

Paediatric Autoimmune Haemolytic Anaemia Presenting with Acute Kidney Injury: A Case Report

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ABSTRACT

Autoimmune Haemolytic Anaemia (AIHA) occurs when an individual's immune system produces autoantibodies against antigens on Red Blood Cells (RBCs). It is a relatively rare haematological disease in the paediatric population. Case reports of paediatric warm AIHA are rare in general and are usually associated with other underlying conditions like haematological neoplasms, viral infections, and drug-induced conditions. This is a case report of a three-year-old male child with warm AIHA who presented with dark urine and decreased urine output for one day. Through laboratory and radiological investigations, it was found that this patient developed acute haemolysis following a bacterial lower respiratory tract infection. The patient was treated with corticosteroids, antibiotics, and Intravenous Immunoglobulins (IVIg). Peritoneal dialysis was also done. The patient was eventually discharged from the hospital on a maintenance dose of oral steroids, which was gradually tapered off. It was concluded that a bacterial lower respiratory tract infection can lead to warm AIHA in children. Even though this illness is rare, it may cause life-threatening complications if prompt treatment is delayed.

Keywords: Autoantibodies, Haemoglobinuria, Haemolysis, Lower respiratory tract infection, Renal disease

CASE REPORT

A three-year-old male child presented to the emergency department with complaints of fever for five days, which was high-grade, intermittent in nature, and acute in onset; cough for five days; difficulty in breathing for two days and dark urine with decreased urine output, having passed urine only once in the previous 24 hours. The patient initially presented to a local hospital four days after the onset of symptoms, where symptomatic treatment was given for one day, and then the patient was referred to this hospital for further management of fever, cough, dark urine, and a suspected acute kidney injury. The patient had no history of surgery, rash, blood transfusion, or bleeding in the past. There was no significant family history.

The physical examination revealed a high-grade fever of 103.2°F, severe pallor, icterus, tachycardia with a heart rate of 140/min, tachypnoea with a respiratory rate of 46/min, and bilateral lower limb pitting oedema [Table/Fig-1]. The patient had an oedema-free weight of 14.5 kg, which was assessed after the oedema was resolved. The patient had a height of 105 cm and was fairly built. There was no lymphadenopathy, rash, petechiae, or bruises noted on examination. Systemic examination revealed tender hepatomegaly and splenomegaly. The patient also had a grade 2 systolic murmur in the left second intercostal space. Respiratory system examination revealed adventitious sounds in the form of crepitations heard over the right upper zone.

Routine laboratory investigations done at the time of admission are shown in [Table/Fig-2]. Blood investigations revealed features indicating severe anaemia, including low haemoglobin, low haematocrit, and a low RBC count. Additionally, the white blood cell count was elevated beyond the normal range. Serum urea and creatinine levels were also significantly higher than normal. Serum total bilirubin was elevated along with elevated serum lactate dehydrogenase. Serological tests for malaria {Peripheral Smear for Malaria Parasite (PSMP)\Rapid Diagnostic Test (RDT)} were negative. In the Direct Antiglobulin Test (DAT), the results revealed a grade 4 reaction indicative of the presence of a significant level of antibody-coated RBCs. The Indirect Antiglobulin Test (IAT) was negative. The DAT was positive for IgG only. Warm autoantibodies were confirmed using the Antibody ID test. Clumps of normocytic normochromic



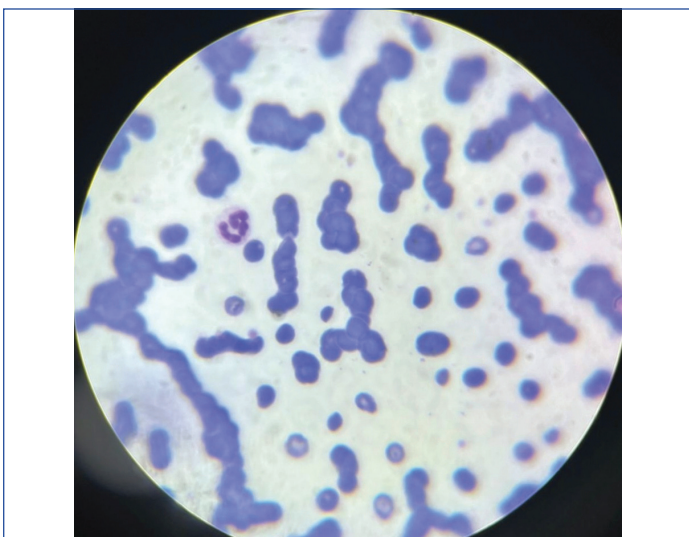
[Table/Fig-1]: Bilateral lower limb pitting oedema.

Investigation	Results (on admission)	Results (12 hours after admission)	Reference range
Haemoglobin (g/dL)	2.30	2.30	Males 13-18 Females 12-16
Haematocrit (%)	6.10	6.10	36-45
RBC count (/mm ³)	0.67×10 ⁶	0.75×10 ⁶	4×10 ⁶ -5.2×10 ⁶
Mean corpuscular volume (fl)	90.80	82.20	80-100
Mean corpuscular haemoglobin (pg)	34.50	30.20	27-32
Mean corpuscular haemoglobin concentration (g/dL)	38.00	36.70	32-36
WBC count (/mm ³)	16.24×10 ³	15.58×10 ³	4×10 ³ -11×10 ³
Platelet count	259.00×10 ³	244.00×10 ³	150.00×10 ³ -450.00×10 ³
S. Urea (mg/dL)	185.00	292.00	10-45
S. Creatinine (mg/dL)	3.17	6.80	0.6-1.4

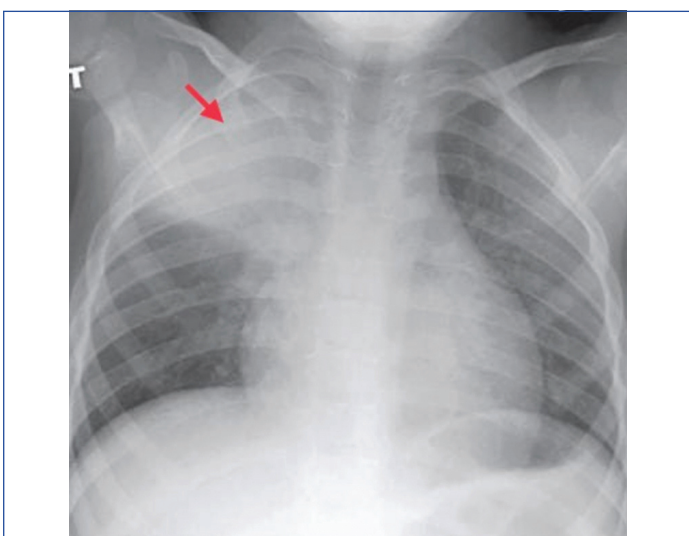
S. Total bilirubin (mg/dL)	2.48	1.98	0.2-1.2
S. Indirect bilirubin (mg/dL)	1.76	1.28	0.2-0.8
S. Direct bilirubin (mg/dL)	0.72	0.70	0-0.2
S. Sodium (Na) (mEq/L)	136.30	132.10	136-145
S. Potassium (K) (mEq/L)	5.90	5.70	3.5-5.1
S. Lactate dehydrogenase (IU/L)	1026.00	732.00	140-280

[Table/Fig-2]: Routine laboratory investigations.
RBC: Red blood cells; WBC: White blood cells; S: Serum

RBCs were seen in the peripheral blood smear [Table/Fig-3]. Rheumatoid factor and anti-nucleic acid titres were negative. Tests for Human Immunodeficiency Virus (HIV) and hepatitis also came back negative. Arterial Blood Gas Analysis (ABGA) revealed non respiratory acidosis {pH=7.359, (HCO₃)=15.0 mmol/L}. The urine analysis disclosed dark brown-coloured urine without the presence of RBCs. The patient's estimated Glomerular Filtration Rate (eGFR) was 13.7 mL/min/1.73 m². A consolidation of the right upper lobe with an air bronchogram was seen on the chest X-ray [Table/Fig-4]. Based on X-ray findings, viral and atypical pneumonia were ruled out. Clinical features along with reports were suggestive of active haemolysis, lower respiratory tract infection, and acute kidney injury.



[Table/Fig-3]: Red Blood Cells (RBCs) are seen in clumps on peripheral blood smear. (Giemsa stain, 100x oil immersion)



[Table/Fig-4]: Chest X-ray showing right upper lobe consolidation. Patient had an oedema-free weight of 14.5 kg

The patient was then admitted to the Intensive Care Unit (ICU) and started on a High-Flow Nasal Cannula (HFNC). After that, two units of IVIg were transfused, and one unit of packed red cells was transfused after cross-matching it with the patient's blood. The patient was then started on intravenous injections of meropenem

13 mg/kg/dose thrice daily and levofloxacin in the dose of 10 mg/kg/dose once daily, both given for seven days. The paediatric nephrologist's opinion was taken for decreased urine output and deranged Renal Function Tests (RFT) for which it was advised to inject furosemide in the dose of 1 mg/kg/dose twice daily and give intravenous fluids according to insensible water loss, which is 20 mg/kg/day, along with replacement of urine output. The paediatric haematologist's opinion was also sought, and it was advised to give IVIg and start systemic steroids. Pulse therapy with methylprednisolone was started with the dose of 30 mg/kg given for three days and then shifted to oral prednisolone at 2 mg/kg/day. Repeat blood investigations done after 12 hours of admission indicated deteriorating renal function with serum creatinine at 6.80 mg/dL and serum urea at 292.00 mg/dL. Also, there was no improvement in urine output noted. However, in the context of DAT, the results exhibited a reduction from grade 4 done on admission to grade 3 conducted after 48 hours of admission, indicating a noteworthy change in the level of antibody-coated RBCs. In a repeat paediatric nephrologist's opinion, peritoneal dialysis was recommended due to further worsening in RFT and urine output. After four days of renal replacement therapy in the form of peritoneal dialysis, normal renal function was restored, and the patient was voiding urine normally. After completing the course of antibiotics, the patient was discharged from the hospital on the maintenance dose of oral prednisolone. The patient was followed-up on an outpatient basis, and systemic steroids were gradually weaned off. Six months after discharge from the hospital, the patient is now clinically well with normal RFTs and without any relapse.

DISCUSSION

The development of autoantibodies by an individual's immune system against antigens on RBCs is the hallmark of AIHA [1]. It is a rare form of haemolysis in the paediatric age group. The direct Coombs test or DAT test is used to identify the antibodies [2]. The ideal temperature at which autoantibodies may bind to RBC antigens is used to classify AIHA [3,4]. In the warm-type of AIHA, IgG class antibodies are produced, which are maximally reactive at body temperature and do not require complements for agglutination. Cold AIHA is further subdivided into Cold Agglutinin Disease (CAD) and Paroxysmal Cold Haemoglobinuria (PCH) [4]. Based on the underlying aetiology, AIHA can be either primary/idiopathic or secondary [3,5].

Presenting features of patients suffering from AIHA include symptoms of haemolysis, anaemia, or symptoms of an underlying illness. In severe cases, hepatosplenomegaly and signs of heart failure are also seen [5,6]. This study reports a paediatric case of AIHA secondary to lower respiratory tract infection, possibly due to bacterial aetiology and associated with acute kidney injury. This patient had a history of fever, cough, dark urine, difficulty in breathing, and decreased urine output for 2-5 days before presenting to this hospital. Physical examination revealed findings of lower respiratory tract infection. Tender hepatosplenomegaly was suggestive of congestive cardiac failure. Blood investigation indicated findings of haemolytic anaemia with acute kidney failure. However, the most crucial step in confirmation of a diagnosis of AIHA is the DAT, which also helps in determining the type of AIHA. Warm-AIHA is mainly caused by the IgG class of autoantibodies, so if the reaction is positive with anti-IgG only, then it is typically suggestive of warm-AIHA [7]. In this patient, at the time of admission, DAT revealed a grade 4 reaction, which was indicative of the presence of a high level of antibody-coated RBCs in the patient's blood.

Warm AIHA may be primary/idiopathic-not related to an underlying cause or secondary-caused by an underlying cause. Primary warm AIHA patients make up around half of all cases, and secondary warm AIHA cases make up the other 50% [8]. The association of secondary warm AIHA includes drugs like penicillins and

chemotherapeutic agents; haematological neoplasms such as non Hodgkin's lymphoma, Chronic Lymphoblastic Leukaemia (CLL); viral infections; immune dysregulation, and a previous history of blood transfusion or transplantation [3-5,8,9]. Given the examination findings and laboratory results, it was deduced that the likely aetiology for the development of warm AIHA in this patient was due to the lower respiratory tract infection, which is rare. Through a screening rheumatologist work-up, hepatitis, and HIV, all of which were normal, other alternative causes of AIHA were ruled out. Warm IgG autoantibodies were found in this patient with a lower respiratory tract infection, which is unique. It was concluded that this patient's AIHA is most likely the result of a lower respiratory tract infection caused by bacteria.

Acute kidney injury is a well-recognised complication in haemolytic diseases, such as AIHA and Paroxysmal Nocturnal Haemoglobinuria (PNH) [10,11]. The mechanism involved is massive haemoglobinuria resulting from intravascular haemolysis, leading to acute tubular necrosis [12,13]. Haemoglobinuria is one of the main signs of excessive intravascular haemolysis. Typical laboratory findings include anaemia, increased serum lactate dehydrogenase and bilirubin, reduced serum haptoglobin and a positive urine dipstick without the presence of RBCs. In this case, laboratory results were consistent with these findings indicating a severe haemolytic reaction occurring in the patient's body.

Corticosteroids are the first-line therapy for warm AIHA. The requirement for blood transfusion depends on the severity of anaemia. When treated promptly, most AIHA patients have been reported to react favourably to steroids and have a good prognosis [9,14,15]. However, some studies have reported that regardless of good prognosis, patients may have a high probability of recurrence and serious infectious complications even after steroid therapy [15,16].

CONCLUSION(S)

This is a rare case report of warm AIHA caused by a lower respiratory tract infection and presenting with complications in the form of acute kidney injury in a paediatric patient. This case illustrates how a warm AIHA can be caused by a potential bacterial

lower respiratory tract infection. Although this illness is uncommon, it can have life-threatening consequences due to congestive cardiac failure and acute kidney injury if treatment is delayed. More research is required to establish causality.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Apr 04, 2024
- Manual Googling: Jun 03, 2024
- iThenticate Software: Jun 11, 2024 (8%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Apr 04, 2024**

Date of Peer Review: **May 30, 2024**

Date of Acceptance: **Jun 12, 2024**

Date of Publishing: **Aug 01, 2024**