Letters to the Editors

Kawasaki disease shock syndrome in Korean children

Sirs,

Kawasaki disease (KD) is a systemic inflammatory vasculitis of unknown cause that predominantly occurs in children under 5 years of age (1, 2). In rare cases, KD can present with shock, and this unique and severe subtype of KD is called Kawasaki disease shock syndrome (KDSS) (3, 4). KDSS has a more severe disease course and worse outcomes than haemodynamically stable KD (3-5). KDSS can be confused with various paediatric conditions that cause severe inflammation, such as septic shock, toxic shock syndrome (TSS), multi-system inflammatory syndrome in children (MIS-C), or macrophage activation syndrome (MAS) (6, 7). Although many studies on KD have been conducted in East Asia, research on KDSS is limited, especially in Korea (8, 9). In this brief report, we investigate the incidence and characteristics of KDSS in Korean children.

This retrospective study reviewed data from nine patients with KDSS hospitalised at four hospitals in Korea (Seoul St. Mary's Hospital, Eunpyeong St. Mary's Hospital, Bucheon St. Mary's Hospital, and Daejeon St. Mary's Hospital) between January 2013 and December 2022 (8). Among the patients with KD (M30.3), those who received vasoactive drugs or had a secondary diagnosis code for hypotension (I95.9) were considered to have developed KDSS. All nine patients with KDSS met both the diagnostic criteria for KD (1) and the case definition of shock (systolic hypotension for age, a decrease in systolic blood pressure from baseline ≥20%, or clinical signs of hypoperfusion) (4). When calculating the incidence of KDSS, patients with KD who received treatment with intravenous immunoglobulin (IVIG) and aspirin during hospitalisation were included in the total number of patients with KD. To estimate the severity of KDSS, 140 patients with KD from our previous study (2) were selected as a control group for comparison.

The study protocol was approved by the Institutional Review Board of the Catholic University of Korea (approval no.: HC24RISI0024).

During the 10-year study period, 1,095 patients with KD were hospitalised, and the incidence of KDSS was 0.8% (9/1,095). Table I presents the characteristics of patients with KDSS. Of the nine patients with KDSS, seven were hospitalised between January 2013 and December 2019 and two were hospitalised between January 2020 and December 2022 (*i.e.* during the COVID-19 pandemic). Age, initial diagnosis, and time to KDSS diagnosis varied among the patients. Rash and conjunctivitis were common KD-related symptoms observed in most patients (8/9). All patients had multiorgan involvement, with gastrointestinal (8/9) and cardiac (7/9) involvement being the most common. Haematologic (6/9), renal (3/9), and neurologic (2/9) involvements were also observed. Notably, some patients (4/9) met the 2016 MAS diagnostic criteria (10). For management, vasoactive drugs (8/9), systemic steroids (7/9), and biologic agents (1/9) were administered in addition to IVIG and aspirin.

The clinical and laboratory findings of patients with KDSS (n=9) and KD (n=140) are shown in Supplementary Table S1. Compared with patients with KD, those with KDSS were older, had longer hospital stays, and showed higher rates of IVIG resistance, coronary artery abnormalities (CAAs), empirical antibiotics, and intensive care unit (ICU) admission. Laboratory abnormalities, such as anaemia, thrombocytopenia, C-reactive protein (CRP) elevation, hypoalbuminaemia, and pyuria, were also observed more frequently in patients with KDSS than in those with KD.

The term KDSS was first introduced by Kanegaye *et al*. (3) in 2009 to distinguish this severe form of KD from haemodynamically stable KD. In their study, IVIG resistance and CAAs were more frequent in patients with KDSS than in those with KD without shock. In addition, KDSS has distinct epidemiological characteristics (5). In contrast to KD, KDSS occurs more frequently in children older than 5 years, in Hispanic populations, and in non-Asian regions (4, 7). In this study, the incidence of KDSS was lower than that reported in non-Asian regions (Table II) (3, 11-16).

The initial diagnoses of the nine patients with KDSS varied, including septic shock, TSS, atypical KD, myocarditis, bacterial cervical lymphadenitis (BCL), urosepsis, or appendicitis. On the day of hospitalisation, one patient showed typical KDSS manifestations that met both the KD criteria and the shock definition, whereas the remaining eight patients showed atypical manifestations. Over half of the patients (5/9) with KDSS were diagnosed with complete KD. However, KD-related symptoms did not appear all at once, so the KDSS diagnosis was delayed. Early KDSS recognition may have been more challenging in patients with incomplete KD and fewer KD-related symptoms. Therefore, KDSS should be considered in the differential diagnosis of children with unexplained organ dysfunction, even

Table I. Characteristics of nine children with KDSS in Korea.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9
Date of hospitalisation	Sep 2013	Aug 2014	Jan 2016	Feb 2016	Feb 2018	Mar 2018	Mar 2018	Jan 2022	Feb 2022
Age (year) / Sex	6.0 / M	13.1 / M	1.8 / M	15.5 / F	1.0 / F	9.3 / F	12.3 / F	9.9 / F	5.9 / M
Initial diagnosis	BCL	Atypical KD	Urosepsis	Septic shock	Myocarditis	TSS	Appendicitis	Septic shock	KDSS
Time to KDSS diagnosis (day)	7th	3rd	4th	6th	13th	7th	5th	6th	1st
KD-related symptoms									
Rash	Y	Y	Y	–	Y	Y	Y	Y	Y
Conjunctivitis	Y	Y	Y	Y	Y	–	Y	Y	Y
Oropharyngeal inflammation	Y	Y	Y	–	Y	Y	–	–	Y
Extremity changes	Y	Y	–	Y	Y	–	–	–	–
Cervical lymphadenopathy	Y	–	Y	–	–	–	Y	–	Y
Type of KD	Complete	Complete	Complete	Incomplete	Complete	Incomplete	Incomplete	Incomplete	Complete
Organ involvement and outcomes									
Shock, systolic/diastolic	68/30	74/38	60/32	80/50	66/39	59/26	72/55	52/40	62/27
Other organs involved	C, G, H, R	C, G, H	G	C, G, N	C, G, H, R	G, H	C, G, H	C, H, N	C, G, R
MAS (met 2016 criteria)*	–	Y	Y	–	–	–	–	Y	Y
IVIG resistance	Y	Y	Y	–	Y	–	–	–	–
CAAs	Y	–	–	Y	Y	–	–	–	Y
Successful recovery	Y	Y	Y	Y	Y	Y	Y	Y	Y

KDSS: Kawasaki disease shock syndrome; KD: Kawasaki disease; M: male; F: female; BCL: bacterial cervical lymphadenitis; TSS: toxic shock syndrome; Y: yes; –: no or not tested; C: cardiac (*i.e.* myocarditis); G: gastrointestinal; H: haematologic (*i.e.* cytopenia or coagulopathy); R: renal (*i.e.* acute kidney injury); N: neurologic; MAS: macrophage activation syndrome; IVIG: intravenous immunoglobulin; CAAs: coronary artery abnormalities.

*MAS is diagnosed when ferritin >684 ng/mL plus 2 of 4 criteria (platelet counts ≤181 × 10^9/L, aspartate aminotransferase >48 U/L, triglycerides >156 mg/dL, or fibrinogen ≤360 mg/dL) (10).

Table II. Incidence and characteristics of KDSS by region.

	KDSS/KD	IVIG resistance	CAAs	Vasoactive drugs	ICU admission
Non-Asian regions					
US, 2009 (3)	13/187 (7.0%)	6/13 (46%)	8/13 (62%)	7/13 (54%)	12/13 (92%)
Mexico, 2013 (11)	11/214 (5.1%)	6/11 (60%)	10/11 (91%)	11/11 (100%)	11/11 (100%)
Spain, 2015 (12)	3/48 (6.2%)	2/3 (67%)	3/3 (100%)	2/3 (67%)	3/3 (100%)
Italy, 2017 (13)	5/84 (6.0%)	3/5 (60%)	3/5 (60%)	2/5 (40%)	3/5 (60%)
Asian regions					
Taiwan, 2015 (14)	9/474 (1.9%)	2/9 (22%)	7/9 (78%)	8/9 (89%)	9/9 (100%)
China, 2019 (15)	27/2203 (1.2%)	19/27 (70%)	15/27 (55%)	8/27 (30%)	13/27 (48%)
Japan, 2021 (16)	6/552 (1.1%)	3/6 (50%)	3/6 (50%)	4/6 (67%)	–
Korea, this study	9/1095 (0.8%)	4/9 (44%)	4/9 (44%)	8/9 (89%)	9/9 (100%)

KDSS: Kawasaki disease shock syndrome; KD: Kawasaki disease; IVIG: intravenous immunoglobulin; CAAs: coronary artery abnormalities; ICU: intensive care unit; –: no or not tested.

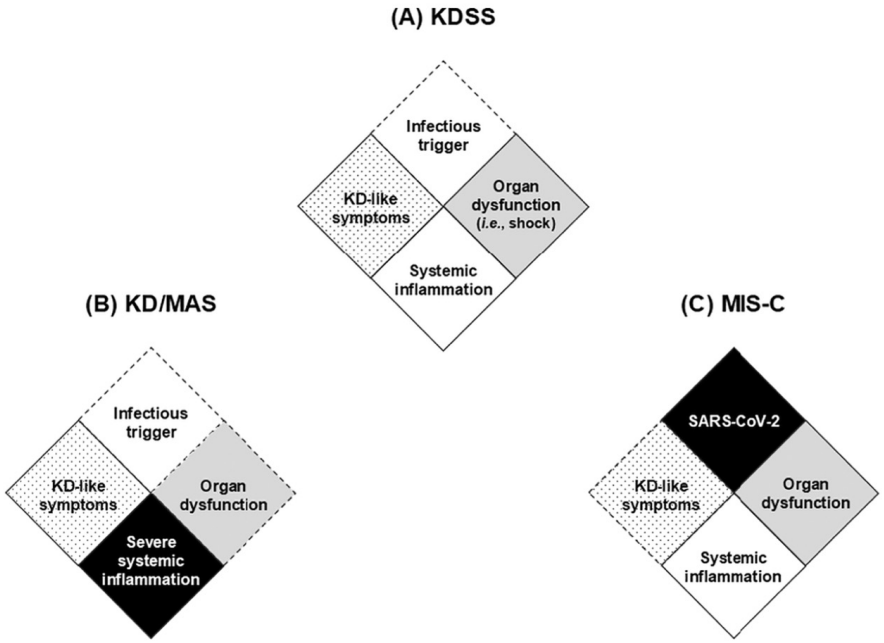

Fig. 1. Conceptual comparison of KDSS, KD/MAS, and MIS-C. **(A)** KDSS is diagnosed when shock presenting as organ dysfunction is observed in children with KD. **(B)** KD/MAS is diagnosed when severe systemic inflammation meets the MAS criteria in children with KD or KDSS. **(C)** MIS-C is diagnosed when SARS-CoV-2 infection is confirmed in children with systemic inflammation and organ dysfunction.
KDSS: Kawasaki disease shock syndrome; KD: Kawasaki disease; KD/MAS: Kawasaki disease complicated by macrophage activation syndrome; MIS-C: multisystem inflammatory syndrome in children; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

if KD-related symptoms are absent (13, 14). When the 2016 MAS criteria were retrospectively applied to patients with KDSS, some patients (4/9) met the criteria. These patients presented with a more severe clinical picture than those who did not meet the criteria. MAS is a life-threatening hyperinflammatory condition caused by excessive activation of T cells and macrophages (10). MAS has been increasingly reported in children with various systemic inflammatory diseases, such as systemic juvenile idiopathic arthritis (SJIA, ~10%), systemic lupus erythematosus (SLE, ~5%), and KD (~2%) (6). Ma *et al*. (9) reported that 10% (2/21) of patients with KDSS had haemophagocytosis on bone marrow examination. Given the relatively high incidence of MAS in KDSS, KDSS should be included among the leading causes of paediatric MAS. Furthermore, distinguishing between KDSS and KD complicated by MAS (KD/MAS) is important because their pathophysiology and therapeutic strategies differ. Two patients with KDSS (cases 8 and 9) were hospitalised during the COVID-19 pandemic. They were diagnosed with KDSS because there was no evidence of SARS-CoV-2 infection. Otherwise, the patient would have been diagnosed with MIS-C (5, 16). The fundamental difference between KDSS and MIS-C is the identification of SARS-CoV-2 (8). Figure 1 compares the components of KDSS, KD/MAS, and MIS-C, showing their similarities and differences. This study has some limitations. First, this is a small retrospective study, and larger nationwide studies are needed to support the findings. Second, the incidence of KDSS may have been underestimated because patients with KDSS who did not receive vasoactive drugs may have been excluded from the study.

In summary, the incidence of KDSS in Korea was low compared with non-Asian regions. Patients with KDSS had more severe clinical and laboratory findings and higher rates of IVIG resistance and CAAs than those with haemodynamically stable KD. Of the nine patients with KDSS, two were hospitalised during the COVID-19 pandemic and four developed MAS. On the day of hospitalisation, only one patient exhibited typical KDSS manifestations that met both the KD criteria and the definition of shock. Therefore, clinical suspicion of KDSS is necessary to avoid diagnostic delay in patients with atypical presentation.

J. Lee, *MD*
S.-Y. Lee, *MD*

Department of Paediatrics, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea.

Please address correspondence to:
Soo-Young Lee
Department of Paediatrics,
Bucheon St. Mary's Hospital,
The Catholic University of Korea,
327 Sosa-ro, Wonmi-gu,
Bucheon 14647, Republic of Korea.
E-mail: sylee@catholic.ac.kr

Competing interests: none declared.

References

1. McCrindle BW, Rowley AH, Newburger JW *et al*.: Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. *Circulation* 2017; 135(17): e927-99. https://doi.org/10.1161/cir.0000000000000484
2. Han SB, Lee SY: Antibiotic use in children with Kawasaki disease. *World J Pediatr* 2018; 14(6): 621-2. https://doi.org/10.1007/s12519-018-0157-3
3. Kanegaye JT, Wilder MS, Molkara D *et al*.: Recognition of a Kawasaki disease shock syndrome. *Pediatrics* 2009; 123(5): e783-9. https://doi.org/10.1542/peds.2008-1871
4. Gamez-Gonzalez LB, Moribe-Quintero I, Cisneros-Castolo M *et al*.: Kawasaki disease shock syndrome: unique and severe subtype of Kawasaki disease. *Pediatr Int* 2018; 60(9): 781-90. https://doi.org/10.1111/ped.13614
5. Gamez-Gonzalez LB, Ramirez-Lopez MJ,

COLMENERO-RASCON M, YAMAZAKI-NAKASHIMADA MA: Kawasaki disease shock syndrome in the COVID-19 pandemic. *Cardiol Young* 2022; 32(3): 506-7. https://doi.org/10.1017/S1047951121003280
6. LEE J, LEE SY: Under-recognised macrophage activation syndrome in multisystem inflammatory syndrome in children. *Clin Exp Rheumatol* 2024; 42(10): 2096-97. https://doi.org/10.55563/clinexprheumatol/qy4pab
7. JAIN SS, HARAHSHEH AS, LEE S *et al*.: Factors associated with shock at presentation in Kawasaki disease versus multisystem inflammatory syndrome in children associated with Covid-19. *Can J Cardiol* 2025: 41(4): 740-48. https://doi.org/10.1016/j.cjca.2024.11.027.
8. LEE J, KIM BJ, CHO KS *et al*.: Similarities and differences between multisystem inflammatory syndrome in children (MIS-C) and Kawasaki disease shock syndrome. *Children* (Basel) 2023; 10(9): 1527. https://doi.org/10.3390/children10091527
9. MA L, ZHANG YY, YU HG: Clinical manifestations of Kawasaki disease shock syndrome. *Clin Pediatr* (Phila) 2018; 57(4): 428-35. https://doi.org/10.1177/0009922817729483.
10. JEONG DC, LEE SY: Macrophage activation syndrome in Kawasaki disease: a literature review of Korean studies. *J Rheum Dis* 2025; 32(2): 105-12. https://doi.org/10.4078/jrd.2024.0118
11. GAMEZ-GONZALEZ LB, MURATA C, MUNOZ-RAMIREZ M, YAMAZAKI-NAKASHIMADA M: Clinical manifestations associated with Kawasaki disease shock syndrome in Mexican children. *Eur J Pediatr* 2013; 172(3): 337-42. https://doi.org/10.1007/s00431-012-1879-1
12. CAMACHO-LOVILLO MS, MELON M, MORENO MD, ARDANUY AV, NETH O: Kawasaki disease shock syndrome (KDSS)-presentation of 3 children and review of the literature. *Klin Padiatr* 2015; 227(6-7): 355-57. https://doi.org/10.1055/s-0035-1548814
13. TADDIO A, ROSSI ED, MONASTA L *et al*.: Describing Kawasaki shock syndrome: results from a retrospective study and literature review. *Clin Rheumatol* 2017; 36(1): 223-28. https://doi.org/10.1007/s10067-016-3316-8
14. CHEN PS, CHI H, HUANG FY, PENG CC, CHEN MR, CHIU NC: Clinical manifestations of Kawasaki disease shock syndrome: a case-control study. *J Microbiol Immunol Infect* 2015; 48(1): 43-50. https://doi.org/10.1016/j.jmii.2013.06.005
15. LI Y, ZHENG Q, ZOU L, WU J *et al*.: Kawasaki disease shock syndrome: clinical characteristics and possible use of IL-6, IL-10 and IFN-γ as biomarkers for early recognition. *Pediatr Rheumatol Online J* 2019; 17(1): 1. https://doi.org/10.1186/s12969-018-0303-4
16. SUZUKI J, ABE K, MATSUI T *et al*.: Kawasaki disease shock syndrome in Japan and comparison with multisystem inflammatory syndrome in children in European countries. *Front Pediatr* 2021; 9: 625456. https://doi.org/10.3389/fped.2021.625456