

Case Report

Mycoplasma pneumoniae-associated severe autoimmune haemolytic anaemia in children: a case report from a resource limited setting

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ABSTRACT

Mycoplasma pneumoniae is a common cause of community-acquired pneumonia and respiratory tract infection in children. While traditionally known for its respiratory manifestations, extrapulmonary manifestations of *Mycoplasma pneumoniae* infections are rare, particularly autoimmune hemolytic anemia (AIHA). Emerging evidence suggests its association with AIHA in pediatric patients, especially with severe respiratory involvement. Here, we present a case of a child with cold AIHA secondary to *Mycoplasma pneumoniae* infection without marked pulmonary manifestations, from a resource limited setting, highlighting the importance of considering atypical presentations of this pathogen in pediatric patients. Understanding this association is crucial for timely diagnosis, appropriate management, and improved outcomes in affected children.

Keywords: *Mycoplasma pneumoniae*, Autoimmune hemolytic anemia, Children, Respiratory tract infections

INTRODUCTION

Mycoplasma pneumoniae is a bacterial pathogen known to cause respiratory tract infections worldwide, particularly in children and adolescents. While its clinical manifestations typically involve the respiratory system, extrapulmonary complications can occur in 20-25% of the infected persons. This may even be present after or in the absence of pulmonary signs.¹ Autoimmune hemolytic anemia (AIHA) is a rare complication of *Mycoplasma pneumoniae* infection, especially in pediatric patients with extensive respiratory system involvement.² We present a case report of a child with *Mycoplasma pneumoniae* associated cold AIHA without pulmonary signs to increase awareness and prompt management of such an atypical presentation of a common infection.

CASE REPORT

A 3-year-old previously healthy boy with normal birth and developmental history presented with generalized

weakness and progressive paleness of the body for the last five days. One week before the day of hospitalization, there was a history of cough, runny nose, and fever, which was getting resolved after symptomatic treatment at home. On physical examination, he was febrile with an axillary temperature of 101°F and tachycardic with a heart rate of 138/min. Severe pallor and mild icterus were noted. Respiratory and other systemic examinations were unremarkable.

Laboratory investigations showed severe anemia with a hemoglobin level of 4g/dl, a total leukocyte count of 22,000/mm³, and a platelet count of 4.7 lakhs/mm³ on admission. Peripheral blood smear showed moderate anisopoikilocytosis, microcytic hypochromic red cells with macrocytes and spherocytes, and WBC showed neutrophilic leukocytosis. Total serum bilirubin level was 2.4 mg% with a direct fraction of 0.7 mg%; serum lactate dehydrogenase was > 1000 IU/l and reticulocyte count was 9% (Corrected 2.3%), suggesting the hemolytic cause of anemia. Direct antibody test (DAT) was positive

for polyspecific IgG (Figure 1). Unexpected red cell antibody test, Donath Landsteiner test, and Solid phase technique test for IgG were all negative. Since these tests other than DAT were negative, it became likely that our patient had IgG negative complement-mediated reaction, i.e., C3d positive AIHA, which is usually seen in cold AIHA type. However, it could not be directly confirmed as a complement gel card test and the cold antibody titre was unavailable intramurally and could not be performed in our set-up. Further workup with IgM *Mycoplasma pneumoniae* antibody level (ELISA) was done and found to be positive, thereby indirectly confirming cold AIHA secondary to *Mycoplasma pneumoniae* infection.

Other relevant blood parameters were normal, such as serum iron level, vitamin B12 level, coagulation profile, Glucose-6-P-Dehydrogenase levels, ANA, and Anti-ds DNA. Kidney function tests, urine analysis, and routine fever workup came within normal limits. Blood and urine cultures were also sterile.

Our patient was managed conservatively with packed red blood cell (PRBC) transfusions (10 ml/kg 2 times), injection methylprednisolone pulse therapy for 3 days, and oral azithromycin for 7 days. His clinical condition as well as laboratory parameters got improved subsequently. His Hb level increased up to 10 g/dl by day 10 of admission. The patient was discharged on oral prednisolone, which was then tapered on follow-up and stopped after a total of 4 weeks duration. Repeat DAT also became negative on follow-up. He remained asymptomatic and had been maintaining a normal Hb level with no further episodes of hemolysis on subsequent follow-ups.

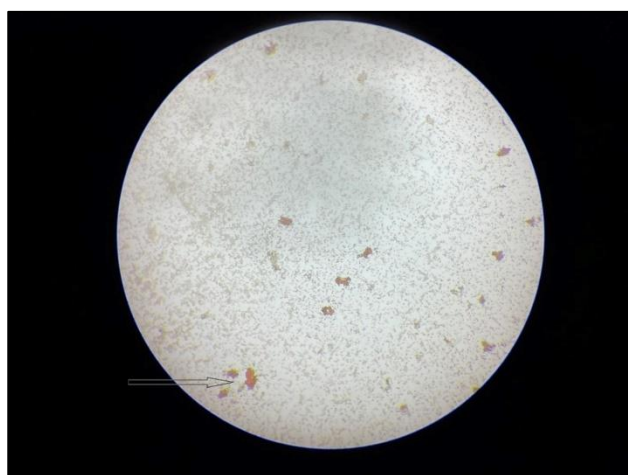


Figure 1: Light microscopic picture (10X, non-stained) showing red cell agglutination, as indicated by arrow.

DISCUSSION

Autoimmune hemolytic anemia is a group of uncommon disorders characterized by hemolysis due to autoantibodies against red blood cell surface antigens

with an approximate annual incidence of 0.81/100,000 in children.³ Warm AIHA (reactive at room temperature at 37°C) is the most common type in the pediatric population. Cold AIHA, (reactive with a temperature optimum way below the normal body temperature) accounts for only 15% of all AIHA cases, with an annual incidence of one per million. It is commonly observed with acute infections like *Mycoplasma pneumoniae* and Epstein-Barr virus.^{3,4}

Around 50-60% of *Mycoplasma pneumoniae* infections have raised cold agglutinin titers and often cause mild subclinical hemolysis, typically within the first two weeks of the onset of infection. Though the exact pathophysiology is unknown, the hypothesis accounts for the production of polyclonal cold antibodies of the IgM class as an immune response to the infection. It acts against the I antigen of the erythrocyte membrane, resulting in mild hemolysis. However, sometimes high-titre, high thermal amplitude cold antibody production can result in transient and severe hemolytic anemia. As most published cases show, marked respiratory involvement is usually noted when such severe anemia occurs.^{3,5}

Our case, however, presented with severe hemolytic anemia in the second week of *M. pneumoniae* infection in the absence of marked pulmonary manifestations. It has been reported that 75-100% of the infected patients had an intractable non-productive cough, whereas only 3-10% had pneumonia.⁶ The present case also had a cough before the onset of anemia, but there was no remarkable examination and imaging findings of the chest. Contrary to the usual peak incidence of the infection in the school-age group, our patient was a three-year-old boy suggesting that it is not so uncommon in children below 5 years of age.¹

Serology or polymerase chain reaction gene amplification technique usually confirms the diagnosis of the *M. pneumoniae* infection.⁵ In our patient, diagnosis of AIHA secondary to *M. pneumoniae* infection was based on a positive Coomb test in the presence of anti-mycoplasma antibody as cold agglutinin titer and thermal amplitude testing are unavailable in low-resource settings like ours. The case also had neutrophilic leucocytosis and normal platelet counts, as seen in *M. pneumoniae* infection.¹

Hemolytic anemia secondary to *M. pneumoniae* associated cold antibodies in adults often requires a more aggressive therapeutic approach. On the contrary, pediatric patients usually recover with conservative management as seen in the literature. As Gertz discussed, packed red cell transfusion should be limited, but sometimes needed as a life-saving measure in cases of severe anemia. Our case with severe anemia also received two units (10 ml/kg) of PRBC. Oral azithromycin was also given after the final diagnosis to treat the underlying infection. Antibiotics, though of limited use, have been associated with the speedy resolution of hemolysis.⁷

Use of corticosteroids, intravenous immunoglobulin, plasmapheresis, and cytotoxic drugs is still doubtful and reserved for refractory cases.⁵ In our patient, the steroid was given in concern of ongoing severe autoimmune hemolysis and the patient responded well.

CONCLUSION

Mycoplasma pneumoniae infection can present with rare extrapulmonary manifestations, such as autoimmune hemolytic anemia, particularly in pediatric patients, even in the absence of marked respiratory involvement. There should be a high index of suspicion for such atypical presentations of a common infection, especially in unexplained severe hemolytic anemia. The prognosis is generally favourable if timely intervention is made. Increased awareness of this rare complication can facilitate prompt recognition and management.

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