A Case of IVIG-Resistant Kawasaki Disease with Gallbladder Hydrops

Safra Kesesi Hidropsu ile Birliktelik Gösteren IVIG-Dirençli Bir Kawasaki Hastalığı Olgusu

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ABSTRACT Kawasaki Disease is an acute systemic vasculitis of childhood affecting small and medium-sized arteries particularly coronary arteries. Intravenous immunoglobulin therapy decreases the major cardiovascular complication of the disease. Atypical clinical conditions may accompany to the disease and these cases seem to be more prone to intravenous immunoglobulin resistance which is an important problem in the management of the cases. Herein, we presented a case of 4-year-old boy admitted to our emergency department with fever of 5 days duration and diagnosed as Kawasaki disease based on the clinical, laboratory and imaging findings. He was resistant to intravenous immunoglobulin treatment and in the follow up resulting abdominal tenderness was explained by gallbladder hydrops.

Key Words: Mucocutaneous lymph node syndrome; gallbladder; immunoglobulins, intravenous

ÖZET Kawasaki Hastalığı küçük ve orta çaplı arterleri özellikle de koroner arterleri etkileyen bir çocukluk çağı akut sistemik vaskülitidir. Intravenöz immunglobulin tedavisi hastalığın major kardiyovasküler komplikasyonlarını azaltmıştır. Atipik klinik durumlar hastalığa eşlik edebilir ve bu olgular vaka yönetiminde önemli bir problem olan intravenöz immunglobulin direncine daha yatkındırlar. Bu yazıda, 5 gündür devam eden ateş yakınması ile acil servisimize başvuran ve klinik, laboratuar ve görüntüleme bulgularına dayanarak Kawasaki hastalığı tanısı alan 4 yaşındaki erkek hastayı sunduk. Olgu intravenöz immunglobulin tedavisine dirençli idi ve izlemde gelişen abdominal hassasiyet safra kesesi hidropsuna bağlandı.

Anahtar Kelimeler: Mukokutanöz lenf nodu sendromu; safra kesesi; immünglobulinler, intravenöz

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Kawasaki Disease (KD) is an acute systemic vasculitis of childhood affecting small and medium-sized arteries particularly coronary arteries. It is the most frequent cause of acquired heart disease in children in developed countries which was first described by Tomisaku Kawasaki et al. in 1960s.[1,2] The diagnostic criteria for KD include fever lasting at least five days and four of the following conditions: bilateral non-exudative conjunctivitis, erythema of the lips and oral mucosa, rash, extremity changes, and cervical lymphadenopathy. Atypical clinical conditions such as aseptic meningitis, arthritis, abdominal pain and gallbladder hydrops may accompany to KD. Whereas its etiology is still unknown, the major cardiovascular complications such as coronary artery aneurysm and myocardial is-

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chemia dramatically decreased with the therapy of intravenous immunoglobulin (IVIG).[3] IVIG resistance seen in 20% of patients with KD is an important problem and these patients are especially under risk of developing coronary artery complications.[3] Herein we report a 4- year- old boy with IVIG- resistant KD who had gallbladder hydrops.

CASE REPORT

A 4-year-old boy was admitted to our emergency department with fever of 5 days duration. On physical examination he was irritable with a temperature of 39°C, respiratory rate of 35/minute and heart rate of 130 beats/minute. He had oral mucosal changes (erythema, dryness and fissuring of the lips, strawberry tongue), erythematous and edematous palms and soles, maculopapular rash, non-purulent bulbar conjunctivitis and lymphadenopathy larger than 1.5 cm on left cervical area. Arms, legs as well as the abdomen were painful to touch. The initial abdominal ultrasound showed minimal ascites with a normal sized and shaped gallbladder. Laboratory studies showed leukocytosis (18 000/mm^3), elevated erythrocyte sedimentation rate (80 mm/hour) and increased C reactive protein (CRP) (10.3 mg/dL). Serum albumin (2.5 mg/dL) and Na levels (133 mmol/l) were low and lipid profile showed decreased levels of HDL mg/dL. Serum cardiac troponin-I levels were normal. The patient was hospitalized with the diagnosis of KD. The initial echocardiographic evaluation of coronary arteries was in normal limits without any perivascular brightness or ectasia. Left ventricular systolic functions were normal. There was no pericardial effusion. ECG was free of the signs of myocarditis and myocardial ischemia. Blood and urine cultures were negative. He received IVIG at a dose of 2 g/kg along with aspirin at a dose of 80 mg/kg/day. No clinical improvement occurred after first IVIG treatment. The fever persisted, leucocyte count and C reactive protein levels increased. Albumin levels decreased to a value of 1.3 mg/dL. Second echocardiographic examination of the coronary arteries performed on the 3rd day of hospitalization was in normal limits. The abdominal tenderness increased and abdominal ultrasound determined hydrops of the gallbladder. Because of the suspicion of the perforation, abdominal computerized tomography was performed but it did not determine any perforation except hydrops of the gallbladder (Figure 1). Second dose of IVIG was given but fever persisted after 24 hours from the second dose. Finally intravenous prednisolone at a dose of 2 mg/kg/day was begun. After prednisolone, clinical symptoms improved rapidly. CRP, leukocyte count and albumin levels normalized. At the 5th day of prednisolone gallbladder hydrops regressed. Intravenous prednisolone was replaced to oral prednisolone and the patient was discharged.

DISCUSSION

Gallbladder hydrops is defined as acute distention of the gallbladder in the absence of mechanical obstruction.[4] Sepsis, KD, leptospirosis, typhoid fever, scarlet fever and polyarthritis nodosa are the clinical conditions that may be associated with gallbladder hydrops.[5] It is an uncommon complication of KD and occurs in 5-13% of patients with KD.[6] In a study of Chen et al., 21% of KD patients who underwent abdominal ultrasound had gallbladder hydrops.[7] Hou et al. reported hydrops as the presenting complaint in 2 of 3 cases.[8] In our patient hydrops developed after the other clinical manifestations.

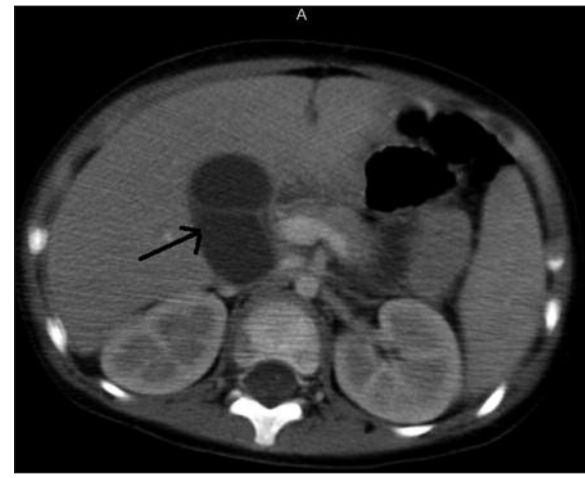

FIGURE 1: Abdominal computerized tomographic view of gallbladder hydrops (arrow).

The recommended treatment of gallbladder hydrops in KD is conservative. Surgical treatment is preferred only for complications such as perforation and peritonitis.[9] We preferred conservative treatment because of the lack of complications.

IVIG resistance occurs in up to 20% of cases and these patients are at risk of developing coronary artery aneurysm unless they receive additional treatment.[10] Patients who have persistent or recurrent fever more than 24 hours after completion of the initial treatment should also be assessed for potential infection, and the diagnosis of KD should be reevaluated. These patients should be retreated for repeating of KD unless there is clear evidence of another explanation for fever, since numerous studies have confirmed an association between prolonged fever and development of coronary artery abnormalities.[11] Young patient age, initial treatment at or before the 4th day of illness, significantly elevated CRP, elevated liver enzymes, platelet count less than 300 000/mm^3, serum sodium levels lower than 133 mmol/l are the clinical factors increased the likelihood of patient nonresponsiveness to initial IVIG therapy.[12] Low serum albumin and high neutrophil levels were reported to be independent predictors of IVIG resistance Chen et al. reported that sonographic gallbladder abnormalities are associated with higher CRP, neutrophil and IVIG resistance.[7] Our patient had low serum sodium, significantly increased CRP and low serum albumin as well as gallbladder hydrops.

Various observational studies suggest that the persistent fever of the patients after initial treatment with IVIG will resolve after retreatment with IVIG. But sometimes multiple doses of IVIG may incompletely control KD and these patients are also under increased risk of coronary artery aneurysms. Corticosteroids, inhibitors of tumor necrosis factor, other immunosuppressive agents and plasmapheresis are the other therapeutic options. Although the results of clinical trials evaluating the use of corticosteroids plus IVIG are confusing, Chen et al. found that significantly fewer patients receiving IVIG plus corticosteroids developed coronary artery aneurysm than those receiving IVIG alone.[13] Our patient underwent the treatment with corticosteroid because he was resistant to 2 doses of IVIG. No coronary artery aneurysm was detected at the end of treatment.

In conclusion gallbladder hydrops is a rare but important complication of KD and these patients may show resistance to IVIG treatment.

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