



COVID-19 MIS-C (MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN) LIKE PRESENTATION WITH RARE ASSOCIATION OF SCRUB TYPHUS : A CASE SERIES.

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ABSTRACT **Introduction:** Recently there is a surge of post COVID-19 MIS-C cases worldwide. Its diagnosis becomes challenging when a case presented with MIS-C like feature associated with scrub typhus infection.

Method: Our cases presented with high fever, neurological and gastrointestinal symptoms, rash and non-purulent conjunctivitis. All the cases have high inflammatory markers like ESR, CRP, LDH, ferritin, IL6 with elevated D-dimer and CPK-MB in case 1 and 2. Echocardiographic abnormality was present in first two cases and SARS-CoV-2 Ab was positive in all. Due to their MIS-C like presentation we treated with methyl prednisolone, IVIG, enoxaparin and oral aspirin but fever did not respond. Then after getting the Scrub IgM Ab positive and discovering eschar in third case we started doxycycline and the patients were discharged in stable condition.

Conclusion: Tropical infections like scrub typhus may be associated with a post COVID-19 MIS-C like presentation.

KEYWORDS : COVID -19, MIS-C, Scrub typhus,

INTRODUCTION

Recently multisystem inflammatory syndrome in children (MIS-C), a post infectious (after 2-6 weeks of SARS-CoV-2 infection) inflammatory syndrome has been reported in the paediatric population in increasing number worldwide¹. In this case series we have described three interesting cases with post COVID-19 MIS-C like presentation, which were also tested positive with scrub typhus IgM. Rarity of the association of MIS-C with scrub typhus prompted us to present these cases.

MATERIAL & METHOD

Case Reports

Case 1 : A 5 year 3 month old female child admitted with chief complaints of high grade fever for 4 days with vomiting, convulsion and altered sensorium. Her positive clinical findings were neck rigidity, right sided diminished breath sound, significant lymphadenopathy and grade II papilledema. Initially treated in the line of meningoencephalitis with CSF finding of lymphocytic pleocytosis (WBC 42/mm³) and mildly elevated protein (76mg/dl). She has low Hb with raised inflammatory markers like ESR, CRP, Serum ferritin, serum LDH, Interleukin-6 along with SARS-CoV-2 IgG antibody positive and increased D-dimer and CPK-MB level (shown in Table 2). Radiological findings of chest shows right sided consolidation and Echocardiography shows global hypokinesia. With these findings we made the diagnosis of MIS-C, excluding common causes of acute febrile illness. Patient was given IVIG, iv methyl prednisolone, s/c enoxaparin and packed RBC transfusion along with ventilator support. But her fever persisted till we started iv doxycycline after receiving the scrub IgM Ab report positive. So a diagnosis of MIS-C like presentation with associated scrub typhus infection was made and the patient was discharged in a stable condition with oral aspirin and prednisolone.

Case 2 : A 4yr 11 month old male child presented with high grade fever for 5 days, pain abdomen, vomiting, bilateral non-purulent conjunctivitis and cervical lymphadenopathy. His reports show leukopenia, thrombocytopenia, high inflammatory markers like ESR, CRP, LDH, ferritin, IL-6 with high D-dimer and CPK-MB. Along with that coronary art dilatation in Echo and SARS-CoV-2 Ab positivity prompted us to make a diagnosis of MIS-C after rule out

common infections and we started iv methyl prednisolone, enoxaparin and other supportive treatment. After one day of afebrile period, fever recurs and ultimately we add oral doxycycline after getting the scrub IgM report positive. Pt was discharge in stable condition with oral prednisolone and aspirin.

Case3: A 3yr 6 month old girl admitted with fever for 10 days, pain abdomen, vomiting, maculopapular rash and significant lymphadenopathy. In her reports, raised values of ESR, CRP, Serum ferritin, serum LDH and Interleukin-6 was found along with SARS-CoV-2 IgG antibody positive. Laboratory and clinical features guided us to think about MIS-C after excluding common tropical infections and we started iv methyl prednisolone. But the fever persisted and on detailed clinical examination we discovered an eschar over neck². So we started oral doxycycline and in the meantime scrub IgM report also came positive. Child become afebrile in 3 days and discharged with oral prednisolone in stable condition.

RESULTS

Table 1 : Clinical presentation of three cases

Features	Case 2	Case 1	Case 3
	Basic information		
Age	5 Y 3 M	4 Y 11 M	3 Y 6 M
Sex	Female	Male	Female
H/O contact to COVID-19 positive individual	Nil	Nil	Nil
	Symptoms		
Fever (duration in days)	+(4)	+(5)	+(10)
Disorientation	+	-	-
Vomiting	+	+	+
Loose stool	-	-	-
Pain abdomen	-	+	+
Headache	-	-	-
Convulsion	+	-	-
Shortness of breath	-	-	-
	Signs		
Altered sensorium	+	-	-
Hypotension ,shock	-	-	-

Non purulent conjunctivitis	-	+	-
Maculopapular Rash	-	-	+
Eschar	-	-	+
Neck rigidity	+	-	-
Lymphadenopathy	+	+	+
Hepatosplenomegaly	-	-	-
Respiratory findings	+	-	-
Direct Ophthalmoscopy	Grade II papilledema	Normal	Normal

Table 2: Important radiological findings and blood parameters of the cases.

Features	Case 1	Case 2	Case 3
	Lab Investigation		
Hb%(gm/dL)	4.5	7.8	11.2
WBC/Platelet(per mm ³)	11200	270000	4500/120000
ESR(mm/hr)	48	77	52
CRP(mg/L)	89	45	88
Serum ferritin(ng/ml)	483.5	275	387
Serum LDH (IU/L)	2982	987	836
Interleukin-6(pg/ml)	>5500	2372	>5500
SARS-CoV-2RTPCR	Negative	Negative	Negative
SARS-CoV-2 IgG antibody	Positive	Positive	Positive
SGPT/SGOT (U/L)	52/69	55/72	56/63
Serum albumin(g/dl)	3.3	3.2	3.6
PT/APTT(sec)	17/40	14.8/37	13.4/32
D-dimer(mg/LFEU)	7.71	4.2	0.6
CPK-MB (IU/L)	32	27	20
Scrub typhus IgM Ab	Positive	Positive	Positive
	Imaging		
CXR	Right sided consolidation	Normal	Normal
HRCT THORAX	Patchy Consolidation over right upper,middle & lower lobe.	Normal	Normal
ECHOCARDIOGRAPHY			
Coronary artery dilatation	-	Proximal part of LCA dilated	-
Pericardial effusion	+	-	-
Any other abnormality	Global hypokinesia	-	-
LVEF%	45%	68%	76%

Table 3: Salient points in the management of the cases.

TREATMENT RECEIVED	Case 1	Case 2	Case 3
Ventilatory support	+	-	-
IVIG	+	-	-
IV Methylprednisolone	+	+	+
Enoxaparin S/C	+	+	-
Oral Aspirin	+	+	-
IV/oral Doxycycline	+	+	+
PRBC transfusion	+	+	-
Oral prednisolone	+	+	+

DISCUSSION

To diagnose a case as MIS-C(WHO definition) we have to fulfil the following six criteria³;

1.Age 0 to 19 years, 2.Fever for ≥ 3 days, 3.Clinical signs of multisystem involvement (at least two of the following five): i)Rash or bilateral non purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands, or feet), ii)Hypotension or shock, iii)Features of myocardial dysfunction, pericarditis, valvulitis or coronary abnormalities (including echocardiographic findings or elevated troponin/NT-BNP), iv)Evidence of coagulopathy (prolonged PT, PTT, elevated d-Dimer), v)Acute gastrointestinal symptoms (diarrhoea, vomiting or abdominal pain), 4.Elevated markers of inflammation (ESR, CRP or procalcitonin), 5.No other obvious microbial cause of inflammation, including bacterial sepsis and staphylococcal/streptococcal toxic shock syndromes, 6.Evidence of SARS-CoV-2 infection(RT-PCR, antigen test or serology positive)or contact with an individual with COVID-19 present.

In our presented three cases clinical features, laboratory investigations and positive covid-19 serology were meeting the criteria for MIS-C , except one that all the children had obvious other evidence of infection that is scrub typhus. Again complicated scrub may present with similar characteristics except that COVID-19 serology would be negative in that case⁴. So here lies the confusion that whether we would categorize the cases as MIS-C or stamp them as MIS-C like presentation with associated scrub infection. Multisystem inflammation is definitely present in all the cases, but question is whether that is due to scrub or due to post covid-19 infection. Or it may be the exaggerated immune response of scrub typhus on the background of SARS-CoV-2 infection. All the cases were treated with IVIG in and/or methylprednisolone and in-spite of that fever was not controlled and ultimately responded with doxycycline. Report of MIS-C with concomitant scrub typhus infection is not available widely in literature. Gupta A et al reported one case of MIS-C with scrub typhus and macrophage activation syndrome recently and D Hazra et al reported a case of scrub typhus and covid-19 co-infection^{2,5}. As the most consistent clinical feature of MIS-C is fever which closely mimics other acute febrile illnesses in children like scrub typhus ,malaria, dengue, enteric fever,seasonal influenza(H1N1) and leptospirosis specially in a tropical country like India, so the co-infection should always be kept in the mind, when a case of MIS-C is not responding to the conventional treatment^{6,7,8}.

CONCLUSION

Case series of these patients highlight the association of MIS-C like presentation with Scrub typhus which is very rarely reported in published literature. As the clinical and laboratory picture of complicated scrub typhus and MIS-C are often very closely related, so it can be a diagnostic challenge to the paediatrician and we must always be aware of the possibility of coexistence of a tropical infection in a case with COVID-19 MIS-C like presentation.

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