Hemolytic Anemia following Mycoplasma Infection
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Citation

Abstract
This is a case report of a 60 year old male with hemolytic anemia secondary to Mycoplasma Pneumoniae pneumonia. He was severely anemic without any respiratory symptoms. His Coombs test was positive for complement (C3). He was transfused blood and investigated for his anemia. He had a raised antibody titer for Mycoplasma. He was treated for his anemia with blood and packed cells along with Prednisolone and Erythromycin for his pneumonia.

INTRODUCTION
Acquired hemolytic anemia may be due to immune or non-immune causes (1). Immune destruction of red blood cell may be due to autoantibodies, alloan antibodies, hemolytic disease of the newborn or drug induced antibodies.

These anemia are characterized by the presence of a positive Direct Antiglobulin Test (DAT) or Coombs test (a test used to red blood cell antibodies. Can be used to detect Rh antibodies and screen for autoimmune hemolytic anemia and determine blood compatibility. Also called Direct Antiglobulin Test (DAT)), which detects the antibodies and complements on the surface of patients' red blood cells (1). Autoimmune hemolytic anemia are divided into ‘warm’ or ‘cold’ types, depending on whether the antibody attaches better to the red blood cells at body temperature (37°C) or at lower temperatures.

Warm autoimmune hemolytic anemia can present as short episodes of anemia, jaundice or may progress to an intermittent chronic pattern. Spleen may become enlarged. These anemia may be associated with lymphoid malignancies or diseases such as Rheumatoid Arthritis, Systemic Lupus Erythematosus or drugs. Antibodies usually are IgG (1).

Cold autoimmune hemolytic anemia are due to antibodies, which attach to red blood cells at lower temperatures and produce complement mediated intravascular hemolysis (1, 7, 11). Low titers of IgM cold agglutinins reacting at 4°C are normally present in serum and are harmless (1). After certain infections (e.g. Mycoplasma, Cytomegalovirus, EB Virus) or Protozoa (e.g. Malaria, Trypanosomiasis) there is an increased synthesis of polyclonal cold agglutinins with a higher thermal range, which may produce transient, mild to moderate hemolysis (10, 13). Direct activation of an immunologic effect such as histiocyte/T lymphocyte-mediated immunosuppression may result in destructive effect of M. pneumoniae (10).

CASE REPORT
A 60 year old male presented with the complaint of off and on precordial pain, radiating to neck for 3 days. He had no past history of hypertension, ischemic heart disease or diabetes mellitus. His blood pressure was 110/70 mmHg., heart rate 120/min and temperature 37.2°C. His EKG and X-ray chest were within normal limits. He looked anemic and icteric. His lab reports showed Hemoglobin (Hb) only 5.6 gm/dl. and Hometocrit 14%. His blood film showed Anisocytosis with Spherocytes positive. His white cell count was 18,800/µl showing reactive leucocytosis. His blood urea was 93 mg/dl and unconjugated bilirubin 8.28 mg/dl, ALT 8 u/l, AST 160 u/l and Alkaline Phosphate 190 u/l. His urine analysis showed positive for albumin, RBC's and pus cells along with their casts. His ultra sound abdomen was within normal limits. He looked anemic and icteric. His lab reports showed Hemoglobin (Hb) only 5.6 gm/dl. and Hometocrit 14%. His blood film showed Anisocytosis with Spherocytes positive. His white cell count was 18,800/µl showing reactive leucocytosis. His blood urea was 93 mg/dl and unconjugated bilirubin 8.28 mg/dl, ALT 8 u/l, AST 160 u/l and Alkaline Phosphate 190 u/l. His urine analysis showed positive for albumin, RBC's and pus cells along with their casts. His ultra sound abdomen was within normal limits except an enlarged prostate consistent with benign prostate hypertrophy. His cold agglutinin blood test was positive along with direct Coombs test for C3. His bleeding time, clotting time, Prothrombin time and Platelet count were in normal range. His Hb remained 5.5 gm/dl. and
his blood urea raised to 252 mg/dl after he was transfused a pint of blood on the next day. But his unconjugated bilirubin decreased to 1.21 mg/dl. He was transfused another 4 pints of blood in the next few days and he responded well. His Hb raised to 8.2 gm/dl and Hematocrit 25%. He was investigated for his hemolytic anemia. There was no drug history. G6PD deficiency was not found. He showed raised titer of anti-I autoantibodies up to 1: 128. He was given Erythromycin along with Prednisilone, and transfused another few pints of blood and packed cells. His Hb became 10.2 gm/dl, blood urea 55 mg/dl and bilirubin within normal range after 10 days of therapy. All his symptoms subsided except for some urinary complaints due to his enlarged prostate and G.I. upsets because of oral steroids.

This patient was diagnosed as a case of cold autoimmune hemolytic anemia with Mycoplasma antibodies positive. He may had Mycoplasma infection leading to formation of cold autoantibodies, most probably IgM type on red blood cells, leading to their destruction and causing anemia (1). He showed positive Coombs test for C3 and a raised antibody titer (IgM) for Mycoplasma pneumoniae. His entire lab investigations and symptoms correlated with the above diagnosis and he was transfused blood to correct his anemia (2). He was treated for his Mycoplasma infection with Erythromycin and Prednisilone to prevent production of red blood cell antibodies and destruction of antibody coated cells (2).

**DISCUSSION**

Mycoplasma Pneumonia is more common in young with scanty pulmonary signs. The extra-pulmonary consequences of Mycoplasma Pneumonia sometimes dominate and remain unexplained (1, 2, 11). Autoimmune reactions may have a role in the pathogenesis of extra-pulmonary complications which may appear before, during, after or in the absence of chest signs as in this case (12). A number of hematological complications are associated with Mycoplasma pneumonia like hemolytic anemia, thrombocytopenia and thrombotic thrombocytopenic purpura (10, 12). Hepatitis, central and peripheral nervous system disease, myocarditis, pericarditis, arthritis and erythema multiforme are some of the other extra-pulmonary complications of Mycoplasma Pneumonia.

Diagnosis of autoimmune hemolytic anemia is usually made on evidence for the cause of hemolysis. Spherocytosis is present as a result of red cell damage. Coombs test is positive with antibody or complement found on the surface of red blood cells. Red blood cells agglutinate in the cold or in the extremities where the temperature is slightly cooler leading to complement-mediated hemolysis (1). In case of cold hemolytic anemia, antibodies are usually IgM that attaches complement on the surface of the erythrocyte, while in case of warm hemolytic anemia they are usually IgG (13). The cold antibodies are also induced by other infectious agents like Epstein-Barr virus, Cytomegalovirus and Klebsiella Pneumonia but certain cold antibody specificities are associated with each infectious agent (3). The presence of anti-I and Sia-b1 autoantibodies have been specified to the M. pneumoniae infection (9). These antibodies are produced not only to lung, but also to brain, smooth muscle and RBCs by Mycoplasma infections (11).

Even though the presence of cold agglutinins is common but excessive hemolysis is very rare in Mycoplasma Pneumonia (9). Hemolysis is usually reported with severe respiratory involvement but the case we reported did not show the signs of respiratory infection. On the other hand the antibody level against Mycoplasma was high, suggesting activation of the immune system. The leucocyte count is usually normal or slightly high in Mycoplasma infections but previous reports of M. pneumoniae with hemolytic anemia showed leucocytosis as we reported (9). The disparity is unidentified but leucocytosis in Mycoplasma Pneumonia may be an indication of the presence of hemolytic anemia (11).

The principle for treatment is to cure the underlying cause if possible. Transfuse blood to make up for the loss of red blood cells. Patients should avoid exposure to cold atmosphere (1). Corticosteroids are effective in inducing a remission in about 80% of patients in case of autoimmune hemolytic anemia (1, 2, 9, 11). Splenectomy may be necessary if there is no response to steroids or if the remission is not maintained when the dose of Prednisilone is reduced. Immunosuppressive drugs such as Azathioprine and Cyclophosphamide may be effective (2).

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**References**

1. A test used to red blood cell antibodies. Can be used to detect Rh antibodies and screen for autoimmune hemolytic anemias and determine blood compatibility. Also called Direct Antiglobulin Test (DAT).

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