ORIGINAL ARTICLE

pISSN 2384-1079 · eISSN 2384-1087

Pediatr Infect Vaccine 2015;22:40-44

DOI: http://dx.doi.org/10.14776/piv.2015.22.1.40

PIV PEDIATRIC INFECTION & VACCINE

뇌척수액세포증가증과 경막외 삼출액이 동반된 비정형 가와사키병 1례

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Incomplete Kawasaki Disease in a 5-Month-Old Girl Associated with Cerebrospinal Fluid Pleocytosis and Epidural Fluid Collection

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Cases of incomplete Kawasaki disease (KD), wherein the patient does not fulfill the full diagnostic criteria for KD, are often detected in infants younger than 6 months of age. The clinical manifestations in infants with incomplete KD may resemble other infectious diseases, including meningitis. For this reason, clinicians may have difficulty differentiating incomplete KD from other infectious diseases in this population. Various neurological features are associated with KD, including aseptic meningitis, subdural effusion, facial nerve palsy, cerebral infarction, encephalopathy, and reversible corpus callosum splenial lesions on magnetic resonance imaging. We report a case of a 5-month-old girl with incomplete KD, associated with cerebrospinal fluid pleocytosis and an epidural fluid collection. Echocardiography indicated dilatation of the main coronary arteries. The girl made a complete recovery, with resolution of both the epidural fluid collection and coronary artery aneurysms. In this case, the child is well, and showed normal developmental milestones at the 7-month follow-up.

Key Words: Kawasaki disease, Infant, Cerebrospinal fluid, Pleocytosis, Epidural abscess

Introduction

The diagnosis of Kawasaki disease (KD) is based on the presence of fever, lasting at least 5 days, and of 4 of the 5 following criteria; bilateral conjunctival injection; changes of the mucous membranes, such as injected or fissured lips and strawberry tongue; polymorphous rash; changes of the extremities including peripheral edema, peripheral erythema and periungual desquamation; and cervical lymphadenopathy[1]. The diagnosis requires that there are no other explanations for the clinical presentation. The term 'incomplete KD' is used for patients presenting with fever of at least 5 days

*The authors declare no potential conflicts of interest related to this study.

Received: 14 October 2014

Revised: 25 October 2014

Accepted: 26 October 2014

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duration, and at least 2 of the 5 additional criteria for KD. It is required that there is no other reason for the illness, and that laboratory findings are consistent with severe inflammation[1,2].

The incidence of incomplete KD appears to be greater in infants of less than 1 year of age[3]. Notably, it is in infants less than 6 months of age with KD that the risk of coronary artery aneurysm is greatest[3]. The clinical presentation of incomplete KD in infants may resemble other infectious diseases, including meningitis[4]. For this reason, the clinician may have difficulty differentiating incomplete KD from other causes of infection.

KD is rarely accompanied by neurological complications, which are reported to include aseptic meningitis, subdural effusion, facial nerve palsy, cerebral infarction, encephalopathy, and reversible corpus callosum splenial lesions on magnetic resonance imaging (MRI)[5-8]. Herein, we report a case of a 5- month-old girl with incomplete KD associated with cerebrospinal fluid pleocytosis and epidural fluid collection. The girl made a complete recovery, with resolution of the epidural fluid collection on MRI of the brain, and the subsequent echocardiogram showed full resolution of the coronary artery dilatation.

Case Report

In March 2014, a previously healthy 5-month-old girl was transferred to our center with a 3-day history of sustained fever (39℃), not relieved by antipyretics. The fever was associated with febrile seizures of a few seconds' duration, associated with eyeball deviation to upward gaze. There was no history of cough or rhinorrhea, but the patient was noted to have reduced activity. There was a single episode of diarrhea, on the background of a loose stool pattern in the 2 days prior to visiting our hospital, but no history of nausea or vomiting. On physical examination, the patient looked acutely unwell, and was noticeably lethargic. She was tachycardic (heart rate, 184 beats/min), tachypneic (respiratory rate, 58 breaths/min), and febrile (body temperature (BT), 39.5℃). Pulse oximetry showed her oxygen saturation to be 95% on air. The anterior fontanelle was flat, and conjunctival injection was not obvious. The lips were red, dry, and fissured. The tongue was dry, but there was no sign of pharyngeal injection or strawberry tongue. The cervical lymph nodes were not palpable. Examination of the skin for an amorphous maculopapular rash was unremarkable. However, it was subsequently noted that the patient had marked redness around the bacillus Calmette-Guérin (BCG) vaccination site. No erythema or edema of the hands or feet was observed.

Laboratory findings on admission were as follows: white blood cell (WBC), 20,400/μL (segmental neutrophil 62.5%, lymphocyte 28.8%); hemoglobin (Hb), 10.8 g/dL; hematocrit (Hct), 30.8%; platelets (PLT), 327,000/ μL; total protein 6.7 g/dL; albumin, 4.0 g/dL; total bilirubin, 0.5 mg/dL; alkaline phosphatase, 360 IU/L; aspartate aminotransferase, 22 IU/L; alanine aminotransferase, 17 IU/L; glucose, 110 mg/dL; and C-reactive protein (CRP), 9.94 mg/dL. Her serum electrolyte data included: sodium, 133 mmol/L; potassium, 4.8 mmol/L; chloride, 101 mmol/L, and bicarbonate level of 18.3 mmol/L. Results of urinalysis were normal, with the exception of microscopic hematuria (red blood cell, 5-9/high power field).

A lumbar puncture was performed at presentation, to rule out meningitis. The cerebrospinal fluid (CSF) cell count was as follows: red blood cell, 0 cell/mm^3 and WBC, 105 cells/μL (polymorphonuclear leukocyte, 3%; lymphocyte, 43%; mononuclear cell, 40%; and other cell (mesothelial cell, atypical cell), 14%). CSF chemistry results included: pH, 8.0; glucose, 62 mg/dL; protein, 42 mg/dL; and lactate dehydrogenase, 51 IU/L.

As a result of these clinical findings and initial investigations, our differential diagnoses included meningitis, roseola infantum, or Kawasaki disease. The patient was treated with intravenous (IV) empirical antibiotics (vancomycin and cefotaxime), an antiviral (IV acyclovir) and antipyretics (acetaminophen and ibuprofen).

On hospital day (HD) 3, the patient's vital signs showed no substantial improvement (HR, 158 beats/min; RR, 50 breaths/min; BT, 39.5℃). An amorphous maculopapular rash was noted on the trunk, which was

present for 2 days; faint conjunctival injection was also noticed. The follow-up laboratory findings were as follows: WBC 13,600/μL (segmental neutrophil 61.5% and lymphocyte 31.9%); Hb, 9.5 g/dL; Hct, 27.4%; PLT, 269,000/μL; erythrocyte sedimentation rate (ESR), 95 mm/hr; total protein, 5.6 g/dL; albumin, 3.1 g/dL and CRP, 18.3 mg/dL. Nasal swab samples, analyzed using polymerase chain reaction (PCR) for 9 respiratory viruses (adenovirus, influenza A, influenza B, metapneumovirus, respiratory syncytial virus, rhinovirus, parainfluenza 1, parainfluenza 2, parainfluenza 3), were all negative. Brain MRI showed fluid collection in the epidural space with high-intensity on T1-weighted images, iso-intensity on T2-weighted images, and high-intensity on fluid-attenuated inversion-recovery (FLAIR) images. Pachymeningeal thickening and a rim of enhancement around the left frontoparietal lobe were also noted (Fig. 1A). After referring to the clinical presentation and laboratory results, KD was considered a likely diagnosis; consequently, treatment with high dose IV immunoglobulin (2 g/kg) and aspirin (80-100 mg/kg/day) was initiated.

On HD 4, the patient's fever, conjunctival injection and skin rash subsided. Blood and CSF cultures were sterile. The dose of aspirin was reduced to 1-3 mg/kg/day. On HD 6, the patient's CSF enterovirus PCR and herpes simplex virus PCR were reported to be negative, so treatment with IV acyclovir was discontinued. On HD 8, thrombocytosis was observed (PLT, 587,000/μL), and the ESR had increased to 120 mm/hr, while the CRP level had decreased to 1.47 mg/dL. Her first echocardiogram revealed mild focal dilatation of the coronary arteries (right coronary artery, 2.2 mm diameter; left main coronary artery, 3.0 mm diameter) and perivascular brightness.

On HD 16, a repeat MRI indicated resolution of the fluid collection in the epidural space (Fig. 1B). The IV antibiotics were discontinued, and the patient was discharged home on a low dose of aspirin. The patient underwent repeat echocardiography 2 months after the onset of disease, in another hospital; the report indicated that the coronary artery dilatation had improved.

Discussion

We suspected KD based on the clinical features and blood, microbiological, and imaging test results. With regard to the clinical features, the patient's fever persisted despite treatment with antibiotics for potential meningitis. Skin rash and conjunctival injection were also observed. Blood tests indicated the presence of inflammation, with a raised ESR and CRP level on serial follow-up tests. Microbiological examination revealed no pathogenic bacteria either in the blood or on CSF culture, reducing the likelihood of an infective etiology. CSF

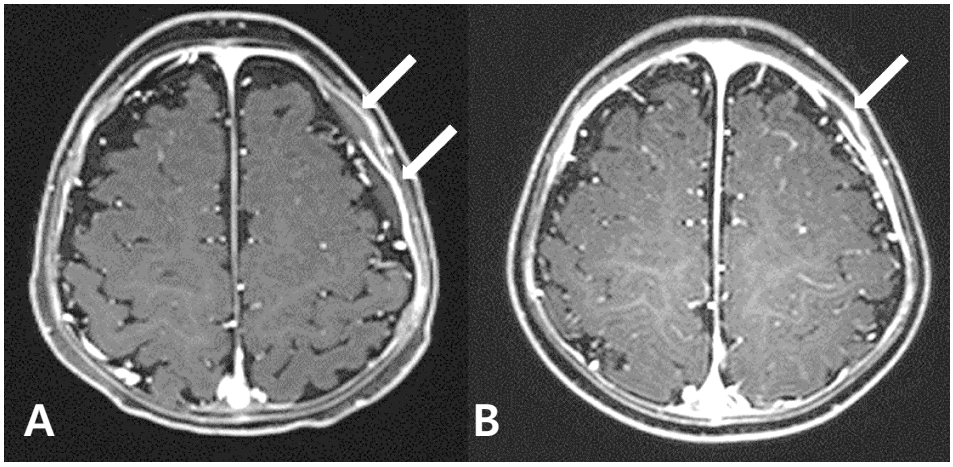

Fig. 1. Magnetic resonance imaging of the brain shows the epidural fluid collection with pachymeningeal thickening on the left frontoparietal lobe on hospital day 3 (A), and on hospital day 16 (B). A and B are axial T1-weighted post-contrast images.

pleocytosis and epidural effusion seen on MRI were likely to have been reactive changes due to KD, rather than bacterial meningitis. Finally, the echocardiogram showed typical features of KD, including coronary artery dilatation and perivascular brightness. The patient's response to IVIg also helped confirm the diagnosis. Desquamation of the fingers and toes, which is a characteristic clinical sign of the subacute phase of KD, was not seen in this case.

Yeom et al[3] mentioned the importance of diagnosis and treatment of infantile KD. The typical presentation of KD, involving mucosal changes and lymphadenopathy, are known to be rare in the first 6 months of life[9]. In addition, unusual symptoms, including aseptic meningitis, appear to occur more frequently in this age group[9]. It is plausible that the infrequent occurrence of typical signs of KD in affected infants is secondary to an inadequate immune response, which results in the weak vasculitis phenomenon observed in this age group[10]. Alternative explanations for the occurrence of incomplete KD in infants include the effect of superantigen neutralization by maternal antibodies, transferred via the placenta, or cross-reaction of antibodies generated by frequent active immunization[10]. As a result of the dearth of typical features of KD, diagnosis of infantile KD younger than 6 months is difficult. Additional factors complicating diagnosis in the present case included the course of the symptoms and signs (typical manifestation of KD presented in sequence, rather than simultaneously), and the absence of both mucosal changes, such as strawberry tongue, and changes to the peripheral extremities. KD should be considered when prolonged fever with nonspecific clinical features is present, mainly in the first 6 months of life in whom incomplete KD is more predominant[4].

Yeom et al[11] reported that KD in infants younger than 3 months was associated with a less prominent CSF pleocytosis, as compared with CSF pleocytosis in enteroviral meningitis; cases of KD in that study had a median CSF WBC count of 8.5 cells (range, 8-27 cells)[11]. In contrast, Dengler et al[12] reported a more prominent CSF pleocytosis (median CSF WBC count, 22.5 cells (range, 7-320 cells)), with a mononuclear cell predominance. In our patient, the CSF WBC count was elevated, and as such, we were obliged to use IV antibiotics and antiviral agents while waiting for the results of CSF culture and PCR.

The reported incidence of neurological complications in KD is approximately 1.1%[13]; while an uncommon occurrence, extracerebral fluid collection has been previously reported[8,14,15] and is generally detected following computed tomography (CT) or MRI of the brain. However, the value of lumbar puncture is unclear, given that some of the patients did not undergo lumbar puncture, and others who did undergo lumbar puncture had normal CSF findings. Takagi et al[14] reported 5 cases of KD associated with meningoencephalitis, in whom CT of the brain showed a fluid collection in the frontal extracerebral space, and whose CSF studies revealed a monocyte-predominant pleocytosis. To the best of our knowledge, there has been no previous report of a case of incomplete KD associated with cerebrospinal fluid pleocytosis and epidural fluid collection in Korea.

The basic mechanism for the CSF pleocytosis in KD remains unknown, but neurological complications in KD are assumed to be secondary to vasculitic involvement of the dura mater[15]. The long-term prognosis for patients with KD complicated by an extracerebral fluid collection is considered to be generally favorable[8,14,15]. In this case, the child is well, and showed normal developmental milestones at the 7-month follow-up.

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요약

비정형 가와사키병은 가와사키병의 진단기준을 충족하지 않는 경우를 말하며, 주로 6개월 미만의 영아에게서 발현하는 경우가 많다. 비정형 가와사키병의 임상소견은 뇌수막염과 같은 감염질환과 비슷할 때가 있어서, 이러한 경우 임상적으로 비정형 가와사키병을 감염질환과 감별하기 어려울 때가 많다. 또한 가와사키병과 연관되어 보고된 신경계 이상은 무균수막염, 경막하삼출, 안면신경마비, 뇌경색증, 뇌병증, 뇌자기공명영상의 가역적 뇌량팽대 변화 등이 있다. 본 저자들은 뇌척수액세포증가증과 경막외 삼출액이 동반된 비정형 가와사키병으로 진단된 5개월 여아에 대해 보고하는 바이다. 환자의 심장초음파검사에서 관상동맥이 늘어나 있었고, 추적관찰에서 경막외 삼출액과 관상동맥 합병증이 모두 회복되었으며 생후 12개월에 발달이정표는 정상이었다.