

Case Report

Multisystem Inflammatory Syndrome in Children Secondary to Surgical Site Infection: A Case Report



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ABSTRACT

Background and Aim: Multisystem inflammatory syndrome in children (MIS-C) is a serious condition in which a patient (typically infected with severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]) manifests symptoms of multiorgan failure a few weeks after exposure due to broad adaptive and innate immune activation. This case report demonstrates that MIS-C can occur in the context of a postoperative surgical site infection (SSI) following orthopedic surgery.

Case Presentation: A 13-year-old boy with a history of multiple trauma and subsequent lower limb fracture followed by orthopedic surgery presented to the emergency department with SSI. After 6 days of admission, the patient developed symptoms of multisystem inflammatory syndrome, including renal shutdown and elevated blood creatinine (Cr) levels. As a result, hemodialysis was performed. The patient's blood culture was negative, and similar clinical situations (such as sepsis and toxic shock) were ruled out during orthopedic surgery and infectious disease specialties' consultations.

Conclusion: MIS-C can emerge not only secondary to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection but also can be triggered by SSI secondary to orthopedic surgeries. Regular organ function monitoring in patients with SSI complications can be very beneficial in early diagnosis and preventing complications.

Keywords: Multisystem inflammatory syndrome in children (MIS-C), Surgical wound infection, Multiple trauma, Limb fracture



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Introduction

Multisystem inflammatory syndrome in children (MIS-C) is a post-infectious situation in which multiple vital organs become inflamed as a result of extensive immune dysregulation caused by SARS-CoV-2 (the virus responsible for COVID-19), commonly 2-6 weeks after exposure [1]. Common components of this syndrome are fever, fatigue, gastrointestinal, cardiovascular, dermatologic, and neurologic involvements [2]. In addition to patients' symptoms, signs, and history of infection exposure, several factors are important and needed for our diagnosis. Paraclinical findings, such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), D-Dimer, and ferritin, are among these factors. In some patients, low platelet count and leukopenia can occur [3]. One of the key factors in the diagnosis is excluding similar differential diagnoses, such as bacterial sepsis and toxic shock syndrome [4]. The importance of exclusion of these conditions is due to the high level of similarity between these conditions' clinical presentation and MIS-C. Key actions in managing this condition include controlling inflammation (by using intravenous immunoglobulin (IVIG), corticosteroids, etc.) and organ support [5]. One of the most important affected organs that should be supported is the kidney. In this case, kidney damage was diagnosed based on a rise in blood Cr level (up to 4.5), which required several sessions of hemodialysis.

By reporting this MIS-C case, this study aimed to bring up the idea that multisystem inflammation syndrome in children can not only be caused by exposure to SARS-CoV-2 infection, but also by a cytokine storm of surgical site infection (SSI), which can be a notable finding.

Case Presentation

A 13-year-old boy with a history of multiple trauma and lower-limb bone fractures followed by orthopedic plate fixation surgery presented to the emergency department with symptoms of SSI, such as erythema, tenderness, and warmth of the surgical site (Figure 1). Purulent discharge was observed at the surgical site. He reported mild fever and chills. He denied other systemic symptoms, such as nausea and vomiting and fatigue. He did not report any other past medical history apart from the crash injury. The only past surgical history in addition to the orthopedic surgery was the circumcision procedure performed when he was 3 years old. He did not report any drug history, allergic history, habitual history, or family history of any disease. He did not report any urinary symptoms, such as oliguria, dysuria, anuria, or hematuria.

Vital signs:

T: 37.9, BP: 110/80, HR: 87, RR: 19, SpO₂: 99.

In examinations, the only sign was erythema, tenderness, and swelling of the surgical site. All other examinations, including head, neck, chest, abdomen, and urogenital regions, were normal.

Laboratory tests upon arrival (including complete blood count with differential, blood urea nitrogen [BUN], creatinine [Cr], sodium [Na], potassium [K], ESR, CRP, and blood culture) did not show any degree of leukocytosis (white blood cell count [WBC]=5,100 / neu=80%). High ESR and CRP levels (ESR=25, CRP=30) were observed. All other laboratory findings, including BUN, Cr, Na, and K, were within the normal range, and blood culture was negative.

He was admitted with a diagnosis of SSI, and empiric treatment (cefotaxime 25 mg/kg every 8 hours, clindamycin 20 mg/kg/day divided every 8 hours) was started. Within the first 6 days, signs and symptoms of infection, such as redness and pain, started to decline, and the patient showed a relative response to empirical antibiotic therapy. On day 6 of admission, precisely after clear improvement of the local infection, new systemic manifestations, such as oliguria, rise of serum Cr (3.2 mg/dL), and alanine aminotransferase (ALT) (680 mg/dL), and seizures emerged. All of these new findings implied multiorgan damage and subsequent renal shutdown (Tables 1, 2, and 3).

Differential diagnosis

Acute kidney injury (AKI) secondary to inadequate hydration

Fluid intake was carefully monitored during hospitalization, and the patient did not show typical signs of dehydration, such as dry mucosa and poor skin turgor. In addition, the patient did not show any significant improvement in response to fluid intake. Based on these facts, we can conclude that the AKI was not secondary to inadequate hydration.

Toxic shock syndrome: The complication occurred several days after admission when source control was in progress, and the patient's general condition began to improve in response to antibiotics. Delayed incidence of the disease, in addition to a negative blood culture, leads to a toxic shock syndrome rule-out.

Table 1. Lab data on day 6

Test	Result	Normal Range
BUN (mg/dL)	79	15-36
Creatine (mg/dL)	3.2	0.7-1.4
WBC ($\times 10^3$)/uL	5.1	4.4-11.3
Neu (%)	80	-
Lym (%)	17	-
MXD (%)	3	-
RBC (/uL)	2.65	4.5-5.9
Hemoglobin (g/dL)	7.4	14-17.5
Hematocrit (%)	22.3	41.5-50.4
MCV (fL)	84.2	80-96
MCH (pg)	28	27.5-33.2
MCHC (g/dL)	33	33.4-35.5
PLT (/uL)	116	150-450
Blood culture	Negative	Negative
COVID PCR	Negative	Negative

Abbreviations: BUN: Blood urea nitrogen; WBC: White blood cell; RBC: Red blood cell count; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; PLT: Platelet count; PCR, Polymerase chain reaction.

Sepsis and septic shock: Sepsis and septic shock syndrome can be ruled out in the same way that toxic shock syndrome was ruled out.

Urinary tract infection (UTI) due to neurologic deficit after multiple trauma: Neurologic deficits and neurogenic bladder can result in recurrent UTIs and mimic the signs of systemic inflammation [6]. Lumbar column inspection and spinal examinations were performed to ensure an intact spine. Negative urine cultures ruled out UTIs.

Treatment and outcome

After confirmation that AKI resulted from MIS-C, the patient underwent several sessions of hemodialysis. After several sessions of hemodialysis and completion of the MIS-C course of disease, blood Cr level returned to its normal value and other organs, such as the liver, showed laboratory data improvements. After Cr level improvements and urine output increased, the patient was discharged from the pediatric nephrology service to continue SSI treatment in pediatric orthopedics and infectious disease services.

Discussion

This patient developed multi-organ dysfunction after crash injury and SSI in the absence of documented recent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The patient's clinical and laboratory features overlapped with MIS-C. The association between SSI and the hyperinflammatory syndrome in this case is largely based on temporal correlation and the lack of an alternative viral trigger. The sequence of severe trauma, development of SSI, and subsequent onset of multi-organ dysfunction is biologically plausible for inducing a cytokine storm.

This suggests that cytokine release resulting from a crash injury and subsequent SSI can lead to MIS-C.

Previous MIS-C cases have been reported several weeks after exposure to COVID-19 and SARS-CoV-2. In contrast, this case suggests that crash injuries and SSIs can also be the source of cytokine release in addition to viral infections.

Table 2. Lab data on day 8 (creatinine peak)

Test	Result	Normal Range
BUN (mg/dL)	109	15-36
Creatine (mg/dL)	4.38	0.7-1.4
Sodium (mmol/L)	127	130-145
Potassium (mmol/L)	6.5	3.5-5
WBC ($\times 10^3/\mu\text{L}$)	6	4.4 – 11.3
Neu	75	-
Lym	20	-
MXD	5	-
RBC (/ μL)	3.09	4.5-5.9
Hemoglobin (g/dL)	8.5	14-17.5
Hematocrit (%)	27.5	41.5-50.4
MCV (fL)	89	80-96
MCH (pg)	28	27.5-33.2
MCHC (g/dL)	31	33.4-35.5
PLT (/ μL)	174	150-450
RDW-cv (%)	14.9	-
PDW (fL)	10.2	-
MPV (fL)	8.5	-
P-LCR (%)	15.2	-
PT (s)	14.5	12-14
PT control	12.5	1-1.2
INR (s)	1.3	30-45
PTT patient	38	Negative:<10
ANA (mg/dL)	4.4	90-180
C3 (mg/dL)	80.0	10-40
C4 (U/L)	10.8	24-190
CPK (U/L)	82740	<683
LDH (mg/dL)	6170	8.6-10.3
Ca (mg/dL)	7.6	2.9-5.1
Phosphorus (mg/dL)	6.4	1.8-2.6
Magnesium (mg/dL)	2.1	0.3-1.2
Bilirubin total (mg/dL)	0.65	<0.3
Bilirubin direct (U/L)	0.12	<40
AST (U/L)	2300	<45
ALT (g/dL)	680	3.5-5.2
Albumin (mg/dL)	2.3	15-36

Abbreviations: RDW-CV: Red cell distribution width-coefficient of variation; PDW: Platelet distribution width; MPV: Mean platelet volume; P-LCR: Platelet-large cell ratio; PT: Prothrombin time; INR: International normalized ratio; PTT: Activated partial thromboplastin time; ANA: Antinuclear antibody; CPK: Creatine phosphokinase; LDH: Lactate dehydrogenase; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; BUN: Blood urea nitrogen; WBC: White blood cell; RBC: Red blood cell count; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; PLT: Platelet count; PCR: Polymerase chain reaction; MXD: Mixed cells.

Table 3. Urine analysis during hospitalization and creatine peak

Color	Brown
Appearance	Semi clear
Specific gravity	1010
PH	6
Glucose	1+
Ketone	Negative
WBC	2-5
RBC	5-10
Epithelial cell	0-5
Crystals	Amorphous urate: Few
Mucus	Not seen
Pus cell	Not seen

Abbreviations: WBC: White blood cell; RBC: Red blood cell count.



Figure 1. Surgical site infection

This study emphasizes the importance of regular organ function monitoring (especially the kidneys) during hospitalization of patients with crash injuries and SSIs. Regular monitoring can lead to earlier MIS-C diagnosis and treatment (intravenous immunoglobulin [IVIG], corticosteroids, hemodialysis, etc.) and, as a result, less organ damage.

Conclusion

MIS-C can be an outcome of cytokine release during crash injuries and SSIs in addition to COVID-19 and SARS-CoV-2.

Regular organ function monitoring during hospitalization for crash injuries and SSIs is crucial for early diagnosis.

Early diagnosis can lead to earlier treatment and less organ damage.

Ethical Considerations

Compliance with ethical guidelines

All parts of the publishing process were explained to the patient's family, and written consent was obtained from his father.

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Authors' contributions

Data curation, visualization, supervision, project administration: Elham Emami; Investigation and writing: Atrin Oroojeni.

Conflict of interest

The authors declared no conflict of interest.

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