

Metformin Induced Hemolytic Anemia-a case report

¹Dr Prakhar Garg, ²Dr Surender Mittal, ³Dr G.N Saxena

Department of Medicine, MGUMST-Jaipur, Rajasthan

I. Introduction

Metformin is a widely prescribed antidiabetic drug that has been implicated as a cause of hemolytic anemia. We report a case of hemolysis that was associated with initiation of metformin as treatment for diabetes.

II. Case presentation

A 54 year old male with type 2 diabetes mellitus was started on metformin to improve glycemic control, shortly after 7 days patient experienced easy fatigability & developed jaundice. There was no history of fever, any other drug ingestion, alcohol intake, liver disease or blood transfusion. Clinically he had pallor and scleral icterus. No other clinical abnormality was seen. Laboratory studies showed severe hemolysis with a fall in Hb from 13.8 to 5.4 gm/dl over 4 days, markedly elevated LDH, bilirubin and reticulocyte counts and a low haptoglobin level. A direct coombs test was positive for anti Ig G and negative for anti C3. A peripheral blood film showed no schistocytes, the glucose-6-phosphate dehydrogenase level was within normal range. Despite corticosteroid treatment, patient showed no improvement and further decline in hemoglobin to 3.3g/dl was noted.

III. Discussion

Anemia may occur as either a direct result of leukemia or a side effect of chemotherapy. Drug-induced immune hemolytic anemia (DIHA) is a rare condition. The most common causative agents are antibiotics, especially second- and third-generation cephalosporins. Although our patient received several drugs including L-asparaginase and prednisone with metformin, hemolysis ceased shortly after discontinuation of metformin. Therefore, the hemolytic reaction was considered to be due to metformin. DIHA can be attributed to many different mechanisms. Some drugs bind covalently to proteins on the RBC membrane. Hemolytic reaction in vivo is dependent on the presence of the drug and ceases shortly after discontinuation. The other and most controversial DIHA mechanism is immune complex reaction, in which antibodies formed to combined RBC membrane proteins and drugs often activate the complement, leading to acute intravascular hemolysis. DIHA can also be associated with drug-independent antibodies. Such antibodies do not need the drug to be present to obtain in vitro reactions. In these cases, the drug affects the immune system, causing production of RBC autoantibodies. Although antibodies against the drug could not be demonstrated, based on the negative Coombs test with complement and no persistence of hemolysis after the discontinuation of metformin, we suppose that the hemolysis was a drug-dependent reaction.

IV. Conclusion

The serologic finding, in this case suggest autoimmune hemolytic anemia, caused either by drug induced auto anti body or a warm auto antibody. We proposed that metformin induced hemolysis with a drug induced auto antibody is a strong possibility physicians should be aware of potential side effect of metformin although it is infrequent.