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Alternative Treatment to Multisystem Inflammatory Syndrome in Children Kawasaki Phenotype

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Immunoglobulin, methylprednisolone, maculopapular rash, fever, COVID 19. coronary artery aneurysms , conjunctivitis.

Abstract
During the COVID 19 pandemic multisystem inflammatory syndrome in children (MIS-C) has been reported quite often in different countries. This case report is about a 4-year-old child who presented with fever , maculopapular rash, abdominal pain for 3 days with exposure to COVID 19 in the past. Child was started on ceftriaxone and doxycycline. Covid antibody IgG detected to be positive. Considering age, mucocutaneous involvement without shock, child was diagnosed as MIS-C kawasaki phenotype without shock. Child was treated with intravenous methylprednisolone. Follow up showed no coronary dilatation. In a resource limiting setting, it is reasonable to consider steroids as a firstline.

1. Introduction

The Novel SARS-COV 2 (COVID 19) pandemic has presented with a wide range of clinical manifestations in children predominantly being asymptomatic to less number of severe acute respiratory distress syndrome cases [1,2]. However many countries have reported systemic hyperinflammation condition defined as multisystem syndrome in children (MIS-C) following COVID infection [3].Since MIS-C has overlapping clinical features to Kawasaki disease, intravenous immunoglobulin(IVIG) has been the preferred treatment regime. But, since IVIG is costly, alternative management options are needed in resource limited settings. In this case report, we are discussing one such alternative to IVIG.

2. Case Report

A previously healthy 4 year old female child presented to the hospital with complaints of

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intermittent high grade fever with body pain for 3 days, maculopapular rashes over hands and face for 2 days. The child also had abdominal pain with non projectile vomiting 2 to 3 times per day for 2 days. One month before ,her father had fever and was tested positive for COVID 19 via nasopharyngeal RT PCR. The mother and child also had fever, cough and cold during the same period, but did not get tested for COVID 19. None of them required hospitalization and recovered well without any complication.

On physical examination, the child was irritable, febrile (103 F), tachycardiac (heart rate of 124 beats/min), blood pressure – 100/75mmHg and normal urine output, with no evidence of shock. Maculopapular rash were noted over hands, face and pubic region as shown in figure 1,2. Ophthalmologic examination revealed bilateral non-purulent conjunctivitis, blepharitis (figure 3) and periorbital puffiness. No eschar was found.

Figure 1: Rashes in the palm

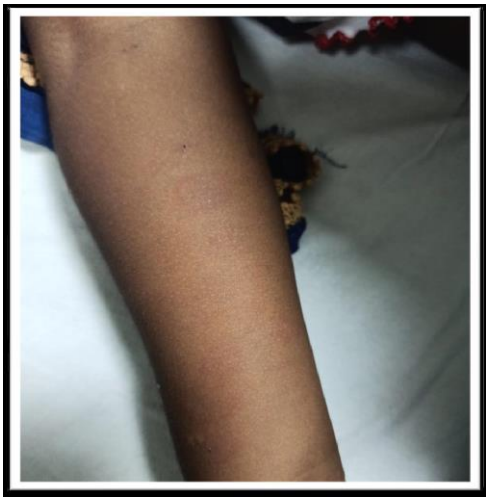

Figure 2: Maculopapular rashes in forearm

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Figure 3: Blepharitis

On abdominal examination, tenderness was present at suprapubic and periumbilical region, with no organomegaly and no free fluid. Other systemic examinations revealed no abnormality.

At the time of admission, complete blood count with peripheral smear, liver function test, renal function test, urine routine analysis, urine and blood culture and sensitivity, Dengue serology, Covid 19 RT PCR, scrub typhus serology, inflammatory markers, coagulation profile was sent. Results are tabulated in table 1 for reference.

TABLE 1: Blood investigation during hospitalisation

Investigation	**Baseline**	**Day4**	**Follow up Day 14**
Haemoglobin	13 gm/dl	11.7 gm/dl	12.3 gm/dl
PCV	35 %	34 %	35 %
WBC	12460mm^3	17,140mm^3	7,233mm^3
Neutrophils	89.3 %	64.2 %	62%
Lymphocytes	9.1 %	32.8 %	34.5%
Eosinophils	0.1 %	1 %	1%
Basophils	0.3 %	0.2 %	0.5%
Monocytes	1.2 %	1.8 %	2%
Platelet Count	1.8 Lakh/mm^3	4.55 Lakhmm^3	8 Lakh/mm^3
CRP	120 mg/L	>130 mg/L	5 mg/L
LDH	476 U/L	500 U/L	250 U/L

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S.ferritin	152 mcg/L	200 mcg/L	180 mcg/L
D.Dimer	1160 ng/ml	1198 ng/ml	150 ng/mL
PT	17.8 seconds		
INR	1.40		
aPTT	31 seconds		
Urea	24 mg/dl		
S.creatinine	0.4 mg/dl		
Scrub typhus IGm	Negative		
Dengue IgM, IGg	0.7 IV (Negative)		
COVID 19 RT PCR	Negative		
COVID IgG	8.76 s/Co (Positive)		

Laboratory investigations suggest leukocytosis with neutrophilia, lymphopenia, elevated C-reactive protein (CRP), D-dimers and LDH. Although COVID RTPCR was negative, viral antibodies for SARS-COV-2 returned positive for IgG. Dengue and scrub typhus serology, urine and blood culture and sensitivity were negative. All other investigations were within normal limits. Chest Radiography and ultrasound abdomen did not reveal any abnormality. 2D Echocardiography (2D ECHO) showed normal contractility and no abnormalities in the coronary arteries.

At the time of admission, the child was started on intravenous ceftriaxone, doxycycline, pantoprazole, paracetamol, emeset. Still she continued to have high grade fever on day 2 and day 3 of hospitalisation. In view of high grade fever, along with rash, gastrointestinal symptoms, elevated markers of inflammation with evidence of positive COVID 19 serology and no other obvious evidence of microbial inflammation we kept a provisional diagnosis of multisystem inflammatory syndrome in children (MIS-C). As per CDC guidelines(2) intravenous immunoglobulin (IvIg) 2g/kg was planned but since parents were not affordable intravenous methylprednisolone was started at 2mg/kg/day 12th hourly.

After 24 hours of starting steroids, fever spikes stopped and rashes disappeared. Intravenous antibiotics were discontinued as blood and urine culture were negative. Intravenous methylprednisolone was continued for 5 days and then changed to oral prednisolone at 2mg/kg/day. Repeat 2D ECHO revealed no abnormalities in coronary arteries and hence discharged on oral steroids.

3. Outcome & Followup

After a week of discharge, inflammatory markers normalised but platelets were elevated to 8 Lakh/mm3. Hence tablet aspirin (75mg) was started and continued for four weeks till platelet returned to normal. Oral steroids were tapered off gradually and

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stopped in 4 weeks. Repeat 2D ECHO at one month and 6 months of discharge showed normal coronaries.

4. Discussion

We are presenting this case of MISC to discuss alternative management we followed and its outcome.

During the COVID 19 pandemic MIS-C has been reported quite often in different countries. The case definition of MIS -C by WHO consists of six criteria: age 0-19 years, Fever for more than 3 days, clinical signs of multisystem involvement, elevated markers of inflammation, no other obvious microbial causes of inflammation and evidence of SARS-COV2-infection(4).

Our case fitted with above WHO criteria for MIS-C. Also in the study of 570 children with MIS-C reported to CDC, investigators identified three different subtypes(5). Our child age is going with rash, mucocutaneous involvement and no shock or myocardial dysfunction, hence can be categorised to "MIS-C overlapping with kawasaki disease " subtype. Patients who meet criteria for MISC with features of Kawasaki disease (KD) should receive standard treatment of KD which includes intravenous immunoglobulin (IVIG), aspirin. Steroids should be added if persistent inflammation or coronary artery dilatation present. The International Best Available Treatment Study (BATS) casortium in their report of 614 patients had no difference between the three treatments: IVIG alone, IVIG and glucocorticoid combination or glucocorticoids alone with regards to need for inotropic support, mechanical ventilation or death(6).

Crosby et al commented that cost of requirement of IVIG for MIS-C in India could be around a 100 million rupees and understanding the role of steroids as a low cost primary treatment for MIS-C is important.Hence in India, methylprednisolone (1-2mg/kg) has been the first line of recommendation for MIS-C with IVIG reserved for nonresponders, Kawasaki-disease phenotype or severe illness(7).

Francesco Liccardi et al were able to treat 31 patients of MIS-C with a treatment protocol that avoids IVIG as first line treatment(8). Evidence is mounting towards the usage of steroids in MIS-C as first line treatment particularly in settings where IVIG is expensive and difficult to access. But till now for Kawasaki disease phenotype IVIG is only recommended even in resource limited settings. Even though our child was diagnosed as a case of MIS-C with Kawasaki-disease phenotype, we couldn't start IVIG due to financial constraints of parents. We gave methylprednisolone 2mg/kg/day for 5 days and oral steroids for 4 weeks. Fever and raised inflammatory markers normalised to baseline and no coronary dilatation was documented till 6 months of follow up.

5. Conclusion

MIS-C has varied presentations involving GIT, skin, heart, Nervous system, kidney, Eye. In the pandemic any presentation that fulfills the mentioned criteria MIS-C should always be considered as differential Diagnosis. In MIS-C kawasaki phenotype, it is reasonable to consider treating children with steroids as firstline, particularly in settings where IVIG is expensive and difficult to access. For kawasaki disease, which has the same pathogenesis, the role of steroids is to be explored.

References

[1] Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DS, Du B. Clinical characteristics of coronavirus disease 2019 in China. New England journal of medicine. 2020 Apr 30;382(18):1708-20.Med 2020;382:1708.https://doi.org/10.1056/NEJMoa2002032

[2] Yang X, Yu Y, Xu J, Shu H, Liu H, Wu Y, Zhang L, Yu Z, Fang M, Yu T, Wang Y. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. The Lancet Respiratory Medicine. 2020 May 1;8(5):475-81.https://doi.org/10.3389/fped.2020.594127

[3] Fouriki A, Fougère Y, De Camaret C, Blanchard Rohner G, Grazioli S, Wagner N, Relly C, Pachlopnik Schmid J, Trück J, Kottanatu L, Perez E. Case report: case series of children with multisystem inflammatory

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syndrome following SARS-CoV-2 infection in Switzerland. Frontiers in Pediatrics. 2021 Jan 5;8:863.https://doi.org/10.3389/fped.2020.594127

[4] Son M, Friedman K, Kaplan SL, Sundel R, Randolph AG. COVID-19: multisystem inflammatory syndrome in children (MIS-C) management and outcome. Up to Date. 2021.

[5] Godfred-Cato S, Bryant B, Leung J, Oster ME, Conklin L, Abrams J, Roguski K, Wallace B, Prezzato E, Koumans EH, Lee EH. COVID-19–associated multisystem inflammatory syndrome in children—United States, March–July 2020. Morbidity and Mortality Weekly Report. 2020 Aug 14;69(32):1074.http://dx.doi.org/10.15585/mmwr.mm6932e2

[6] McArdle AJ, Vito O, Patel H, Seaby EG, Shah P, Wilson C, Broderick C, Nijman R, Tremoulet AH, Munblit D, Ulloa-Gutierrez R. Treatment of multisystem inflammatory syndrome in children. New England Journal of Medicine. 2021 Jul 1;385(1):11-22.https://doi.org/10.1056/NEJMoa2102968

[7] Crosby L, Balasubramanian S, Ramanan AV. Steroids or intravenous immunoglobulin as first line in MIS-C in LMICs. The Lancet Rheumatology. 2021 Sep 1;3(9):e615-6.https://doi.org/10.1016/S2665-9913(21)00223-X

[8] Licciardi F, Baldini L, Dellepiane M, Covizzi C, Mogni R, Pruccoli G, Orsi C, Rabbone I, Parodi E, Mignone F, Montin D. MIS-C Treatment: Is IVIG Always Necessary?. Frontiers in Pediatrics. 2021;9.https://doi.org/10.3389/fped.2021.753123