DOI: 10.1111/pan.14121

Postoperative inflammation to "*hyper*"-inflammation: *cryptic COVID-19 connections!*

To The Editor,

Over the past few months, a considerable literature has accumulated on the possibility of a multisystem inflammatory syndrome in children (MIS-C) associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.[1] Appropriate to this context, we wish to share our experience emanating from a pediatric cardiac surgical setting.

A 2-year-old tetralogy of Fallot child with mild preoperative central cyanosis and no obvious respiratory complaints (deemed COVID-19 negative on 2 preprocedural reverse transcriptase polymerase chain reaction (RT-PCR) 7 days apart) underwent an uneventful intracardiac repair following a written informed parental consent. With an adequate surgical correction performed on cardiopulmonary bypass (CPB) of 90-minute duration, the patient was weaned on a minimal hemodynamic support of 5 mcg/kg dobutamine and 0.025 mcg/kg epinephrine. The postoperative echocardiography was also unremarkable for any residual intracardiac shunts or any degree of right ventricular dysfunction or outflow gradients, which could classify as concerning. Nevertheless, 8–10 hours into the postoperative period, the child manifested persistently high core temperatures (>40°C) alongside declining urine output, deteriorating hemodynamics (escalated vasopressor requirement), poor Horowitz index on blood gases, elevated D-dimer, liver enzymes and total leukocyte count, and worsening myocardial pump function on serial echocardiography.

Subsequently, the child tested positive for SARS-CoV-2 IgG serology suggesting COVID-19 convalescence from a past mild infection as an important harbinger of the postoperative deterioration to the current status. The index case was categorized as a COVID-related MIS-C by all means of the syndromic criteria (pediatric age, persistent fever, laboratory evidence of inflammation, multisystem involvement, serious illness, and a temporal association with COVID-19 infection).[1] However, an inexorable systemic immune-inflammatory response to CPB alongside additional perioperative aggravators such as bleeding, coagulation disturbances, positive pressure ventilation, and transfusion-related lung injury (second hit) is likely to have exasperated the underlying indolent SARS-CoV-2 infection (first hit) to manifest as a peculiarly lethal postoperative *"hyper"*-inflammation wherein the patient succumbed to death despite a satisfactory surgical correction (in background of a false security attributable to negative RT-PCRs).

Quite reasonably, one might question the relative contributions of the SARS-CoV-2 infection and an open-heart surgery, to the so-called postoperative MIS-C. Nevertheless, the liaison between the two is doubtlessly perilous with the resultant *"hyper"*-inflammation at the *"heart"* of life-threatening postoperative multi-organ failure.[2-4] Moreover, a wide range of 2–29% false negativity of the current gold standard of preoperative screening with RT-PCR (performed twice preoperatively in the present case to minimize this problem) and the recommendation on the role of antibody testing being limited to the RT-PCR results not correlating to the clinical circumstance (as in the index postoperative scenario) compound the situation furthermore.[5,6] The preoperative testing recommendations cite the lack of cost-effectiveness of a routine preoperative antibody screening in addition to a considerably variable seroprevalence rate.[6]

As an extension of our discussion of a cryptic preoperative COVID-19 infection *"hiding in the shadows,"* the shadows are unfortunately only expected to turn murkier as we navigate further into the pandemic with more elective surgical settings being reopened. Damodaran et al's very recent description of a related perioperative scenario in an adult coronary artery revascularization setting bears testimony to the same.[7] The research group intriguingly questions whether COVID-19 convalescence emerges as a boon or a bane in the cardiac surgical arena.[7]

To conclude, the aforementioned experience highlights the present-day relevance of a sound perioperative risk comprehension, consent appropriate to the level of planned surgical intervention to be equally backed by a case-based approach for the anticipation, and the attenuation of the second inflammatory hit aimed at ameliorating the overall severity of the postoperative disease.[8,9] Meanwhile, prudent feasible suggestions from our colleagues on minimizing such perioperative circumstances are more than welcome.

KEYWORDS

COVID-19 convalescence, cryptic infection, hyper-inflammation, multisystem inflammatory syndrome in children, RT-PCR, SARS-CoV-2 serology, second hit

CONFLICTS OF INTEREST

None.

AUTHOR CONTRIBUTIONS

RM conceptualized and wrote the original draft, IS conceptualized and edited the manuscript, and JKK and RK supervised the data.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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