coronavirus Disease 2019 (COVID-2019) or bacterial infections. His biochemical, hematological parameters and acute phase reactants at admission were in the normal reference range. On the 3rd day of admission, he developed tachycardia and became restless and inconsolable. His laboratory results revealed elevated C-reactive protein level [8.75 mg/dl–(0–0.5 mg/dl)]. Empirical antimicrobial treatment (ampicillin and cefotaxime) was initiated after sepsis workup was performed. *Enterobacter cloaca* was isolated from the 2 consecutive blood cultures.

COVID-19 seems to have a favorable clinical course in children; however, knowledge about the course of disease in symptomatic infants is scarce.[1] A study of pediatric SARS-CoV-2 cases in China reported that 11% of infants had a severe or critical illness.[2] In infants, findings such as fever, lethargy, poor feeding, vomiting, tachypnea and tachycardia attributed to the SARS-CoV-2[3] can be also seen in bacterial sepsis. Laboratory parameters may not always help distinguish between COVID-19 and bacterial sepsis. Bacterial coinfection has been previously reported in SARS-CoV-2-positive infants.[4] A preterm neonate was reported to develop sepsis caused by Enterobacter species as in our case.[5] It is important that clinicians be aware of the development of bacterial sepsis during SARS-CoV-2 infection, especially in infants.

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MIS-C and Identical Twins: A Case Series

To the Editor:

Multisystem inflammatory syndrome in children (MIS-C) caused after coronavirus disease 2019 (COVID-19) was first reported in patients presenting with shock in Europe and North America in mid-April 2020.[1,2] Here, we present 3 pediatric cases with MIS-C who had identical twins (Fig. 1). In all 3 cases, while the twin was infected, they did not develop MIS-C.

CASE 1

A 2-year-old previously healthy boy presented with a 4-day fever, diffuse rash, nausea-vomiting, and diarrhea. Vital signs at the time of examination included a temperature of 39.6°C, heart rate of 146 beats/min, blood pressure of 95/60 mm Hg, respiratory rate of 33 breaths/min, and oxygen saturation of 94% on room air. On admission, physical examination showed a diffuse urticarial rash that localized face and lower extremities, bilateral conjunctivitis, and periorbital edema, papillitis of the tongue, lip cracking, and fissuring. He was tachycardic with 3/6 systolic murmurs and had clear lungs to auscultation bilaterally. He was admitted to pediatric intensive care unit (PICU) with a diagnosis of MIS-C. His identical twin was asymptomatic, his physical examination was normal. Clinical and laboratory findings were shown in Table 1. Nasopharyngeal swab for SARS-CoV-2 by RT-PCR was negative, but SARS-CoV-2 antibodies were positive. Also, his identical twin and his parents were antibody positive. An echocardiogram revealed ventricular systolic dysfunction and left ventricular ejection fraction (LVEF) 45% with mitral insufficiency. Treatment was initiated with fluid replacement therapy, milrinone (0.5 μg/kg/min) infusion, aspirin 100 mg, IVIG 1 g/kg for 2 days, and methylprednisolone 30 mg/kg/day for 3 days followed by a prednisone taper. The patient experienced a near resolution of symptoms and normalization of vital signs within 4 days. Inflammatory markers improved rapidly over 9 days. On day 10, the patient was discharged home on prednisone and aspirin 100 mg. Although the identical twin was antibody positive, he developed no symptoms and laboratory values were normal.

CASE 2

A 12-year-old previously healthy boy presented with a 7-day history of fever, vomiting, diarrhea, and abdominal pain. One month ago, our patient, his identical twin, and parents were PCR positive for SARS-CoV-2 from nasopharyngeal swabs. Vital signs at the time of examination included a temperature of 39.1°C, heart rate of 149 beats/min, blood pressure of 88/42 mm Hg, respiratory rate of 36 breaths/min, and oxygen saturation of 92% on room air. On admission, physical examination showed a diffuse erythematous rash that localized on bilateral axillary and inguinal regions, bilateral conjunctivitis, and papillitis of the tongue, lip cracking, and fissuring. He had signs of meningeal irritation, decreased breath sounds at the lung bases. He was tachycardic with 3/6 systolic murmurs and hypotensive, so he was admitted to PICU with a diagnosis of MIS-C. His identical twin was asymptomatic, his physical examination was normal. Clinical and laboratory findings were shown in Table 1. An echocardiogram revealed ventricular systolic dysfunction and LVEF 40% with mitral insufficiency. Brain magnetic resonance imaging (MRI) showed hyperintensity on T2-weighted images in the splenium of the corpus callosum with restricted diffusion. Treatment was initiated with fluid replacement therapy, milrinone (0.5 μg/kg/min) and noradrenaline (0.1 μg/kg/min) infusion, enoxaparin (low molecular weight heparin) 6000 U, IVIG 1 g/kg for 2 days, and methylprednisolone 1 g/day for 5 days followed by a prednisone taper. The patient experienced a near resolution of symptoms and normalization of vital signs within 5 days. Inflammatory markers improved rapidly over 7 days. Repeated brain MRI on day 7 was normal, indicating the resolution of the lesion in the splenium of the corpus callosum. On day 10, the patient was discharged home on prednisone and aspirin 100 mg. Although the identical twin had COVID-19 infection 1 month ago and was positive for antibodies, he developed no symptoms and laboratory values were normal.

CASE 3

A 10-year-old previously healthy boy presented with a 4-day history of fever,

N.A., M.O., M.E.M., K.B.G., A.I.S., and E.Ş. treated the patient. N.A. and E.Ş. wrote and revised the article. All authors approved the final article.

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TABLE 1. Clinical Characteristics, Laboratory Findings, and Outcome in 3 Patients With MIS-C

	Case 1	Case 2	Case 3
Age/Gender	2/Male	12/Male	10/Male
Concomitant illness	Yes	Yes	Yes
Symptoms	Fever, diffuse rash, diarrhea, vomiting	Fever, diarrhea, vomiting, abdominal pain	Fever, diarrhea, vomiting, abdominal pain
Consanguinity	Yes	No	No
Vital signs			
SpO_2 (%)	94	92	94
Heart rate (per min)	146	149	159
Blood Pressure (mm Hg)	95/60	88/42	85/69
Respiratory Rate (per min)	33	36	30
Body Temperature (°C)	39.6	39.1	38.6
Laboratory findings			
White blood cell (per µL)	3290	6330	8910
Lymphocyte (per µL)	630	260	960
Neutrophil (per µL)	2280	5490	7760
Platelet (per µL)	84,000	98,000	111,000
Hb (g/dl)	11.4	10.9	10.5
CRP (mg/L)	123	350	415
Procalcitonin (ng/mL)	11.28	29.05	100.32
Ferritin (µg/L)	251	1037	1115
Urea (mg/dL)	19	30	17
Creatinine (mg/dL)	0.26	0.63	0.36
AST (U/L)	45	101	163
ALT (U/L)	29	43	462
Fibrinogen (mg/dL)	493	556	528
D-dimer (µg FEU/mL)	1.22	5.44	2
Pro-BNP (ng/L)	13,400	6470	3720
Troponin (ng/ml)	24	124	57
IL-6 (pg/mL)	256	318	43
SARS-CoV-2 PCR	Negative	Negative	Positive
SARS-CoV-2 Antibody	Positive	Positive	Positive
Echocardiography	LV systolic dysfunction LVEF %45	LV systolic dysfunction LVEF %40	LV systolic dysfunction LVEF %50

ALT indicates alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; LVEF, left ventricular ejection fraction.

vomiting, diarrhea, and abdominal pain. One month earlier, his mother was positive for PCR for SARS-CoV-2 in the nasopharyngeal swab. Vital signs at the time of examination included a temperature of 38.6°C, heart rate of 159 beats/min, blood pressure of 85/69 mm Hg, respiratory rate of 30 breaths/min, and oxygen saturation of 94% on room air. On admission, physical examination showed nonspecific erythema that localized his trunk and inguinal region. He was tachycardic with 3/6 systolic murmurs and had clear lungs to auscultation bilaterally. He was admitted to PICU with a diagnosis of MIS-C. His identical twin was asymptomatic, and his physical examination was normal. Clinical and laboratory findings were shown in Table 1. Nasopharyngeal swab for RT-PCR for SARS-CoV-2 and the SARS-CoV-2 antibodies were positive. Also, his identical twin was PCR and antibody positive. An echocardiogram revealed ventricular systolic dysfunction and LVEF 50% with mitral insufficiency. Treatment was initiated with fluid replacement therapy, aspirin 100 mg, IVIG 1 g/kg for 2 days, and methylprednisolone 2 mg/kg/day for 7 days followed by a prednisone taper. The patient experienced a near resolution of symptoms and normalization of vital signs within 1 days. Inflammatory markers improved rapidly over 7 days. On day 8, the patient was discharged home on prednisone and aspirin 100 mg. Although the identical twin was positive for COVID-19 PCR and antibody he developed no symptoms.

We, herein, describe 3 children with MIS-C who had identical twins who did not develop MIS-C. Although MIS-C is indeed related to infection with SARS-CoV-2, the pathophysiological mechanism of disease is unknown.[5] Researchers suspect that adaptive immune mechanisms have a major role to play in pathogenesis of MIS-C.[4] Since only a small percentage of patients develop MIS-C, it is possible that there are genetic factors that make some children susceptible.[6] Identical twins share a common genotype. On the other hand, monozygotic twin pairs are not identical; due to epigenetic differences. While identical twins are epigenetically indistinguishable during the early years of life, older identical twins exhibited remarkable differences in their epigenetic information.[7] In addition, the timing of the immune response to SARS-CoV-2 infection may vary with viral load and genetic differences in host response. When viral load is high or genetic factors slow antiviral responses, virus replication can delay IFN response and cytokine storm can result before adaptive responses clear the virus, which may result in MIS-C.[5]

Our case series we did not study the contribution/role of epigenetic modifications.

In conclusion, the occurrence of MIS-C in one of the identical twins may be due to epigenetic differences as well as the difference in exposure to viral load.

CONSENT

The written inform consent to publication has been obtained from the parents.

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Features of COVID-19 Among Children and Adolescents Without Risk Factors Before and After the Delta Variant Outbreak in South Korea

To the Editors:

As the Delta variant of coronavirus disease 2019 (COVID-19) pandemic spreads, the number of children and adolescents infected with this lineage is increasing. However, the relationship between the prognosis of pediatric patients and the Delta variant has not been fully elucidated. In this regard, two studies using the national big data reported a similar incidence of intensive care unit (ICU) admission and mechanical ventilation in the age group of 0–17 years before and after the Delta variant outbreak in the USA.[1,2] However, additional data reflecting various races and regions are still needed. In South Korea, mild-to-moderate COVID-19 patients without risk factors are isolated in residential treatment centers (RTCs). We retrospectively compared the clinical features of unvaccinated children and adolescents admitted to RTCs before and after the Delta variant outbreak in South Korea.

We collected demographics, COVID-19 symptoms, chest radiograph findings and hospital transfer of patients <18 years of age who were admitted to two RTCs in Gyeongsangnam-do, South Korea from December 2020 to August 2021. Based on the nationwide surveillance data of SARS-CoV-2 variants, we divided the patients into the following two groups: (1) the Delta-minor group (diagnosed from December 2020 to June 2021, detection rate <10%) and (2) the Delta-dominant group (diagnosed during August 2021, detection rate >90%). Patients diagnosed during July 2021 were excluded because of inconclusive detection rates of the Delta variant (53.7%). The collected medical information was compared between the two groups. This study was approved by the Institutional Review Board of Gyeongsang National University Changwon Hospital (No.2021-09-023). Descriptive/inferential statistics and regression analysis were used.

Among the 235 patients, 92 (39.1%) were in the Delta-minor group and 143 (60.9%) were in the Delta-dominant group. The Delta-dominant group patients were younger (mean age 13.8 vs. 10.2 years, $P < 0.001$). Neither group had any underlying diseases considered as risk factors for severe COVID-19, such as hypertension or diabetes. There was no significant difference between the two groups

TABLE 1. Characteristics and Outcome of Children and Adolescents COVID-19 Patients in the Residential Treatment Centers

Characteristic and outcome	Delta-minor (n = 92)	Delta-dominant (n = 143)	*P* value
Age (mean ± SD, years)	13.8 ± 3.3	10.2 ± 4.4	<0.001
Children (<10 years of age)	13 (14.1)	66 (46.2)	<0.001
Male	56 (60.9)	75 (52.4)	0.21
Underlying disease	0	0	NA
Period from diagnosis to RTC enter date (mean ± SD, days)	0.7 ± 1.1	1.6 ± 1.4	<0.001
Symptom during isolation			
Fever	5 (5.4)	7 (4.9)	>0.99
Duration of fever (mean ± SD, days)	1.4 ± 0.9	1.7 ± 1.9	0.74
Chill	4 (4.3)	2 (1.4)	0.21
Myalgia	7 (7.6)	3 (2.1)	0.051
Fatigue	3 (3.3)	2 (1.4)	0.38
Anorexia	5 (5.4)	3 (2.1)	0.27
Cough	26 (28.3)	52 (36.4)	0.21
Sputum	24 (26.1)	27 (18.9)	0.2
Shortness of breath	0	1 (0.7)	>0.99
Rhinorrhea	23 (25)	15 (10.5)	0.003
Nasal stuffiness	32 (34.8)	22 (15.4)	0.001
Sore throat	22 (23.9)	18 (12.6)	0.02
Chest pain	1 (1.1)	0	0.39
Nausea/vomiting	4 (4.3)	4 (2.8)	0.72
Diarrhea	7 (7.6)	8 (5.6)	0.54
Abdominal pain	2 (2.2)	3 (2.1)	>0.99
Headache	10 (10.9)	20 (14)	0.49
Parosmia	8 (8.7)	14 (9.8)	0.78
Parageusia	9 (9.8)	12 (8.4)	0.72
Asymptomatic during isolation	27 (29.3)	62 (43.4)	0.03
Pneumonia during isolation	2 (2.2)	1 (0.7)	0.56
Length of isolation (mean ± SD, days)	9.3 ± 2.0	8.4 ± 1.9	0.001
Transfer to hospital	5 (5.4)	3 (2.1)	0.27
COVID-19 related cause	1 (1.1)	0	0.39
Non-COVID-19 related cause	4 (4.3)	3 (2.1)	0.44
Oxygen supply	0	0	NA
ICU admission	0	0	NA
Length of hospital stay (mean ± SD, days)	10.8 ± 10.2	8.7 ± 8.1	0.77

SD, standard deviation; NA, not available; RTC, residential treatment center; ICU, intensive care unit.
Data are number (%) of patients, unless otherwise indicated.

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