A Case of Kawasaki Disease Presenting with Aseptic Meningitis

Aseptik Menenjit Başlangıçlı Kawasaki Hastalığı Olgusu

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Abstract

Early recognition and prompt treatment of Kawasaki disease(KD) are essential to ensure a succesful outcome of the coronary artery involvement. However, some patients lack sufficient clinical signs to fulfill the diagnostic criteria, and this may lead to problems in diagnosing children presenting with atypical symptoms. Central nervous system involvement, including aseptic meningitis, can be a presenting feature of KD itself. In this article, we describe a 9-year-old boy who presented with an unusual onset of disease, characterized by fever, erythematous maculopapular rash, vomiting and abdominal pain. He was diagnosed as aseptic meningitis with an unusual onset of Kawasaki Disease (KD) clinical pattern together with the echocardiographic coronary arteries anomalies. Since the cardiovascular sequelaes of the disease could be prevented by early diagnosis and effective drug therapy, KD should be considered in the differential diagnosis in children with fever, erythematous maculopapular rash and vomiting that may be associated with clinical features of aseptic meningitis.
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Key Words: Kawasaki disease; fever; aseptic meningitis

Özet

Kawasaki hastalığının erken tanısı ve hızlı tedavisi, koroner arter tutuluşu üzerinde olumlu sonuçların elde edilmesi için esastır. Hastalığın özgül bir tanısı yoktur ve tanı karakteristik klinik bulgular ile konur. Bazı hastalarda klinik tanı için yeterli sayıda kriter olmadığından atipik bulgularla başlangıç gösteren olgularda hastalığın teşhisi güçleşebilmektedir. Ender bulgular ile başvuran hastalarda tanı güçlükleri olabilmektedir. Merkezi sinir sistemi tutulumunu gösteren aseptik menenjit tablosu, hastalığın atipik bir başlangıcı olabilmektedir. Bu makalede, ateş, eritematöz cilt döküntüleri, kusma ve karın ağrısı şikayetlerini takiben aseptik menenjit tanısı alıp sonrasında klinik ve ekokardiyografik olarak Kawasaki Hastalığı teşhisi alan olan 9 yaşında bir erkek olgu sunulmuştur. Hastalığa bağlı kardiyolojik sekeller hastalığın erken tanı ve tedavisi ile önlendiğinden, ateş, döküntü, kusma gibi menenjit bulgularının ön planda olduğu olgularda ayırıcı tanıda Kawasaki Hastalığı da akılda bulundurulmalıdır.
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Anahtar Kelimeler: Kawasaki hastalığı, ateş, aseptik menenjit

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Kawasaki disease is an acute systemic vasculitis which effects the small and moderate-sized arteries (1). This disease is also known as mucocutaneous lymph node syndrome and it was first reported in Japan in 1967. The etiology is still unknown (2). Kawasaki disease can be seen in every ethnic group, also in Japan, and it is seen mostly in infants, between 6-12 months and more commonly in males (3).

The typical property of Kawasaki disease is fever, lasting for at least 5 days. There is no specific laboratory test. In addition to fever, there are bilateral non-purulent conjunctival injection, cervical lympadenopathy (LAP), edema in hands and feet, erythema and desquamation (4). Central nervous system involvement, including aseptic meningitis, can be a presenting feature of KD. Approximately one-third to one-half of patients with KD who undergo lumbar puncture will have a cerebrospinal fluid (CSF) pleocytosis (5).

With early diagnosis and treatment, especially the development of cardiovascular sequelae can be prevented. Therefore, the aim of this article is to focus on the importance of early diagnosis and treatment of atypical onset of the Kawasaki disease.

Case

A 9-year-old male patient, admitted to our emergency room with fever. The case was considered as an upper respiratory tract infection; thus, amoxicillin-clavulanate threapy was initiated. Two days after the antibiotic therapy, the patient visited the emergency room again with fever at 38.6ºC. Thus, therapy with another class of antibiotic (clarithromycin) was initiated. Although still febrile and there was no meningismus, he was discharged without a diagnosis. The next day, the patient visited the emergency room again with skin rash and continuining of fever. After consultation with the dermatology clinic, the patient was diagnosed with multiformed erythema. Then, he was hospitalized in the dermatology clinic for further examination. The patients' fever was still high as above 38ºC after 6 days of antibiotic therapy. On the second day after his hospitalization, he suffered from vomiting, headache, diarrhea and gastric pain. Since meningeal irritation signs were present in the patient, he was transferred to the pediatrics clinic with the prediagnosis of meningitis.

On physical examination, he was conscious, active and cooperated. Axillar temperature was 38.3ºC, and arterial blood pressure was 80/60 mmHg. His oropharynx and tonsills were hyperemic and hypertrophic, lips were red, there was a red strawberry appearance in his tongue, and a mobile, 2 cm cervical lymphadenopathy (LAP). Examination of the abdomen showed tenderness and defence with no rebound. He had hepatomegaly (2 cm), nuchal rigidity, Kernig and Brudzinski signs were present. Skin examination revealed erythematous maculopapular rash particularly on the legs.

The laboratory findings were as follows; leukocyte count: 8600/mm^3; hemoglobin: 11 g/dL; hematocrit: 24%; platelet count: 305,000/mm^3; C-reactive protein:14.81 mg/dL; erythrocyte sedimentation rate (ESR): 64 mm at 1-hour; aspartate aminotransferase: 66 U/L; alanine aminotransferase: 49 U/dL; urea: 20 mg/dL; creatinine: 0,66 mg/dL; antistreptolysin-O titer: 1001 IU/mL; anti-nuclear antibody, anti-DNA and rheumatoid factor were negative. Prothrombin time, activated partial thromboplastin time, international normalised ratios were normal, and TORCH indicators were negative. Total urinanalysis was normal. Cerebrospinal fluid (CSF) glucose and protein levels were within normal limits, Pandy test was negative. In CSF leukocyte count was 40/mm^3, and erythorocyte count was 160/mm^3.

Samples were taken for culture and the patient was started with ceftriaxone 100 mg/kg/day. With the antibiotic treatment the fever was not taken under control and on the second day of the treatment, the patient had bilateral conjunctivitis. We consulted the patient with the ophthalmology department and the case was diagnosed with non-purulent conjunctivitis. Thus, at the ninth day of fever, the patients had erythematose rashes, oral symptoms, unilateral cervical LAP (2 cm) in addition to fever, and thereafter he had bilateral conjunctivitis, mild hepatomegaly with ultrasonography, and minimal dilatation in the coronary arteries with echocardiography (ECHO). With these signs and symptoms, the patient was diagnosed with Kawasaki disease. The antibiotic therapy was stopped and the patient was started with aspirine 80 mg/kg/day and intravenous immunoglobulin (IVIG) 2 g/kg. His ESR was 105 mm at 1-hour and platelet count was 788,000/mm^3.

During the follow-up, he experienced bradycardia (3 times) which was recovered without any treatment. Our patient's fever was under control and one week after the treatment he had desquamations in his hands and feet. After 14 days, the dose of aspirine was reduced to 5 mg/kg/day. ESR was 35 mm at 1-hour, platelet count was 273,000/mm^3, and ECHO was normal. The aspirine treatment was ended after 8 weeks, because of normal echocardiographic finding without any cardiac sequles, and normal sedimentation rate. The patient had no problems during the follow-up as assessed in both our clinic and the pediatric cardiology clinic.

Discussion

For diagnosis of classical KD four of five main criteria should be appear (6). Incomple or atypical forms of KD are related with higher risk of coronary abnormalities because diagnosis presents more difficulties and therapy starts after 10 days of illness (1, 7). In the present case. the full diagnostic criteria for KD were present, and the diagnosis of atypical onset of KD was based on the presence of prolonged fever without a focus infection, skin rash, vomiting and meningeal irritation signs in the subacute phase of the illnesss. There was no other underlying cause fort his childs presentation of aseptic meningitis because all investigations were negative. Because of this, in our case, coronary involvement may be associated with delaying the accurate diagnosis (7).

There is no specific laboratory tests for the diagnosis of this disease. Thus, the diagnosis primarily depends on the clinical findings (8, 9). The presence of prolonged fever, especially in the absence of bacterial infection, and the presence of some clinical and laboratory findings might suggest incomple KD (7). Fever and erythematosis rash are frequently confused with staphylococcal or

Table 1. Kawasaki disease, diagnostic criterias (8, 9)

Additional to the fever, lasting for at least 5 days; 4 of the 5 criterias written below.
1. Non-purulent bulbar conjunctival injection
2. Oropharyngeal changes (orophangeal erythema; dry, swollen lips, strawberry tongue, compact erythem on the buccal and pharingeal surfaces)
3. Extremite changes (erythema on the feet surfaces and on the palm of the hands, periungeal desquamation, edema on the hands and feet)
4. Maculopapular, erythema multiforme or scarlatiniform
5. Unilateral, cervical, more than a diameter of 1,5 cm, acute non-suppurative lymphadenopathy (LAP)

streptococcal toxic shock syndrome. In these types of infectious diseases, the differential diagnosis is usually made by local epidemiologic data, history of a travel, history of vaccination and the results of the cultures (6). In some centers, prolonged fever and subsequent peripheral desquamation were the most common findings in children with atypical onset of KD (6). In our patient, one week after the treatment he had desquamations in his hands and feet.

Neurologic complications in KD have been described to affect 1.1% of children in a Japanese cohort of 450 children with KD (10). Aseptic meningitis is the most common, accounting for 5% of all neurologic complications (11). Other neurologic associations and complications of KD have been described and include extreme irritability, meningoencephalitis, subdural collection, ataxia and sensorineural hearing loss (5,11,12). Our patient had vomiting and headache on the sixth day of the disease. The considering these symptoms and CSF results, we suspected of aseptic meningitis accompanying Kawasaki disease. Muzaffer et al. (13) evaluated 3 cases with aseptic meningitis among 13 patients with Kawasaki disease. Dengler et al. (6) conducted a study in 46 patients having Kawasaki disease. In the first 10 days of the disease (prior to IVIG theraphy) they performed lumbar puncture to evaluate CSF. They found that 39.1% of the patients had pleocytosis in CSF, 2.2% had low CSF glucose levels (<45 mg/dL) and 17.4% had high CSF protein levels. There is no data in the literature showing patient presenting with aseptic meningitis Kawasaki disease in in our country.

Aseptic meningitis in children with KD can be caused by vasculitis of small arteries,arterioles and venules(3,4). In the differential diagnosis of KD , infantile polyarteritis nodosa, mercury intoxication, Stevens-Johnson syndrome, juvenile rheumatoid arthritis and drug reactions need to be excluded. In the history of our patient, there was no contact with mercury and or drug use. The clinical aspect was not compatible with Stevens-Johnson syndrome. Acute rheumatic fever (ARF) should be excluded when a child has fever and carditis. Our patients' clinical symptoms were not compatible with Jones criteria, and there were no ARF carditis symptoms. There was only dilatation in the coronary arteries with ECHO. Although high level ASO titer and hyperemic tonsils were seen in our patient, unresponsiveness to the antibitics, a good response to the aspirin treatment and, ECHO findings we exclude to the possible a streptococcal infection. Additionally, Adenoviral infections can mimic of KD with some signs. Although, we did not obtain further viral serologic study, presence typical erythematosis rash on the extremities, response to the aspirin treatment andtypical ECHO finding, we exclude an adeno-conjunctival fever, also. In some unusual onset of KD, may be present with clinical signs and symptoms of acute cholestasis (14). In our case also, have got abdominal pain and vomiting that may be associated gallbladder involvement but there was no jaundice, hepatomegaly and typical ultrasonographyc findings may be typical signs of cholestasis.

The clinicians must look for additional criteria to confirm the diagnosis of Kawasaki disease (Table 1). In a patient, the presence of 4 criteria in addition to fever is enough to diagnose Kawasaki disease. For the diagnosis of atypical Kawasaki disease, 4 criteria plus coronary artery aneurysm should be present (7,8). Our patient had fever, erythematose rash, oral symptoms, and LAP. Then, he developed conjunctival infection. According to these signs and symptoms, we diagnosed him with Kawasaki disease. The coronary artery dilatation in his ECHO supported our diagnosis, also.

Once the Kawasaki disease is diagnosed, the treatment must be started immediately. Otherwise in 25% of untreated patients, there is a risk of severe cardiovascular injury (15). Although it is difficult to diagnose the disease, it can be treated very effectively. IVIG and aspirine are used for the treatment of these patients. This treatment regimen was shown to prevent the cardiovascular organs from damage and regress the damage which was developed before (2,13). The symptoms of our case were not compatible with those of the infectious and noninfectious diseases. Indeed, IVIG and aspirine treatment were dramatically successful and we observed clear recovery both clinically and biochemically after the treatment. He did not have any problems during the follow-up visits which were made every 3 months.

As a conclusion, neurologic manifestations like as aseptic meningitis may preceed in some KD. The atypical form of KD seem to predict a higher risk to have coronary dilata-

tion; so pediatrician must a high index of suspicion fort this diagnosis. Our case shows that in a child presenting neurologic manifastation with prolonged fever, erythematose rash, and bilateral conjunctivitis, in spite of absence full criteria, w emay consider KD as possible illness.

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