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Multi-System Inflammatory Syndrome in Children: Varied Presentations and Implications in the Context of COVID-19

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Abstract: ***We present a case of a 5 ½-year-old boy initially admitted with high-grade continuous fever, vomiting, and loose stools for two days. Despite empirical treatment with intravenous broad-spectrum antibiotic administration, the fever persisted. On Day 6, he developed bilateral non-purulent conjunctival congestion, facial puffiness, and tachycardia. Subsequent diagnosis revealed Multisystem Inflammatory Syndrome in Children (MIS-C) associated with COVID-19, confirmed by positive COVID-19 IgG antibodies in both the child and mother. Laboratory investigations revealed elevated Troponin-T and N-terminal pro-B-type natriuretic peptide (NT-pro BNP), indicating cardiac involvement. Treatment with intravenous immunoglobulin (IVIG), Methylprednisolone, and Aspirin led to immediate fever subsidence and improvement in blood pressure. Despite transient bradycardia lasting for 48 hours, the child showed significant clinical improvement and was discharged after stabilization. This case was managed in a peripheral resource-limited setting, underscoring the varied presentations of MIS-C and highlighting the importance of early recognition and management in improving patient outcomes.***

Keywords: Multisystem inflammatory syndrome in children, sars-cov-2, MIS-C, COVID 19

1. Introduction

The emergence of Multi-System Inflammatory Syndrome in Children (MIS-C) has posed significant challenges in the management of Paediatric COVID-19 cases. MIS-C represents a rare but severe complication associated with SARS-CoV-2 infection, characterized by hyperinflammation and multi-organ involvement. Unlike typical COVID-19 presentations in children, MIS-C manifests with diverse clinical features, resembling toxic shock syndrome, Kawasaki disease, and other inflammatory conditions. This syndrome's varied presentations underscore the importance of early recognition and intervention to mitigate its potentially life-threatening consequences. In this report, we present a case of MIS-C in a 5 ½-year-old boy, highlighting the challenges in diagnosis and management and emphasizing the need for heightened awareness among healthcare providers.

2. Case Presentation

A 5 ½-year-old boy was admitted to our Paediatric unit with a history of fever persisting for two days. The fever was high-grade and continuous, accompanied by significant clinical manifestations, including vomiting (5-6 episodes/day) and loose stools (6-8 episodes/day). Notably, there was no history of previous documented COVID-19 infection in the child's past medical records or among family members. Additionally, the child was not vaccinated against COVID-19.

On admission, the child presented with a temperature of 102°F, tachycardia with a heart rate of 120 beats per minute, and a blood pressure of 78/46 mm Hg. Physical examination revealed pallor without signs of jaundice, cyanosis, or edema. The child appeared irritable but did not exhibit signs of meningeal irritation. Cardiovascular examination revealed normal heart sounds without murmurs, and lung auscultation revealed clear breath sounds bilaterally. Abdominal examination was unremarkable, with no evidence of organomegaly.

Initial investigations, including True Nat for COVID-19 and tropical infection screening, returned negative results. Despite empirical treatment with intravenous broad-spectrum antibiotics, the child continued to experience high-grade fever beyond 48 hours. On Day 4 of admission, the child developed bilateral non-purulent conjunctival congestion, facial puffiness, and tachycardia, prompting further investigations. Laboratory investigations indicated anemia, hypoalbuminemia, and mild ascites. COVID-19 antibody (IgG) testing for both the child and the mother returned positive.

Subsequent evaluations revealed grade II Mitral Regurgitation on echocardiography with an ejection fraction of 65%. Additional tests revealed very high NT-pro BNP, high Trop-T, and marginally elevated ferritin levels. The child was managed in line with MIS-C protocols, which included intravenous immunoglobulin (IVIG) at a dose of 2g/kg, intravenous Methyl Prednisolone at 2mg/kg, and Aspirin at 5mg/kg/day. Following this treatment regimen, the child's fever subsided, and blood pressure improved. The child's condition was diagnosed as MIS-C, a hyperinflammatory syndrome associated with COVID-19, characterized by multi-organ involvement. Notably, after starting IVIG and Methylprednisolone, the child experienced sinus bradycardia (heart rate: 40-50/min) without hemodynamic instability, which persisted for 48 hours.

Treatment was given with intravenous Methyl Prednisolone for three days followed by a switch to oral Prednisolone, tapered over seven days. Aspirin therapy was continued throughout the hospitalization. After 12 days of admission, the child was discharged. Follow-up evaluation with a 2D Echo at six weeks revealed normal findings, and Aspirin was discontinued.

The case was managed at a peripheral centre with limited resources. After discharge, the child was advised to defer live vaccines for a duration of nine months since he had received IVIG. All other vaccines were advised to be continued as per schedule.

3. Discussion

Our case exemplifies the complex nature of Multi-System Inflammatory Syndrome in Children (MIS-C) associated with COVID-19, reflecting a growing concern among pediatric healthcare providers. The child presented with fever, gastrointestinal symptoms, and hemodynamic instability, aligning with the diverse clinical spectrum observed in MIS-C cases.

MIS-C shares several clinical features with other hyperinflammatory conditions such as Kawasaki disease, toxic shock syndrome, and macrophage activation syndrome. The overlapping symptoms necessitate a high index of suspicion and comprehensive evaluation to differentiate MIS-C from these conditions. Early recognition and prompt initiation of treatment are critical in preventing morbidity and mortality associated with MIS-C [1].

Comparing our case with existing literature, More et al. (2022) reported cases of MIS-N (Multisystem Inflammatory Syndrome in Neonates) in neonates, emphasizing respiratory distress, shock, and encephalopathy as common presentations. While MIS-N primarily affects neonates, our case highlights MIS-C in an older pediatric age group with similar systemic involvement and hyperinflammatory responses [2]

Furthermore, Greene et al. (2020) described MIS-C as a toxic shock-like syndrome characterized by distributive shock and multi-organ injury. Our patient's clinical course included hemodynamic instability but did not require vasopressors or mechanical ventilation [3]. This suggests that MIS-C can present with varying degrees of severity, and not all cases necessitate intensive care interventions.

Saeed et al. (2023) highlighted MIS-C post-COVID-19 vaccination, suggesting immune dysregulation triggered by SARS-CoV-2 [4]. Although our case did not involve vaccination, it underscores MIS-C's association with COVID-19 infection, necessitating prompt recognition and management to prevent complications. This reinforces the need for continuous monitoring and reporting of MIS-C cases to better understand its pathophysiology and triggers.

Moreover, Casavecchia et al. (2022) reported arrhythmic myocarditis in an adolescent with MIS-C, highlighting cardiac involvement in MIS-C pathophysiology. Our patient's echocardiographic findings of mitral regurgitation and cardiac dysfunction corroborate these observations, emphasizing the importance of cardiac monitoring in MIS-C cases [4]. The bradycardia observed in our patient could be either due to primary cardiac involvement or due to IV Methylprednisolone. Case reports indicate that bradycardia has occurred in both adults and children following pulse methylprednisolone therapy [5]. Additionally, arrhythmias such as atrial fibrillation, ventricular fibrillation, and cardiac arrest have been observed in adults. Slowing of the heart rate has also been reported after high-dose oral prednisolone and pulse dexamethasone therapy.

Lastly, Berardicurti et al. (2021) discussed MIS-C as a manifestation of systemic hyperinflammation, suggesting SARS-CoV-2 triggers severe immune dysregulation in children [6]. Our case adds to this understanding, underscoring MIS-C's role as a consequence of COVID-19-induced hyperinflammation. The immunopathogenesis of MIS-C involves a complex interplay between viral factors and host immune responses, resulting in widespread inflammation and multi-organ dysfunction.

Additional studies have explored the cytokine profiles and immune responses associated with MIS-C, indicating a unique immunological signature compared to other pediatric inflammatory conditions. For instance, Carter et al. (2021) observed elevated levels of interleukin-6 (IL-6), interleukin-10 (IL-10), and tumor necrosis factor-alpha (TNF-α) in MIS-C patients, suggesting a cytokine storm as a key component of the syndrome's pathogenesis [7]. This cytokine storm can lead to significant endothelial damage, vasculitis, and capillary leak syndrome, further complicating the clinical management of affected children.

Cardiac involvement is a critical aspect of MIS-C, with studies highlighting varying degrees of myocardial dysfunction, coronary artery abnormalities, and arrhythmias. Valverde et al. (2021) conducted a comprehensive review of cardiac manifestations in MIS-C, reporting that a significant proportion of patients exhibit decreased left ventricular ejection fraction, coronary artery dilation, and aneurysms [8] . The long-term cardiac sequelae of MIS-C remain an area of active research, with ongoing studies aiming to understand the potential for chronic cardiac issues in survivors.

Neurological manifestations have also been documented in MIS-C, with symptoms ranging from headache and irritability to seizures and encephalopathy. Abdel-Mannan et al. (2020) reported on the neurological complications associated with MIS-C, noting that some patients develop acute encephalopathy, stroke, and demyelinating syndromes [9]. These findings underscore the necessity for multidisciplinary care involving pediatric neurologists, cardiologists, and intensive care specialists to address the multi-organ impact of MIS-C effectively.

Management of MIS-C involves a multi-faceted approach, incorporating immunomodulatory therapies such as intravenous immunoglobulin (IVIG), corticosteroids, and biological agents like anakinra and tocilizumab. The choice of therapy is often guided by the severity of inflammation, organ involvement, and patient response to initial treatments. McArdle et al. (2021) compared the efficacy of IVIG alone

versus IVIG combined with corticosteroids in MIS-C management, concluding that combination therapy resulted in faster resolution of inflammation and improved clinical outcomes [10]. Such insights are invaluable in refining treatment protocols and optimizing patient care.

4. Conclusion

Our case underscores the importance of recognizing MIS-C's varied presentations and initiating appropriate treatment promptly. Educating healthcare providers about MIS-C can aid in early diagnosis and improved patient outcomes. Continued research and documentation of MIS-C cases are essential to elucidate its pathophysiology, improve management protocols, and ultimately enhance patient care.

Furthermore, the diverse clinical manifestations of MIS-C, ranging from mild to severe, highlight the need for individualized treatment plans tailored to each patient's specific needs. The integration of multidisciplinary teams in the management of MIS-C ensures comprehensive care, addressing the syndrome's multifaceted nature. As the understanding of MIS-C evolves, ongoing collaboration and knowledge sharing among healthcare professionals will be pivotal in advancing the standard of care for affected children.

The importance of post-discharge follow-up cannot be overstated, given the potential for long-term sequelae in MIS-C survivors. Regular monitoring of cardiac function, inflammatory markers, and overall health status is crucial in detecting and managing any late-onset complications. As more data becomes available, standardized follow-up protocols will play a critical role in ensuring the well-being of children recovering from MIS-C.

In conclusion, our case contributes to the growing body of evidence on MIS-C, emphasizing the syndrome's complexity and the critical need for timely intervention. By enhancing our understanding of MIS-C through continuous research and clinical observations, we can improve outcomes for children affected by this serious condition and provide them with the best possible care.

References

[1] Multisystem inflammatory syndrome in children during the coronavirus disease pandemic of 2019: a review of clinical features and acute phase management. J Anesth.2021; 35: 384-395.
[2] More K, Aiyer S, Goti A, Parikh M, Sheikh S, Patel G, Kallem V, Soni R, Kumar P. Multisystem inflammatory syndrome in neonates (MIS-N) associated with SARS-CoV2 infection: a case series. Eur J Pediatr.2022 May; 181 (5): 1883-1898.
[3] Greene AG, Saleh M, Roseman E, Sinert R. Toxic shock-like syndrome and COVID-19: Multisystem inflammatory syndrome in children (MIS-C). Am J Emerg Med.2020 Nov; 38 (11): 2492. e5-2492. e6.
[4] Saeed S, Cao J, Xu J, Zhang Y, Zheng X, Jiang L, Jiang C, Zhang X. Case Report: A case of multisystem inflammatory syndrome in an 11-year-old female after COVID-19 inactivated vaccine. Front Pediatr.2023 Feb 14; 11: 1068301.
[5] Casavecchia G, Corbo MD, Gravina M, Barone R, Magnesa M, Mele M, D'Alessandro D, Ieva R, Iacoviello M, Macarini L, Brunetti ND. Arrhythmic myocarditis in an adolescent male: A unique presentation of multi-organ inflammatory syndrome (MIS-C). Am J Emerg Med.2022 Apr; 54: 122-126.
[6] Stroeder J, Evans C, Mansell H. Corticosteroid-induced bradycardia: Case report and review of the literature. Can Pharm J (Ott) 2015; 148: 235–40.
[7] Berardicurti O, Conforti A, Ruscitti P, Cipriani P, Giacomelli R. The wide spectrum of Kawasaki-like disease associated with SARS-CoV-2 infection. Expert Rev Clin Immunol.2020 Dec; 16 (12): 1205-1215.
[8] Current Allergy and Asthma Reports. Pathogenesis of MIS-C: Carter et al. observed elevated levels of IL-1β, IL-6, IL-8, IL-10, IL-17, and IFNγ, and decreased T and B cell subsets in the acute phase of MIS-C patients, with normalization of levels at follow-up visits. Current Allergy and Asthma Reports.2021; 21 (12): 37-47.
[9] Valverde, I., Singh, Y., Sanchez-de-Toledo, J., et al. (2021). Cardiac manifestations of multisystem inflammatory syndrome in children (MIS-C) following COVID-19. *Curr Cardiol Rep*.
[10] Abdel-Mannan O, Eyre M, Löbel U, Bamford A, Eltze C, Hameed B, et al. Neurologic and Radiographic Findings Associated With COVID-19 Infection in Children. JAMA Neurol.2020; 77 (11): 1440-1445.
[11] McArdle AJ, Vito O, Patel H, Seaby EG, Shah P, Wilson C, et al. Treatment of Multisystem Inflammatory Syndrome in Children. N Engl J Med.2021; 385: 11-22