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Case Report

Hypothermia in a 6-Week Infant-an Atypical Presentation of Multisystem Inflammatory Syndrome (MIS-C)

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Introduction

MIS-C is a rare complication of covid-19. The definition across the organizations is based on 6 principle elements: pediatric age, persistence of fever, presence of laboratory markers of inflammation, manifestation of signs or symptoms of organ dysfunction, lacking an alternative diagnosis, and a temporal relation to COVID-19 infection or exposure [1]. We describe an atypical case of MIS-C with myocarditis in a 6-week-old infant presenting with hypothermia rather than fever.

Case Report

Six weeks old, exclusively breast-fed, male born out of non-consanguineous marriage to COVID RT-PCR negative mother with uneventful birth history presented with sudden onset of excessive crying, refusal to feed, bluish discoloration of extremities. Child was extremely cold to touch. There was no history of fever, vomiting, seizures and breathing difficulty. On admission, the child had inconsolable cry, erythematous rash over the body and mottling over extremities. On examination, his core(rectal) and peripheral temperature was 31 degree Celsius with heart rate of 190/min, respiratory rate of 74 /min, capillary refill time 8 sec, poor peripheral pulses, blood pressure 104/59 mmHg (50th centile) and saturation of 87% on room air. Systemic examination showed muffled heart sounds with hepatomegaly. Chest auscultation revealed normal breath sounds. Child was immediately put on warmer and humidified high flow oxygen. Shock was managed as per the standard protocol [fluid bolus followed by ionotropic support (adrenaline and nor adrenaline)]. Bedside echocardiography was done which showed left ventricular dysfunction (ejection fraction 30%) with pericardial effusion. In view of catecholamine resistant shock iv hydrocortisone infusion was started. After 8 hours, peripheral temperature improved to 37 degree Celsius with better perfusion. In view of myocarditis, immunoglobulin was admistered (1gm/kg). Blood investigations showed no evidence of sepsis although inflammatory (including cardiac) markers were high (Table 1). Due to outbreak situation and baby exclusively breast fed, COVID-19 RTPCR and IgG antibody tests were done both for the baby and the mother which showed negative RT-PCR but positive IgG titres 38 AU/ml (done by CLIA method: normal range <12AU/ml) in baby and both were negative in mother. Child gradually improved on supportive treatment with downward trends in inflammatory markers. Ionotropic support was tapered and stopped by day 3. Child got discharged on cardiac support therapy (Enalapril and Aldactone) and is doing well in follow up.

Discussion

Our case is unique as child had MIS-C with Kawasaki disease like presentation with cardiogenic shock but with severe hypothermia rather than fever, which is the mandatory criteria to diagnose the same. MIS-C associated with COVID-19 is thought to occur secondary to a cytokine storm that damages numerous organ systems. At the time of writing, multiple case reports on mixed picture of possible Kawasaki with features of MIS-C associated with COVID-19 have been published but none had stated hypothermia as presenting feature [2,3]. A case report has been published where an adult with SARS-CoV-2 infection presented with hypothermia and lethargy [4]. In our case, the pathophysiology of hypothermia is unclear as

Table 1:

Investigations	Normal values	Da- 1	Day-4 (post immunotherapy)
Hemoglobin (g/dl)	9-13	10.5	9.8
*TLC (per-ul)	4-10	8700	9800
†ALC (per-ul)	1-3	3820	3470
Platelets (per-ul)	15000-450000	32700	35400
‡hsCRP mg/dl	<0.1	35	13
§ESR mm 1st hr	0-10	70	24
Procalcitonin (ng/ml)	<0.5	0.4	0.1
Lactate (mmol/L)	5	2.1	1.5
||AST (U/l)	<35	85	43
¶ALT (U/l)	<35	78	38
Fibrinogen (mg/dl)	150-400	297	305
Ferritin (ng/ml)	23.9-336.2	678	435
D-dimer (ng/ml)	0-200	301	290
Troponin-I (ng/ml)	0.00-0.07	0.12	0.05
**Pro-BNP (pg/ml)	125-450	3541	878.9
Cortisol (random) ug/dl	<10	22.9	25.8
Blood culture	Sterile	Sterile	Not done
COVID IgG (AU/ml)	<12	38	Not done
2D ECHO	Ejection Fraction (EF) >55%	LV dysfunction, EF-30%, Pericardial effusion	EF-45%, Pericardial effusion

*TLC-Total Leucocyte Counts, †ALC-Absolute Lymphocyte Counts, ‡hsCRP-High Sensitive C Reactive Protein, §ESR-Erythrocyte Sedimentation Rate, ||AST-aspartate aminotransferase, ¶ALT-Alanine Transaminase, Pro-BNP-Pro B-Type Natriuretic Peptide.

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we did not find any evidence for sepsis or bacterial infection (normal procalcitonin levels and sterile blood culture). It could have been a specific brain lesion in the hypothalamus or brainstem, which was not visible on neuroimaging or could also be a systemic inflammatory response (as in sepsis cases), where fever is usually present. However, in about 10% of the patients with sepsis, hypothermia instead of hyperthermia can be observed with the same elevated inflammatory cytokines. Here again neither the mechanism, nor the usefulness of the reaction, is yet truly recognized [4]. Possible explanation of hypothermia with hyper inflammation syndrome could be the young age (less than 2 months) where these children have impaired thermoregulation with poor compensatory mechanisms and are prone to decreased core temperature [5]. As we improve our understanding of MIS-C secondary to COVID-19, we recognize that there is likely a broader spectrum of signs and symptoms beyond those of classical inflammatory syndrome [6].

Conclusion

MIS-C can present with a wide range of clinical symptoms. Early recognition of MIS-C is critical as patients can deteriorate rapidly. Given the worldwide COVID-19 pandemic, it is important for all providers to be familiar with MIS-C and to keep this entity in their differential diagnosis, even in cases where classic diagnostic criteria are not initially fulfilled. We suggest to give special attention to very low temperatures during the SARS-CoV-2 pandemic.

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