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Case Report

Autoimmune hemolytic anemia: a rare case report in a post-COVID patient

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ABSTRACT

Autoimmune hemolytic anemia (AIHA), a rare disease in pediatrics, affecting one's own immune system, is one of the causes for the acquired hemolytic anemia. For the past two years, the COVID-19 pandemic had emerged, evolved and manifested with a wide range of symptoms causing threat to human race. In recent times, there have been literatures focused on AIHA manifesting, with novel SARS-CoV-2 infection, or as its late sequelae (secondary). The pathophysiology causing hemolysis in SARS-CoV-2 infection remains vague making it a very rare association with COVID-19. The acute symptoms of jaundice, giddiness, shortness of breath are noted, with investigations depicting hyper-inflammatory state as a most common etio-pathogenesis. This acute presentation, at times could be fatal and make the patient refractory to steroids. There are complications due to COVID-19 infection like pneumonia, respiratory failure, acute respiratory distress syndrome etc., known until lately where AIHA secondary to COVID-19, a very rare phenomenon is taking the spot light. A few cases of AIHA manifestation with ongoing SARS-CoV-2 have been reported and few cases which presented as a secondary infection. Here we are presenting an extremely rare case of a 16-year-old girl, with late onset anemia, post COVID-19 infection 4 weeks back.

Keywords: AIHA, SARS-CoV-2 infection, Hemolysis, Inflammatory state

INTRODUCTION

The SARS-CoV-2 infection, is a disease with a wide spectrum of manifestations whose pathophysiology and the immune-pathogenic mechanism are barely being understood. There are proofs available pointing towards cytokine storm and hyper-inflammatory responses acting as the diagnostic and prognostic factors.[1] AIHA is one of the causes for the acquired hemolytic anemia occurring due to antibodies produced by one's on immune system against the antigens present on its own red cells. The association of COVID-19 with AIHA or as a secondary infection is a rare incidence.[2,3]

The incidence of AIHA accounts to 1-3/100000 people per year worldwide with an average of 79 cases per year being reported from India, amongst which 52 are of primary etiology and 27 with secondary etiology of a the AIHA. Warm-AIHA is the most common type accounting for 80% of the adult cases and 50% of the pediatric cases.[4]

Causes for AIHA in children remain obscure in majority of the cases which eventually end up in labelling them as idiopathic or primary. The incidence of secondary AIHA accounts for only 40-50%.[5] Secondary AIHA cases are most commonly associated with malignancies, underlying autoimmune diseases or infections like adenovirus, parvovirus, HIV, HCV etc. Recent literatures have been come up with cases of secondary AIHA post COVID-19 wherein 31 cases of AIHA with acute SARS-CoV-2 are

reported and one case reported with AIHA as a late COVID-19 syndrome.[2,3]

There could be various extra-pulmonary complications seen as a SARS-CoV-2 sequelae like Gullian Barre syndrome, anti-phospholipid syndrome, or most common, multisystem inflammatory syndrome in children. Yet AIHA trigger due to past COVID-19 infection is very rare and here we are presenting one such case. The usual presenting symptoms include tiredness, dizziness, shortness of breath, palpitations. Most of the cases remain responsive for blood transfusions and steroids but the acute presentation could lead to refraction or relapse in future.[5]

CASE REPORT

A 16-year-old female child, made a visit to the pediatrics OPD with the complaints of fever and decreased appetite for 7 days. A detailed history was elicited where the patient complained of breathlessness on exertion, which was not improved on taking rest, and child felt lethargic with restriction in performing daily activities (New York Heart Association class 2). There was no history of chest pain, cough, jaundice, weight loss, altered sensorium, drug allergy or any other comorbidities. Past history revealed COVID-19 infection 4 weeks back, for which she had got treated then.

On general physical examination the young girl, conscious, co-operative, poorly built and nourished, and was well oriented to time, place and person. The vitals (Temperature, pulse rate, blood pressure, oxygen saturation) were found to be within normal limits.

Clinically the child appeared icteric and pale suggesting of anemia and bilateral lower limb edema of grade 2 was noticed with tender hepatomegaly and no other abnormality detected on systemic examination. The blood investigations showed hemoglobin of 3 gm%, and peripheral smear depicted a picture of dimorphic anemia with hemolysis. The reports of Iron profile, Lactate dehydrogenase, Vitamin-B_{12} were found to be deranged and D-dimer, C-Reactive protein normal (details provided in Table 1). 2D ECHO revealed a grade I mitral regurgitation.

The RT-PCR for COVID-19 infection was negative and the child tested positive for direct anti-globulin test (DAT) IgG with positive direct and indirect Coombs test: suggesting autoimmune pathology. The test for COVID-19 antibodies was positive and further the (double stranded nuclear antibodies) anti-nuclear antibody and antiphospholipid tests turned out to be negative suggesting absence of any preexisting autoimmune pathology.

Blood transfusion was done under careful monitoring considering it as a case of severe anemia (Hb-3g%) with congestive cardiac failure. Further the child responded well for methyl-prednisolone (1 g/day), prednisolone (1 mg/kg/day) and azithromycin (500 mg/day). Subsequent blood transfusions and following blood investigations showed betterment of symptoms and increasing trend in hemoglobin concentration. The patient was thus diagnosed as a case of secondary Acquired AIHA to COVID-19 infection of late onset.

The child had a Hemoglobin of 9.8g% at the time of discharge with negative RT-PCR. Regular follow up was advised every week and ongoing steroid treatment was prescribed to be continued and planned for tapering at every visit.

Table 1: Blood investigations.

Parameters	On admission	At discharge
Hemoglobin	3 g%	9.8 g%
Red blood cells	1.35×10^6/mm^3	2.86×10^6/mm^3
Mean corpuscular volume	76.1 fL	98 fL
Mean corpuscular hemoglobin	22.4 pg	25.3 pg
Retic count	3%	1.2%
Serum iron	114 µg/dL	156 µg/dL
Serum transferrin	142.3 mg	202.6 mg
Total iron binding capacity	252 µg	256 µg
Vitamin B12	137 pg/dL	182 pg/dL
Platelets	1.98 lakhs/mm^3	4.06 lakhs/mm^3
Lactate dehydrogenase	543 U/L	162 U/L
D-dimer	0.2 µg/mL	0.4 µg/mL
C-reactive protein	1.0 mg/L	3.2 mg/L

Investigations of the patient done on admission and at discharge.

DISCUSSION

AIHA has numerous causative agents like, malignancies, auto immune diseases, collagen diseases, drugs, prior blood transfusions, post viral infections etc., amongst which the most common cause being the immune hemolytic anemia.[4,6-9] Antibody mediated hemolysis results in trapping /phagocytosis / complement mediated hemolysis taking place intravascular or extravascular.

The warm AIHA is more common than cold AIHA, where IgG coated RBCs are removed by the reticuloendothelial macrophages and sequestered in the spleen, this sometimes would be the cause for splenomegaly.[3] The warm-AIHA is most commonly mediated through IgG reacting at ≥37ºC and cold AIHA is generally mediated through C3 component of complement.[5,8,9] Warm AIHA commonly has direct antibody test positive for IgG with or without complement-3, with the incidence for C3 only warm

AIHA is less than 25%.[9] The rare association of secondary AIHA post COVID-19 is being noticed very recently.

The most common presenting symptoms being fever, jaundice, fatigue, dyspnea, followed with the findings of tachypnea and splenomegaly. The median time period noted for development of COVID-19 symptoms and onset of anemia is 9 days (range of 4-15 days) or in certain cases more than 25-days.[5] This is a rare case reported with a late onset after 4 weeks (one case presenting 3 months after infection is mentioned in literature).[3]

The clinching diagnostic tests in this condition are direct anti-globulin test, peripheral smear with hemolytic changes and deranged retic counts. The positive direct Coombs test suggests an autoimmune pathology and normal C- reactive protein, D-dimer levels and negative RT-PCR for COVID-19 in our case suggest absence of active SARS-CoV-2 infection. The various treatment modalities include steroids, blood transfusions and refractory cases of warm-AIHA post COVID are seen responding to rituximab (a monoclonal antibody).[2] Other modes of treatment are plasmapheresis, intravenous immunoglobulin therapy where steroid resistance is seen. The probability of relapse is based on the hemoglobin level at the time of presentation: Lower the hemoglobin, higher the risk of relapse.[5]

Altogether the association of SARS-CoV-2 with AIHA is uncommon and a delayed onset in an otherwise healthy individual is extremely rare.[2]

CONCLUSION

AIHA one among the leading cause of death due to anemia, can occur at any age. But the association of AIHA secondary to SARS-CoV-2 infection is an extremely rare and unpopular phenomenon.

This case notifies the need for vast research required in considering AIHA as a sequela of SARS-CoV-2 infection.

Generally, steroids act as a first line therapy in these cases (like in the present case scenario) and warm AIHA post COVID with steroid resistance need the consideration of various treatment modalities like immunoglobulins, plasmapheresis. Relapse cases have been having some hope with rituximab therapy. More research is to be done in regard to this topic of secondary AIHA as a late onset of SARS-CoV-2, which in future can be a great matter of concern.

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