Case Report

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Multisystem inflammatory syndrome in children with COVID-19 in a multitransfused patient

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Abstract:

Multi-system inflammatory syndrome in children associated with COVID19 (MIS-C) is a unique clinical syndrome characterised by fever, gastrointestinal symptoms, skin and oral rash and or neurological symptoms in the presence of raised acute phase reactants and coagulopathy. Ferritin is an acute phase reactant which is used as a marker of inflammation. Diagnosis of MIS-C in the background of transfusion dependent thalassemia with iron overload needs a strong clinical suspicion. Early diagnosis and prompt treatment are necessary to ensure a rapid uneventful recovery. A three-year-old male child born to non-consanguineously related parents reported to pediatric emergency with difficulty breathing and pain abdomen for one day. The child was a diagnosed case of Beta thalassemia major since the age of one year and was on regular transfusions and was on iron chelation for past eleven months with deferrasirox. Initial clinical examination showed a sick and irritable child with tachypnea tachycardia and hypoxia. Initial investigations showed raised acute phase reactants along with severe anemia. The child was investigated for MIS-C because of unexpected rise of serum ferritin from 1980 ng/mL (October 2020) to 6686 ng/mL (in January 2021) despite being on regular chelation. Antibody titre for SARS COVID-19 was positive. The patient was treated with intravenous corticosteroids and improved with the same. The advent of COVID19 pandemic saw most children having a mild disease with no or minimal symptoms. Some kids however presented with more serious delayed symptoms of MIS-C. To diagnose same in multi transfused patients a strong clinical suspicion and just judgement based on the clinical and laboratory findings should be done. Unexplained rise in ferritin levels, typical symptoms and high probability of exposure to COVID19 helped in clinching diagnosis.

Keywords:

Case report, child, COVID-19, ferritin, multisystem inflammatory syndrome in children, thalassemia

Introduction

The pandemic of coronavirus disease-2019 (COVID-19) had catastrophic effect on global health with more than 240 million cases and 4.92 million deaths reported worldwide.[1] Multisystemic inflammatory syndrome in children (MIS-C) is a new disease phenotype, which emerged in children and has lethal potential. This condition was first described in May 2020 in a cluster of children admitted to the critical care unit in South London.[2,3]

MIS-C has been defined by the Centers for Disease Control and Prevention (CDC) in an individual aged <21 years presenting with fever (lasting for >24 h and >38°C), laboratory evidence of inflammation (as shown by raised acute-phase reactants such as C-reactive protein [CRP], serum ferritin, and erythrocyte sedimentation rate [ESR]), and evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic, or neurological); in the absence of alternative possible diagnoses; in a patient who is positive for current or recent COVID-19 infection by reverse

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transcriptase polymerase chain reaction (RT-PCR), serology, or antigen test; or exposure to a suspected or confirmed COVID-19 case within the 4 weeks before the onset of symptoms.[4]

Serum ferritin is an acute-phase protein, which is raised in many conditions such as acute and chronic inflammation and hepatocellular damage.[4] It is an important marker for the diagnosis of MIS-C. Ferritin, being an intracellular iron storage protein, is also a marker of iron stores, and values are expected to be very high in a patient with chronic transfusion. Children with thalassemia major and other conditions requiring frequent transfusions invariably present with elevated ferritin levels. In the background of chronic transfusion, the sudden unexpected rise in ferritin level often challenges the physician, especially in a compliant patient. MIS-C cases present with high ferritin levels and have to be thought of as a common differential diagnosis in a febrile chronically transfused kid. This is especially important since the chances of getting COVID-19 infection are more in these groups of patients due to frequent hospitalizations.

Case Report

Patient information

A 3-year-old male child presented to the pediatric emergency room with complaints of fever, pain abdomen, vomiting, and irritability. The child is a known case of beta-thalassemia major since the age of 1 year and was on regular transfusion and iron chelation.

Clinical findings

At admission, the child was sick-looking, irritable with tachypnea. Systemic examination showed pallor. The child also had mucositis but no skin rash. The abdominal examination showed gross distension of the abdomen and diffuse tenderness. Initial blood investigations revealed anemia (Hb 6.2 g/dl), thrombocytopenia (80,000/µL), raised CRP 13.72 mg/mL, and increased liver enzymes (Bilirubin normal serum glutamate oxaloacetate transaminase (SGOT) 67 U/L serum glutamate pyruvate transaminase (SGPT) 121 U/L and low serum albumin 2.4 g/dL). Ultrasound of the abdomen was unremarkable except for hepatomegaly and mild splenomegaly.

Timeline and diagnostic assessment

The child developed a high spiking fever from the next day. There was a history of exposure to a family member who had SARS-COVID-19 2 months before hospitalization. The patient was screened for COVID-19 by RT-PCR which was negative.

Because of typical history, markers of acute inflammation were sent, which showed ferritin of 6886 ng/mL. ESR was 47 mm in 1 h and lactate dehydrogenase (LDH) 931.6 U/L (normal <330 u/l). CRP was further raised to 87.14 mg/L along with a D-dimer 3.28 µg/mL, and pro-brain natriuretic peptide was raised 1466 pg/mL, with positive anti-SARS-Cov-2 immunoglobulin G of 10 S/CO. Echocardiography was done showed normal left ventricular function with an ejection fraction of 66% without coronary artery dilatation.

With a history of beta-thalassemia major, his serum ferritin levels were reviewed. His ferritin levels remarkably increased from 1980 ng/mL to 6886 ng/mL, even though he was on deferasirox at 30 mg/kg/day. After that, he had received two packed red blood cell transfusions at 15 ml/kg in subsequent months and was compliant with iron chelation. With the background of being positive to SARS-CoV-2 antibody with unexplainedly high ferritin levels and raised D-dimer and CRP values, the child was diagnosed with MIS-C in COVID-19 as per the CDC criteria for diagnosis. Serological tests sent for dengue, scrub typhus, and typhoid came negative. Blood and urine cultures did not grow any organism, and bacterial sepsis and urinary tract infections were also ruled out. Peripheral smear for malaria was negative, and malaria was ruled out in this patient before confirming the diagnosis as MIS-C.

Therapeutic interventions

The child was started on injectable methylprednisolone at 10 mg/kg/day along with supportive treatment. The child was given two units of packed red blood cell transfusion before discharge. The child became afebrile at 48 h after starting steroids.

Follow-up and outcomes

The child was discharged after the completion of injectable methylprednisolone for 3 days, on tapering doses of oral steroids. Ferritin was repeated had fallen to 4806 ng/mL suggesting raised levels were acutely due to MIS-C, with normalization of complete blood count and CRP. The child was discharged on deferasirox and on follow-up after 2 weeks, ferritin levels have further reduced to 2132 ng/ml.

Discussion

MIS-C is a newly evolving illness and is considered a late complication of COVID-19 in children. Typically presents 4 – 6 weeks after initial COVID-19 infection, although causal association not established. Possible mechanisms of hyperinflammation are (1) viral mimicry and resulting autoantibodies, (2) antibody or T-cell recognition of viral antigens expressed on infected host cells, (3) formation of immune complexes which activate inflammation, and (4) SARS-CoV-2 spike protein behaves like superantigen which mediates hyper-inflammation

observed in MIS-C.[5] Timing of SARS-CoV-2 infection and interferon (IFN) response can vary with viral load and the genetic difference in host response. When viral load is low, IFN response is engaged, leading to viral clearance and milder infection. When viral load is high and or genetic factors slow the antiviral and IFN response it leads to cytokine storm.[6] Usual presentations are persistent fever, abdominal pain, vomiting, diarrhea, skin rash, mucocutaneous lesions, and severe cases present with respiratory distress, hypotension, and shock along with high levels of inflammatory markers such as CRP, ESR, serum ferritin, LDH, D-dimer, fibrinogen, and increased biomarkers of organ dysfunction. Leukocytosis with lymphopenia, thrombocytopenia, and anemia is common. Any child with persistent fever >3 days, who is moderate-to-severely ill with clinical signs of organ dysfunction should be suspected of MIS-C. In this case, a disproportionately high rise of serum ferritin was the clue toward hyperinflammation.[7,8] A high index of suspicion, early diagnosis, and treatment is the key to an uneventful recovery.[9,10] As the cardiovascular system is the most frequent organ system involved and contributes to the severity of illness, frequent cardiac function monitoring is required. Immunomodulators are the mainstay treatment. Intravenous immunoglobulin (IVIG) (2 gm/kg) is considered first-line therapy.[6] Glucocorticoids should be used as adjunctive (1-2 mg/kg/d) therapy in patients with severe disease or at (10-30 mg/kg/d) refractory to IVIG. Low-dose aspirin (3-5 mg/kg/d, maximum 81 mg/day) should be used in patients with MIS-C and continued till normalization of platelet count and confirmed normal coronary at >4 weeks after diagnosis. In our case, we used methylprednisolone due to the financial constraints of parents.

Conclusion

Diagnosing MIS-C requires a strong clinical suspicion with clinical and laboratory findings. Serum ferritin should not be considered a solitary marker of acute inflammation in multitransfused patients and should be commented based on the clinical features, serial levels and history of chelation use and other acute-phase reactants. Typical symptomatology, unexplained rise in ferritin levels, and high probability of exposure to COVID-19 helped in clinching the diagnosis in our case.

Informed consent was obtained from parents.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. WHO Coronavirus Disease (COVID-19) Dashboard | WHO Coronavirus Disease (COVID-19) Dashboard. Available from: https://covid19.who.int/. [Last accessed on 2021 Oct 13].
2. Radia T, Williams N, Agrawal P, Harman K, Weale J, Cook J, *et al.* Multi-system inflammatory syndrome in children & adolescents (MIS-C): A systematic review of clinical features and presentation. Paediatr Respir Rev 2021;38:51-7.
3. Ahmed M, Advani S, Moreira A, Zoretic S, Martinez J, Chorath K, *et al.* Multisystem inflammatory syndrome in children: A systematic review. EClinicalMedicine 2020;26:100527.
4. Centers for Disease Control and Prevention. Emergency Preparedness and Response: Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with Coronavirus Disease 2019 (COVID-19). Health Advisory. Available from: https://emergency.cdc.gov/han/2020/han00432.asp. [Last accessed on 2021 Oct 13].
5. Koperdanova M, Cullis JO. Interpreting raised serum ferritin levels. BMJ 2015;351:h3692.
6. Al Ameer HH, AlKadhem SM, Busaleh F, AlKhwaitm S, Llaguno MBB. Multisystem Inflammatory Syndrome in Children Temporally Related to COVID-19: A Case Report From Saudi Arabia. Cureus 2020;12:e10589. [doi: 10.7759/cureus.10589]. PMID: 33110725; PMCID: PMC7580961.
7. Rowley AH. Understanding SARS-CoV-2-related multisystem inflammatory syndrome in children. Nat Rev Immunol 2020;20:453-4.
8. Lee PY, Day-Lewis M, Henderson LA, Friedman KG, Lo J, Roberts JE, *et al.* Distinct clinical and immunological features of SARS-CoV-2-induced multisystem inflammatory syndrome in children. J Clin Invest 2020;130:5942-50.
9. Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, Son MB, *et al.* Multisystem inflammatory syndrome in U.S. children and adolescents. N Engl J Med 2020;383:334-46.
10. Godfred-Cato S, Bryant B, Leung J, Oster ME, Conklin L, Abrams J, *et al.* COVID-19-associated multisystem inflammatory syndrome in children – United States, March-July 2020. MMWR Morb Mortal Wkly Rep 2020;69:1074-80.