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Multisystem Inflammatory Syndrome in Children (MIS-C) with Involvement of Cardiovascular, Respiratory and Gastrointestinal System: a Case Report

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Summary

MIS-C is a rare complication after COVID-19 infection that manifests with multi-system involvement. This case report presents a 7-year-old girl with MIS-C with involvement of the cardiovascular, respiratory, and gastrointestinal systems. The patient was treated with intravenous immunoglobulins (IVIG) and glucocorticoids, resulting in recovery and hospital discharge after two weeks.

Keywords: MIS-C, COVID-19, hepatitis, case report.

Aim of demonstration

This case report aims to highlight the need for immediate treatment in MIS-C, which can manifest with severe multi-organ involvement. However, diagnosing MIS-C can be challenging due to the wide range of differential diagnoses (1). Therefore, this case report serves to draw attention to the heterogeneous clinical presentations observed in MIS-C, emphasizing the need for clinical awareness and prompt management.

Case report

This is a case of a 7-year-old female patient who presented to the emergency department with complaints of fever, headache, nausea, fatigue, and jaundice for two days.

The patient was previously healthy, with a history of rhinitis and cough one month ago, and SARS-CoV-2 infection four months ago. On admission, the patient had icterus, abdominal pain, hepatomegaly, and palmar erythema. Laboratory results showed leucopenia (3.29 x 109/L), thrombocytopenia (58 x 109/L), prolonged clotting time, increased levels of ferritin (3278 ng/mL), bilirubin (117.34 μmol/L), ALT (2003.11 U/L), AST (2224.82), LDH 1165 (U/L), D- dimers (4.63 mg/L FEU), CRP (50.57 mg/L) and NT-ProBNP 504.4 pg/ml., as shown in Table 1.

Table 1. Clinical laboratory results during hospitalization

Hospitalization day	1	2	3	4	5	6	Reference range
WBC (x 109/L)	3.29	2.31	2.20	2.63	2.37	4.64	4.27 - 11.4
NEUT (x 109/L)	-	1.51	1.18	1.31	0.78	2.15	1.64 -7.87
LYMPH (x 109/L)	0.69	0.62	0.76	0.94	1.20	1.96	1.16 - 4.28
PLT (x 109/L)	58.00	46.00	33.00	44.00	64.00	150	199 - 367
CRP (mg/L)	50.56	43.47	33.79	-	-	7.91	0 - 2.8
Ferritin (ng/mL)	-	3278	2800	-	-	-	20 - 200

Table 1 countinued

Hospitalization day	1	2	3	4	5	6	Reference range
LDH (U/L)	-	1165	611	-	225	-	120 - 300
ALT (U/L)	2003	2208	1923	-	-	701	0 - 39
AST (U/L)	2224	-	1469	-	-	131	0 - 51
Total bilirubin (umol/L)	117.34	125.93	135.78	-	54.20	40.29	0 - 21
Conjugated bilirubin (umol/L)	88.64	-	122.53	-	-	36.83	0 - 5
Protrombin (%)	48.20	49.70	51.90	78.00	-	106.00	76.6 - 116.2
INR	1.55	1.51	1.45	1.15	-	0.98	0.8 - 1.2
APTL (s)	34.50	36.70	38.00	32.20	-	27.90	24 - 43
Fibrinogen (g/L)	3.72	3.03	2.28	2.22	-	1.54	1.7 - 4.2
D-Dimers (mg/L)	4.63	4.90	5.33	6.83	-	11.01	0 - 0.55
NT-ProBNP (pg/ml)	-	504.4	-	217.4	-	622.1	0 - 125

Abdominal ultrasonography showed polyserositis, ascites, pericholecystitis, hepatolienal syndrome, and fluid accumulation in pleural space. Echocardiography showed pericardial effusion, tricuspid, and mitral valve insufficiency. ECG and chest X-ray were without pathology.The patient received empiric antimicrobial treatment with intravenous Cefuroxime, Furosemide 20 mg/day, and Spironolactone 25 mg/day upon suspicion of an infectious cause. Serology tests for Parvovirus B 19, Borrelia burgdorferi, hepatitis C virus, hepatitis E virus, hepatitis B virus, human immunodeficiency virus (HIV), Ehrlichia, Ehrlichia chaffeensis, Enthenoplasma phagocitophylum were all negative. Cytomegalovirus, Ebstein-barr virus, Parvovirus B19, E.coli, Haemophilus influenzae, Listeria monocytogenes, Neisseria meningitidae, Streptococcus agalactiae, Streptococcus pneumoniae, Enterovirus, Herpes simplex 1/ 2, Human parechovirus, Varicella zoster virus, Cryptococcus neoformans/gattii, Tick-borne encephalitis virus were all undetectable in blood with real-time polymerase chain reaction (PCR). The results of stool swab analysis revealed the absence of Campylobacter jejuni/coli/upsaliensis, Clostridium difficile, Plesiomonas shigelloides, Salmonella, Yersinia enterocolitica, Adenovirus F40.1, Astrovirus, Norovirus G1/G2, Apovirus, Enterovirus, Sapovirus 1/2/4/5, and Vibrio cholera in all samples tested.

Parasites including Giardia lamblia, entamoeba histolytica, Cryptosporidium spp, Blastocystis hominis, Cyclospora cayetanensis were excluded. Real-time polymerase chain reaction (PCR) of nasopharyngeal swab for Adenovirus, Influenza A, B, Respiratory syncytial virus (RSV) type A and B, Metapneumovirus, Coronavirus 229E/NL63 un OC43, SARS-CoV-2, Parainfluenza virus type 4, Rhinovirus, Enterovirus, Bocavirus were negative. The urine culture also revealed no bacterial growth. It was found that the patient has positive serology for IgG against adenovirus, SARS-CoV-2 recombinant antigen antibodies 165.6 COI, and SARS-CoV-2 spike (s) protein antibodies 1951 U/ml. Platelet level on day 6 of hospitalization was 150 x 109/L. Therefore, therapy with Acetylsalicylic acid was started. Serologic testing for autoimmune hepatitis was also performed and resulted in positive for antinuclear antibodies (1:40) and anti-smooth muscle antibodies (1:40). Autoimmune hepatitis was excluded after normal Serum electrophoresis and immunoglobulin G levels in plasma. On the basis of the clinical picture of multisystem involvement and positive serology against SARS-CoV-2, the diagnosis of MIS-C was made, according to the Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO) diagnostic criteria. Consequently, therapy with intravenous immunoglobulin (IVIG) at a dose of 1g/kg and intravenous Methylprednisolone at a dose of 30 mg/ day was started on day 4 of hospitalization. After 12 days of hospitalization, the patient's condition normalized, and she was discharged home with recommended follow-up. After 6 months during

follow-up, Next Generation Sequencing (NGS) panel analysis for inborn errors of metabolism and genes associated with fulminant hepatitis and hemophagocytic lymphohistiocytosis was done. Results were negative, but it was found that the patient is heterozygous for genes associated with Canavan disease. The patient was tested for metabolic diseases by detection of Volatile Organic Compounds in Urine and Blood Spot acylcarnitines. No inborn errors of metabolism were found.

Discussion

This case report described a 7-year-old girl with MIS-C with involvement of the liver, lungs, and heart. Patients with MIS-C exhibit a wide variety of clinical and laboratory manifestations (2,3). It therefore is a challenge to differentiate MIS-C from other differential diagnoses such as autoimmune diseases, macrophage activation syndrome, sepsis, acquired hemophagocytic lymphohistiocytosis (HLH), or other infectious conditions (1,4,5). However, prompt initiation of immunoglobulin therapy holds significant importance in ensuring the patients' recovery and should not be postponed once there is a suspicion of the diagnosis (6).

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