N.D.

Conflict of Interest

None declared.

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Nozokomiyal Sepsis ve Kawasaki Hastalığı Birlikteliği: Bir Olgu Sunumu

Kawasaki hastalığı etiyojisi bilinmeyen akut ateşli sistemik bir vaskülitir. Tedavi edilmeyen olgularda %15–25 oranında koroner arter ektazisi ve anevrizma gelişerek ani ölümlere ve ileri yaşlarda hastalıklara neden olabilmektedir. Bu nedenle erken teşhis ve intravenöz immünglobülin ile asetil salisilik asit tedavisinin en kısa sürede başlanması çok önemlidir. Tedavi başlangıcından 24 saat sonra nüksetme veya persistan ateş durumlarında, sepsis de dahil olmak üzere diğer ateş nedenleri dışlanarak refrakter Kawasaki hastalığı tanısı düşünülmelidir.

Anahtar Sözcükler: Kawasaki hastalığı; nozokomiyal; sepsis.