CASE REPORT

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Kawasaki Disease Shock Syndrome with Acute Kidney Injury and Hypertension

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Kawasaki disease (KD) is an acute febrile mucocutaneous lymph node syndrome that commonly presents with stable hemodynamic status during the acute phase. An 8-year-old boy initially presented with severe hypotension and acute kidney injury. He was placed in the intensive care unit and was diagnosed with KD. Observed clinical features were defined as KD shock syndrome. His coronary artery was dilated during the subacute phase. Furthermore, he was given anti-hypertensive medications, owing to hypertension as an unusual complication of KD. We knew the importance of monitoring for blood pressure considering vasculitis as an aspect of the main pathogenesis of KD.

Key Words: Mucocutaneous lymph node syndrome; Shock; Acute kidney injury; Hypertension

Introduction

Kawasaki disease (KD) is an acute febrile mucocutaneous lymph node syndrome with generalized systemic vasculitis predominantly involving medium and small-sized blood vessels[1,2]. KD predominantly occurs in infants and young children, particularly in Asian countries such as Japan, Korea, and Taiwan. The etiology of KD is yet ill-defined. The coronary arterial lesions are important complications which often occur during the subacute phase of KD.

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Most researches concerning KD have mainly focused on the coronary artery lesions; however, long-term experiences with KD have informed researchers about its various clinical manifestations. The spectrum is diverse from self-limited mild symptoms to severe forms such as hemophagocytic lymphohistiocytosis, macrophage activation syndrome, and shock syndrome[3,4]. Especially, hemodynamic instability during the acute phase of KD is uncommon. Several reports have described the initial presentation of shock syndrome in KD patients[4-6]. Kanegaye et al.[7] have reported children requiring critical care support due to shock and hypotension and defined this condition as Kawasaki disease shock syndrome (KDSS). Children with KDSS may have various clinical courses and are known to have higher risk for coronary artery dilation[8]. We report a case of an 8-year-old boy with KDSS and complications following acute kidney injury (AKI) including coronary artery dilatation and hypertension.

Case

A previously healthy 8-year-old boy was transferred to Jeju National University Hospital with a 4-day history of fever and altered consciousness. He presented with fever and right submandibular swelling in a local clinic 4 days before the transfer. He was admitted to the local clinic because of persistent fever. Although he was treated with ampicillin/sulbactam, fever was not relieved. Abdominal pain and erythematous macular rash appeared 1 day before the transfer. History of cough and rhinorrhea was not noted.

When he was transferred, he was ill-looking and generally edematous. Initial vital signs were as follows: blood pressure (BP) of 78/35 mm Hg (5th percentile of systolic BP for same age: 86 mm Hg), pulse rate of 113 beats per minute, respiratory rate of 22 breaths per minute, and body temperature of 38.3℃. Neurological assessment showed a Glasgow Coma Scale score of 12 (E3, V4, M5). His body weight was 39.4 kg, which was increased 6 kg higher than his usual weight. The pupil reflex was prompt and conjunctivae on both eyes were slightly injected. The tongue was dry, but strawberry tongue was not noted. The cervical lymph node was not palpable. Skin rash was prominent and coalescing. Erythema of the hands and feet, or the injection of Bacillus Calmette-Guérin (BCG) site was not observed. His abdomen and costovertebral area were not tender. His extremities had non-pitting edema. Laboratory findings on admission were as follows: white blood cell (WBC), 6,700/μL (85.9% segmental neutrophil, 11.2% lymphocyte); hemoglobin, 11.7 g/dL; hematocrit, 33.4%; platelet 35,000/μL; albumin, 2.4 g/dL; total protein, 4.6 g/dL; total bilirubin, 2.4 mg/dL; aspartate aminotransferase, 161 IU/L; alanine aminotransferase, 146 IU/L; blood urea nitrogen, 40.8 mg/dL; creatinine (Cr), 1.3 mg/dL; sodium, 128 mmol/L; potassium, 3.8 mmol/L; calcium, 7.1 mg/dL; phosphorus, 3.0 mg/dL; and uric acid, 5.9 mg/dL. C-reactive protein (CRP) was elevated at 24.95 mg/dL (normal range, 0 to 0.3 mg/dL) and erythrocyte sedimentation rate (ESR) was 8 mm/hr. Urinalysis results were as follows: specific gravity, >1.03; pH, 5.5; red blood cells, 1-4/high-power field (HPF); protein, 1+; WBC, 1-4/HPF; and protein to creatinine ratio, 0.95.

We initially suspected septic shock or myocarditis. He was treated with inotropics (dopamine and dobutamine), empirical antibiotics (vancomycin and cefotaxime), and intravenous immunoglobulin (IVIG; 1 g/kg) for suspected septic shock. On his fourth hospital day (HD), hypotension was controlled without inotropics; however, his fever persisted. Conjunctival injection was more prominent, and strawberry tongue had just appeared. KD was considered a likely diagnosis, and hence, additional high dose of IVIG (2 g/kg) and aspirin (50 mg/kg) was administered.

On HD 5, his fever and skin rash subsided. No virus or bacteria were found in blood, urine, stool, or nasopharyngeal aspirates. Echocardiography revealed no dilatation of coronary arteries (left main coronary artery [LMCA], 3.6 mm; right coronary artery [RCA], 2.8 mm; and left anterior descending [LAD], 2.5 mm), and no perivascular brightness. The dose of aspirin was reduced to 5 mg/kg/day on the following day. CRP level decreased to 3.83 mg/dL on HD 9, whereas ESR increased to 58 mm/hr. Thrombocytosis was observed (platelet, 494,000/μL) and Cr decreased to 0.7 mg/dL. The intravenous antibiotics were discontinued. His BP was incidentally checked at 139/86 mm Hg and intermittent hypertension was subsequently observed.

Kidney Doppler revealed no tardus parvus waveform suggesting arterial stenosis in the kidney on HD 12. He was discharged with low-dose of aspirin as home medication. One week after discharge, his body weight was 33.2 kg, which was similar before the illness, and both hands and feet were desquamated. A 24-hour ambulatory BP monitoring revealed that his mean BP was 126.2/84.9 mm Hg and 119.0/75.8 mm Hg during the day and night, respectively (Fig. 1). Systolic or diastolic BP was higher than 121/81 mm Hg, corresponding to the 95th percentile which is approximately 77%. We started carvedilol for treatment of stage 1 hypertension. Follow-up echocardiography 7 weeks after the onset of disease revealed coronary dilation (LMCA, 3.7 mm, Z score=1.32; LAD, 4.7 mm, Z score=5.86; RCA, 3.8 mm, Z score=3.05) and low-dose aspirin was

maintained. Proteinuria disappeared (protein-to-creatinine ratio, 0.04) and BP was checked at 134/76 mm Hg.

Discussion

Half-century experiences with KD have revealed its diverse clinical spectrums. Especially, hemodynamic instability during the acute phase of the illness is uncommon, except for infusion of IVIG. The rates of admission to the intensive care unit during the acute phase of KD were reported to be from 1.9% to 3.3%[7,9]. Several reports commented that most patients with KD and severe hypotension had delayed diagnosis because of treatment for unstable hemodynamic status[4,9]. These uncommon conditions of KD have led to terminology

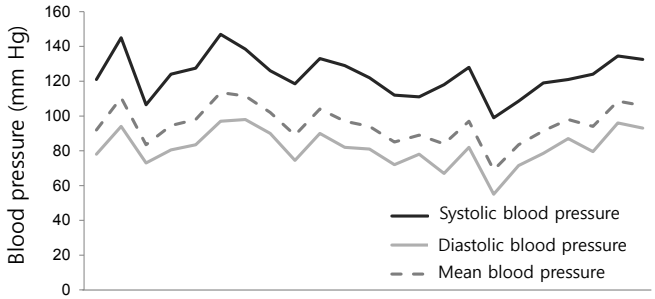

Fig. 1. A 24-hour ambulatory blood pressure monitoring 19 days after disease onset.

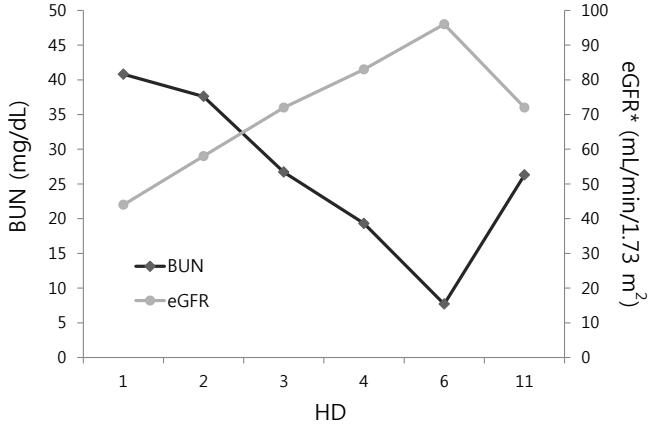

Fig. 2. Changes in the estimated glomerular filtration rate (eGFR) and blood urea nitrogen (BUN) related to the hospital day (HD). *eGFRs were calculated using the creatinine-based "Bedside Schwartz" equation.

of KDSS as a severe variant of KD characterized by hypotension and hemodynamic support in the critical care setting[7]. Initially, we suspected shock due to myocarditis or other bacterial infections. During the management of shock, other diagnostic clinical features of KD were found. The IVIG response, desquamation of extremities, and coronary artery dilatation on echocardiogram confirmed the diagnosis.

The pathogenesis of KD including KDSS was unknown. Kim and Kim[10] hypothesized the etiology was associated with the immature immune response to infection, autoimmune factors. After that, striking immune derangement, various changes of immune cells and over-produced cytokine have been considered the main immunopathogenic role in KD. We hypothesized that KDSS has similar pathogenesis with KD in a view of immunopathogenesis. By genetic susceptibility, more excessive immune dysregulation could produce overwhelming cytokines, and then result in endothelial damage and capillary leak. Compared to KD, more severe immune dysregulation and persistent inflammation in KDSS could explain the high IVIG resistance in KDSS. KDSS is associated with more severe changes in inflammatory markers, thrombocytopenia, and greater risk of coronary artery abnormalities in several case-control studies[8,9].

In our case, AKI, which is generally uncommon in KD, resolved for a relatively short time after controlling hypotension and IVIG administration (Fig. 2). Moderate proteinuria without hematuria at disease onset disappeared within 2 weeks. Renal complications in KD are uncommon, except for sterile pyuria[11,12]. Pathogenesis of AKI associated KD has been suggested including prerenal AKI due to acute heart failure, immune-complex mediated nephropathy, tubulointerstitial nephritis, and hemolytic uremic syndrome[12]. Gatterre et al.[4] reported 10 patients with KDSS with AKI who recovered from AKI without any renal sequelae. Out of 10 patients, eight had multiple organ dysfunction syndrome. Mac Ardle et al.[13] reported a 2-year-old boy with clinical features of KDSS who developed AKI that required peritoneal dialysis. In that case, renal biopsy was performed and evidence of acute tubular necrosis was

observed. We presumed that AKI was related with acute tubular necrosis because of sustained hypotension and development of transient nephrotic syndrome with azotemia related to KDSS.

Unexpectedly, hypertension was found without a headache or palpitation in our case. His BP was higher than 95th percentile based on the European hypertension guideline[14]. Hypertension is an uncommon complication in patients with KD; however, controlling hypertension in patients with KD is important because of coronary artery aneurysmal rupture risk[15]. Hypertension in KD can be explained by renal artery stenosis, which is a characteristic feature of vasculitis syndrome. Arterial inflammation of extra-coronary artery including kidney was known to be milder than that present in the coronary arteries[16,17]. The evidence of renal artery stenosis was not radiologically found in our patient, and we cannot explain the cause of his hypertension. However, we planned to follow-up this complication for a long time based on case reports of renal artery stenosis found several years after onset of KD[18,19]. Transient hypertension in patients with KD as a side effect of IVIG infusion has been reported; however, the mechanism was unclear[20].

In conclusion, we report a KDSS patient who had uncommon two complications including AKI during the acute phase and hypertension during the subacute phase. The prognosis of our patient was expected to be poor, considering the high rates of cardiac complications of KDSS and his older age. However, until now, he has had a complication of dilated coronary artery without mitral regurgitation or myocardial dysfunction. Reviewing this case, we know that initial presentation, such as shock syndrome, can be diagnosed as KDSS. In addition, the unusual complication of hypertension showed that regular BP monitoring should be highlighted in patients with KD.

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요약

가와사키병은 다른 원인이 없는 발열과 함께 피부점막에 특징적인 병변을 보이는, 소아에서는 비교적 흔한 질환으로 일반적으로 급성기에는 혈역학적으로 안정적이다. 저자들은 심한 저혈압과 함께 급성 신손상이 있는 상태에서 내원한 8세 남아가 치료 중에 가와사키병으로 진단된 증례를 경험하였다. 최근에는 가와사키병 초기에 불안정한 혈역학적 상태를 가와사키병 쇼크증후군이라는 개념으로 정의하고 있다. 환아는 면역글로불린 치료 후 임상적으로 회복되었으나 관상동맥 확장 합병증이 확인되어 아스피린을 복용하고 있으며, 가와사키병의 합병증으로서는 비교적 드문 고혈압이 확인되어 베타 차단제를 사용하고 있다. 본 증례를 통해 가와사키병 쇼크증후군의 임상 양상을 알고, 혈관염이라는 가와사키병의 특성을 고려해볼 때 혈압 모니터링의 중요성을 깨닫게 되었다.