Digital Journal of Clinical Medicine

Volume 6 | Issue 3 Article 9

2024

A Rare Case of Cold Agglutination Syndrome Secondary to Mycoplasma pneumoniae

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Recommended Citation
Shahri D, M DK, Chethan D, Vijayakumar D, B.S. D. A Rare Case of Cold Agglutination Syndrome Secondary to Mycoplasma pneumoniae. *Digital Journal of Clinical Medicine*. 2024; 6(3): -. doi: https://doi.org/10.55691/2582-3868.1207

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Abstract

Mycoplasma pneumoniae (M. pneumoniae) is one of the foremost causes of community acquired pneumonia. Most of the cases are, however mild. Although, complications may seldom occur. One such known complication of M. pneumoniae infection is cold agglutinin hemolysis, which is usually benign and transient. This hemolysis is due to formation of cold agglutinins during the course of infection. Cold Agglutination Syndrome (CAS) is a type of acquired Autoimmune Hemolytic Anaemia (AIHA), which exists due to an underlying disorder, like a viral illness or lymohoid malignancy. It is generally self-remitting, in contrast to Cold Agglutination Disease (CAD), which is a chronic disorder. The antibody implicated in CAS is IgM. Here, we present a case of a young female, presenting with acute and severe hemolysis secondary to M. pneumoniae.

Keywords

Autoimmune hemolytic anemia, Cold agglutinin syndrome, Mycoplasma pneumoniae

A Rare Case of Cold Agglutination Syndrome Secondary to Mycoplasma pneumoniae

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Word Count: 1216

Conflict of interest: None

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Abstract

Mycoplasma pneumoniae (M. pneumoniae) is one of the foremost causes of community acquired pneumonia. Most of the cases are, however mild. Although, complications may seldom occur. One such known complication of M. pneumoniae infection is cold agglutinin hemolysis, which is usually benign and transient. This hemolysis is due to formation of cold agglutinins during the course of infection. Cold Agglutination Syndrome (CAS) is a type of acquired Autoimmune Hemolytic Anaemia (AIHA), which exists due to an underlying disorder, like a viral illness or lymohoid malignancy. It is generally self-remitting, in contrast to Cold Agglutination Disease (CAD), which is a chronic disorder. The antibody implicated in CAS is IgM. Here, we present a case of a young female, presenting with acute and severe hemolysis secondary to M. pneumoniae.

Introduction

M. pneumonia is a small bacterium, lacking a cell wall and is a frequent respiratory tract pathogen. Infections with M. pneumoniae are frequent, but mild generally not requiring antimicrobial therapy and hospitalization. Severe pneumonia, although uncommon, is observed. M. pneumoniae also has a variety of extra-pulmonary manifestations which include, but are not limited to skin rashes, encephalitis, myocarditis and hemolysis. It can also cause kidney injury, mainly as glomerulonephritis. These extra-pulmonary manifestations are seen in as many as 25% of the affected individuals.[1,2] Here, we present a case of severe hemolysis, secondary to M. pneumoniae infection in a young patient.

Case Discussion

An 18-year-old female presented to the outpatient department with the complaints of easy fatiguability and swelling of both lower limbs for the past week. She also gave history of fall following giddiness, without loss of consciousness. There was history of fever 2 days prior to presentation, which was intermittent and moderate grade, which subsided on its own without any medications. She did not complain of chest pain, palpitations, orthopnea, yellowish discolouration of eyes, frothy urine, decreased urine output or rashes. The patient, however gave history of pain in the small joints of both hands.

She was born out of a non-consanguineous marriage and was the eldest among two siblings. There was no history of similar complaints in the siblings and she had no history of receiving blood transfusions in the past.

On examination, she had a pulse rate of 112/min, which was regular in rhythm, low volume and blood pressure was 110/70 mm of Hg. At the time of examination, she was afebrile. Severe pallor was noted. Cardiovascular assessment revealed an ejection systolic murmur in the pulmonary area. Rest of the clinical examination was unremarkable.

Routine laboratory investigations were sought. Complete hemogram showed presence of agglutination of RBCs which were normocytic, normochromic with polychromatophils and

spherocytes. Few nucleated RBCs were also noted. This picture was suggestive of autoimmune hemolytic anaemia, cold agglutinin disease. Hemoglobin was 5g/dl with normal platelets and total counts. Reticulocyte proliferation index was >2. Renal function was normal. LFT showed mild hyperbilirubinaemia (1.59mg/dl). Direct coomb's test was positive (4+) and serum levels of LDH were elevated. Urine routine was within normal limits. Ultrasonography of the abdomen and pelvis showed splenomegaly, which was not clinically palpable. In order to work up for the cause of hemolysis, a monospecific DAT was performed which was positive for C3d and negative for IgG. Complement C3 and C4 levels were low indicating complement activation. A diagnosis of cold autoimmune hemolytic anaemia was made and secondary causes were looked into. Serology was sent for HIV, Hepatitis B and Hepatitis C, which came negative. Chronic lymphocytic leukemia was ruled out because of young age of patient and absence of B symptoms. An ANA by immunofluorescence was negative. EBV IgM was sent which was negative. Mycoplasma IgM tested positive. Mycoplasma pneumoniae was considered as the cause of cold agglutination.

Management

The patient was treated appropriately with antibiotics and steroid therapy was initiated. The patient was given Tab. Azithromycin 500mg once a day for a duration of 5 days and a pulse dose of Inj. Methyl Prednisolone 1mg/kg was given for 3 days. Since there was no significant improvement in hemoglobin levels, along with an oral tapering dose of steroids, the patient was also started on Tab. Azathioprine 50mg after completion of pulse therapy. A repeat evaluation done a week later revealed a substantial improvement in the general condition of the patient and correction of the hemoglobin levels.

Discussion

M. pneumoniae commonly causes some degree of hemolysis, which is usually mild. M. pneumoniae associated hemolysis is due to cold agglutinin antibodies which react against I antigen, which is a carbohydrate antigen seen on erythrocytes as well as epithelial cells lining the respiratory tract.[1] The formation of these antibodies is triggered by interaction of the bacteria with the antigen in the respiratory epithelium.[3] Binding of these antibodies in triggered by lower temperatures and hence is seen as complement mediated hemolysis.[4] Most case of M. pneumoniae show mild or subclinical hemolysis, which can be demonstrated by elevated reticulocyte levels.[5] Severe hemolysis is rarely seen. Reasons for severe hemolysis and high levels of antibodies remain unknown. Mainstay of treatment is keeping the patient warm.[1] Other modalities which can be used, but have no established benefits include glucocorticoids, which are one of the primary drugs used in warm autoimmune hemolytic anaemia.[6] In our patient, administration of pulse dose of glucocorticoids did not yield satisfactory results. Antibiotics are recommended but have a limited role. In theory, antibiotics can cause faster clearance of pathogen from blood stream and hence inhibit production of antigens causing agglutination, leading to a more rapid resolution of the hemolytic process.[1] Other agents which can be used are Rituximab, Azathioprine and interferon. Plasmapheresis may be tried, but has a doubtful role. [7] Newer drugs include B-cell

receptor inhibitors and proteosome inhibitors. Warmed blood may be transfused, depending on the degree of the anaemia.

Conclusion

In conclusion, M. pneumoniae should be suspected as a cause for acute presentations of hemolytic anaemia. It may present with complications involving other organ systems as well, like, encephalitis, myocarditis and glomerulonephritis. Management includes warming of the patient, blood transfusions and antibiotics. Glucocorticoids, cytotoxic drugs and plasmapheresis have a questionable role, but may be tried in refractory cases.

Acknowledgement

I wish to thank Dr. Srinath K.M. for this opportunity as well as the Department of General Medicine, JSS AHER.

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