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COVID-19

Kawasaki Disease and Invasive Pneumococcal Infection

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To the editor,

We have read the article by Watanabe et al. [1] with special interest. We have also experienced an infant with Kawasaki disease (KD) secondary to invasive pneumococcal disease (IPD).

In 2018, a 20-month-old girl was admitted to our hospital because of a series of febrile seizure. She had been a healthy infant with no particular medical history. She had completed 13-valent conjugate vaccination (PCV13) according to the Japanese immunization schedule. Ten days before the admission, she had a fever, which persisted for 4 days, and was followed by transient rash.

Fever and a rash developed again 2 days before the admission, and a rash spread to a whole body on the next day. She had a convulsion for 10 min in the evening, which stopped spontaneously.

Several hours later, she had a second convulsion, which also subsided, and visited the emergency department of our hospital with her parents at midnight.

On admission, her consciousness was clear, and the temperature was 39.5 °C. There were no abnormal neurological findings. Blood examination presented a white blood cell count (WBC) of 20,100/μL (69% of neutrophils), hemoglobin of 11.1 g/dL, platelet count of 54.3×10^4/μL, lactate dehydrogenase of 805 IU/L, aspartate aminotransferase of 71 IU/L, alanine aminitransferase of 27 IU/L, sodium of 133 mEq/L, total protein of 7.2 g/dL, albumin of 3.0 g/dL, C-reactive protein (CRP) of 7.86 mg/dL, immunoglobulin (Ig) G of 815.7 mg/dL, IgM of 160.4 mg/dL, IgA of 69.4 mg/dL, and D-dimer of 3.0 μg/mL. There was no gross abnormality on the head computed tomography, and pleocytosis in the spinal fluid was absent. Rapid tests for pharynx adenovirus and group A *Streptococcus* were both negative. Intravenous cefotaxime (CTX) administration was started empirically. In the morning, she developed five out of six major KD symptoms (except for lip findings), and intravenous immunoglobulin (2 g/kg; IVIG) and oral aspirin (30 mg/kg/day) were started according to the definite diagnosis of KD with a Kobayashi score of 4 [2]. The blood culture became positive for GPC in the evening, and intravenous ampicillin (ABPC) was added to cover enterococcus infection, empirically. Both spinal fluid and urine culture were negative. On the next day, fever decreased transiently. However, fever increased again to 39.0 °C on the 3rd day after admission and systemic rash and edema became further deteriorated. Blood examination revealed WBC of 11,100/μL, CRP of 7.52 mg/dL, sodium of 136 mEq/L, albumin of 2.4 g/dL, and D-dimer aggravated to 13.7 μg/mL. GPC was determined to be *Streptococcus pneumoniae* with penicillin susceptibility, and antibiotic treatment was switched to ABPC only. Considering of unresponsiveness to IVIG, prednisolone (2 mg/kg/day; PSL) was added. The follow-up blood culture performed on the same day was found to be negative later. Fever decreased to normal level, and a rash and edema improved dramatically on the 4th day. The pneumococcal serotype was determined as 24B (non-vaccine strain) later. The patient was discharged on oral aspirin after 14 days antibiotic treatment. During the course, the coronary lesion was absent.

In our case, KD was unresponsive to IVIG in spite of proper antibiotic treatment for IPD, and KD was well responsive to PSL instead. It is considered that IPD might be a triggering factor of KD and highly elevated D-dimer is a significant risk factor of IVIG unresponsiveness in KD as we have previously reported [3]. Concerning the preceding febrile episode which occurred 10 days before the admission, the likelihood of exanthem subitum was speculated, although it was not confirmed serologically. It is very interesting to speculate that the preceding viral infection might be a prerequisite background of KD which was later triggered by IPD, when considering the unknown immunological pathology of KD [4, 5]. Furthermore, when once induced, KD requires specific treatment for itself, even if the triggering infection such as IPD as in our case is controlled by proper antibiotic therapy.

This article is part of the Topical Collection on *Covid-19*

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Recently, the relationship between KD and the novel coronavirus infection (COVID-19) has been reported and noticed with great concerns [6, 7]. Further investigation should be required to disclose the association of KD with infections.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval Informed consent was obtained from the patient's parents under institutional ethical approval.

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