CASE REPORT

Hyperleukocytosis: A Rare Manifestation of Autoimmune Hemolytic Anemia

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ABSTRACT

Autoimmune hemolytic anemia (AIHA) is described by destruction of Red Blood Cells (RBCs) as a result of binding of antibodies to red blood cell surface antigens. White blood cells are usually normal and hyperleukocytosis is rare. The most common microorganism that has been associated with these hemolytic processes is *Mycoplasma pneumoniae*. We presented a case study, a 4-year-old boy child who was diagnosed AIHA by warm antibody testing with high leukocyte count. The patient was treated with methylprednisolone, intravenous immunoglobulin and clarithromycin. During treatment, the leukocytosis became normal. The clinical condition and vital signs improved. The purpose of this study was to highlight hyperleukocytosis in AIHA caused by *Mycoplasma pneumoniae*.

Keywords: Autoimmune Hemolytic Anemia, Child, Leukocyte, Mycoplasma.

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INTRODUCTION

Autoimmune hemolytic anemia (AIHA) is rarely seen in children[1]. Warm Immunoglobulin G (IgG) or cold Immunoglobulin M (IgM) antibodies initiate RBC destruction[2]. *M. pneumoniae* commonly causes respiratory tract infection, but inducing AIHA is exceptional. White blood cells are usually normal in AIHA. Leukocytosis could mostly accompany with lymphoproliferative diseases. Even though cold agglutinins may occur in *M. pneumoniae*, hemolysis is more frequently seen with warm antibodies[3].This unusual case exhibited AIHA with severe warm antibody and excessive leukocytosis associated with a *M. pneumoniae* infection. We wanted to emphasize a rare pediatric AIHA case with high leukocyte counts without lymphoproliferative or any other hematological malignancies.

CASE PRESENTATION

The parents of a 4-year-old twin-boy rushed him to the emergency department in the middle of the night due to recent generalized fatigue, shortness of breath and occasional vomiting. His mother noticed sudden with yellow discoloration of his eyes two days ago. During his life, he grew properly, with normal development. He decreased oral intake, with occasional postprandial vomiting of gastric contents, with no other major symptoms such as cough, abdominal pain, or urinary complaints. He had no significant medical or family history, and he was not taking any medications.

On physical examination, the patient was pale appearing, fatigued, and anxious. He had a blood pressure of 116/66 mm Hg, a heart rate of 150 beats/min with a regular rhythm, a respiratory rate of 22 breaths/min, and an oxygen saturation of 96% while breathing room air. A mild bilateral conjunctival jaundice and 2cm spleen below the costal margin were noticed. At the time of his admission, laboratory tests were performed that revealed a markedly elevated WBC of 37.6×10^3 cells/µL (reference range: $4.8\text{-}10.8\times10^3$ cells/µL). In addition, with 75% neutrophils; significantly low hemoglobin level

of 5.2 g/dL (reference range: 11.5-15.5 g/dL), mean corpuscular volume (MCV) of 118 fl (reference range: 80-94 fl), reticulocyte count of 23.3% (reference range: 0.5-2.00; 8% when corrected for hematocrit). All other elements of the complete blood count were normal. An elevated lactate dehydrogenase (LDH) of 783U/L (reference range: 110-295 U/L) and indirect bilirubin of 3.81 mg/dl (reference range: 0-0.2 mg/L) were recorded. Direct antiglobulin test (DAT), direct Coombs test, for both IgG and C3d was positive. The serum level of C-reactive protein was 6.4 mg/L (reference range: <3.5 mg/L). Hemoglobinuria was determined. Viral tests (Epstein–Barr virus, adenovirus and influenza virus), hepatitis markers and antibodies to human immunodeficiency virus were all negative. The complement fixation test for *M. pneumoniae* was positive for IgM at 3.15 Index (reference range: <0.9 negative). Peripheral blood smear examination displayed polychromasia, anisocytosis, poikilocytosis, macrocytosis, neutrophils and shift to left of granulocytes. Chest X ray showed interstitial infiltrates in the middle third of right lung.

After eliminating of all other causes of autoimmunity and hemolytic anemia, leukemoid reaction due to warm type autoimmune hemolytic anemia caused by *M. pneumoniae* infection was diagnosed. The patient had tachycardia and red cell transfusion was ordered. Because of cross-match incompatible, serocompatible O Rh (-) red blood cell was transfused. No blood transfusion complication was seen. Meanwhile the leukocyte count increased on hospital day 2 and was up to 47×10^3 cells/µL. Since steroids are the first-choice treatment in all cases of warm-type AIHA[5], methylprednisolone (3 mg/kg/d) was given. Intravenous immunoglobulin and antibiotics (clarithromycin 15 mg/kg/d) were empirically initiated for suspicion of *M. pneumoniae*. Concurrent diagnosis of *M. pneumoniae* infection, clarithromycin was continued. During treatment, the leukocyte count declined to normal values after day 5. He responded to red blood cell transfusion, steroid and intravenous immunoglobulin and remained well. The hemoglobin level (Figure 1) and leukocyte count were improved.

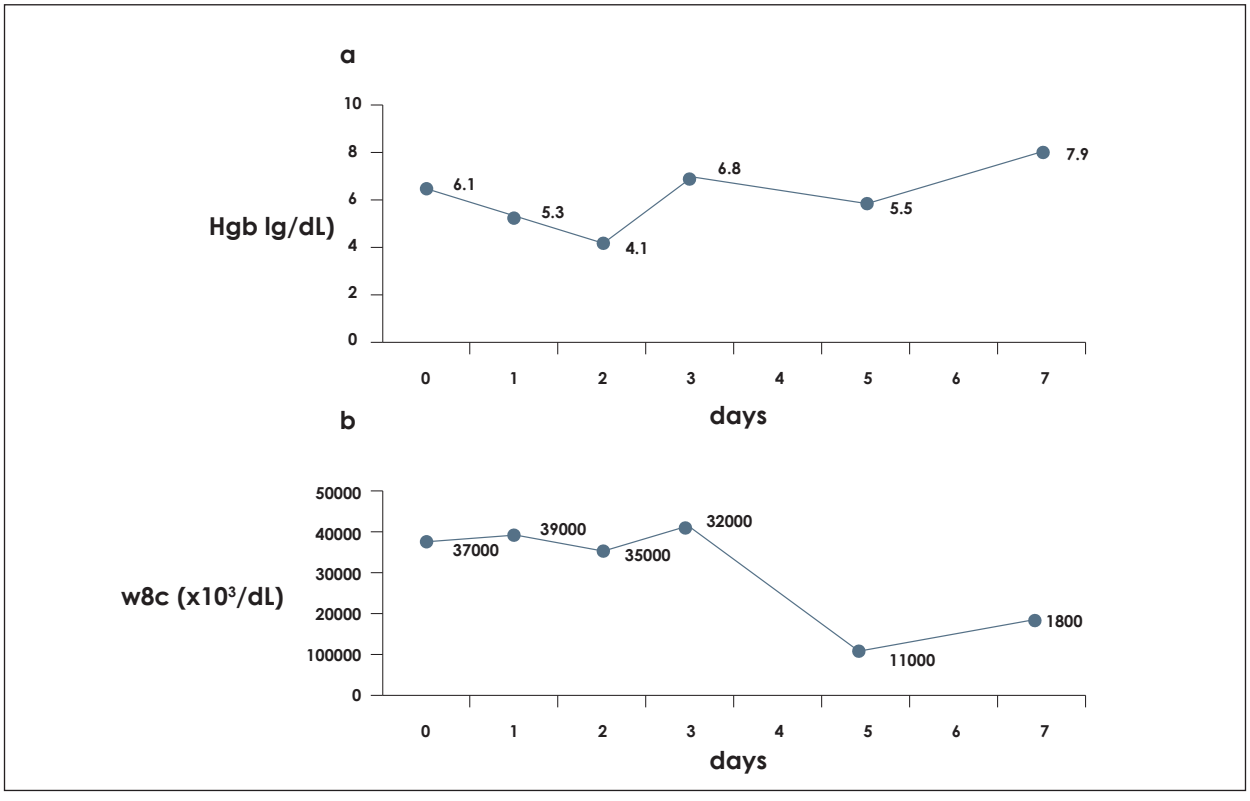

Figure 1: The hemoglobin levels and leukocyte count during hospital days.

DISCUSSION

Warm typed AIHA is mostly diagnosed after viral infection in children. Even though the significant relationship between infection and AIHA is rarely reported, *M. Pneumoniae* is the most important pathogen caused to AIHA[4]. Generally, infections in infants, immunodeficiencies and autoimmune disorders included collagen vascular disorders in adolescents are etiological factors for AIHA[5]. The incidence of warm autoimmune hemolytic anemia is significantly high in adults than that of children. In one pediatric study, the median age was 10 years, and almost two-thirds of the cases were male[6]. The largest cohort from France presented warm autoimmune hemolytic anemia in children[7]. The present

case was also a child, 4-year-old boy and serological findings showed typically warm autoimmune hemolytic anemia.

Occasionally an unusual clinical manifestation of *M. Pneumonia* presenting with extrapulmonary signs can be seen. Extrapulmonary involvement in children with *M. pneumoniae* infection is required for confirmation by clinical, laboratory and radiological data[6]. Our case had mycoplasma mediated with hemolyticanemia, presenting jaundice without respiratory symptoms. Serum test results are fundamental for rapid diagnosis in terms of early therapeutic planning in autoimmune hemolytic anemia. Therefore, the diagnosis of common and rare clinical presentations caused by *M. pneumoniae* is unavoidable.

Hemolytic anemia caused by *M. pneumoniae* associated cold antibodies is described in adults with more aggressive treatment modalities. Conversely, most of the children have had self-limited anemia and supportive care ameliorated the disease. The successful outcome of *M. pneumoniae* infection can be obtained with the defining of uncommon and severe findings, which lead to an early specific treatment at the right time. Regardless of warm or cold antibodies, steroid is a good option for the initial treatment. Frequently decreased DAT level indicates improvement of hemolysis[5]. The present patient with mycoplasma infection induced AIHA had negative DAT and presented a favorable outcome with receiving methylprednisolone, intravenous immunoglobulin and antibiotic.

Generally, thrombocyte and leukocyte counts are normal in AIHA, unless hemolysis is associated with high leukocyte count in lymphoproliferative diseases or thrombocytopenia in Evans syndrome. In one study, severe hemolytic anemia with extreme high leukocyte level was pointed in mycoplasma pneumonia. High leukocyte and platelet count may be related to thrombopoietin, which stimulates leukocyte and thrombocyteformation[8]. At the hospital admission of our case, his platelet count was normal but white blood cell count was significantly high. Hyperleukocytosis should be taken into consideration with excluding lymphoproliferative diseases in AIHA.

Finally, and importantly, an existing alloantibody could be resulted in cross-match incompatible in AIHA patients. Not only red blood cells destructed by autoantibodies but also transfusion reactions may result in hemolysis. It is important to use the same ABO and Rh group with less incompatibility for transfusion safety[9]. Our patients who had B Rh (+) blood type was not able to compatible for the same blood type transfusion and given compatible O Rh (-) red blood cell transfusion. Since cross matching can be complicated by panagglutinating warm autoantibodies, ABO group discrepancies should be resolved for correct blood typing in terms of preventing blood transfusion reactions in patients with autoimmune hemolytic anemia.

CONCLUSION

Autoimmune hemolytic anemia is an important issue for many pediatricians, who have to deal with the diagnosis and treatment of critically ill patients. We presented here a case of warm agglutinin-related severe hemolytic anemia secondary to *M. pneumoniae* infection who recovered completely after steroid, intravenous immunoglobulin and medical treatment with clarithromycin. Even though very uncommon, *M. pneumoniae* may induce the occurrence of warm agglutinins and cause immune hemolytic anemia. It is worth that multiple and atypical clinical manifestations of *M. pneumoniae* infection should be suspected, mainly in severe hemolytic anemia cases in order to start early specific therapy.

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CONFLICT OF INTEREST

No financial or non-financial benefits have been received or will be received from any party related directly or indirectly to the subject of this article.

ETHICS APPROVAL

The Ethics Committee in Health Science University, Kartal Dr. Lutfi Kirdar City Hospital, approved this study.

PATIENT CONSENT

Verbal and written informed consent was obtained from patient's family.

AUTHORS' CONTRIBUTION

SY conceived the idea, wrote the manuscript; IU, NC and ET recorded patient and obtained written informed consent. SY and ES overall supervised the project and finalized the manuscript. All authors had read and approved the content of the case report.

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