

Undetectable Glycosylated Hemoglobin in Autoimmune Hemolytic Anemia

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Abstract We encountered two cases of autoimmune hemolytic anemia (AIHA) with undetectable glycosylated hemoglobin (HbA1C) level at diagnosis. Hemolytic anemia improved by administration of prednisolone (PSL) and HbA1C became measurable after response.

Key words: autoimmune hemolytic anemia, glycosylated hemoglobin

Introduction

HbA1C is formed by the non-enzymatic glycation of the N-terminus of beta-chain hemoglobin A. In the control of diabetes mellitus, the glycosylated hemoglobin (gHb, HbA1C) is measured by cation-exchange chromatography or immunoassay.¹⁾ HbA1C reflects the mean daily blood glucose concentration over the preceding two to three months. However, sometimes, the discrepancy between the measured blood sugar and HbA1C levels is observed; in hemoglobinopathies, hemolytic anemia, iron deficiency anemia, liver cirrhosis (hypersplenism), blood transfusion and uremia, giving falsely low or high HbA1C levels.¹⁻³⁾ We encountered two cases of autoimmune hemolytic anemia (AIHA) whereby the levels of HbA1C were below detectable at presentation and they became measurable after anemia improved responding to the administration of prednisolone.

Case report

The first patient was a 55-year old woman

(Fig. 1). The patient had not history of diabetes mellitus, or had not received corticosteroid. At presentation, Hb was 6.1g/dl with spherocytosis and reticulocytosis of 13%, Coombs test, direct and indirect, was positive, haptoglobin was decreased and screening for hemoglobinopathy was negative. The patient also suffered from arteriosclerosis obliterans (ASO) of the right leg. At that time, fasting blood sugar was normal, but HbA1C measured by immunoassay was below the detectable level (<1.5%) (normal value, 4.3-5.8%). Glycosylated albumin was not measured in this patient. Autoimmune hemolytic anemia (AIHA) was diagnosed. Anemia rapidly improved and reticulocyte count dropped responding to the administration of prednisolone (PSL) of 30mg/day, and HbA1C became measurable at 6.1%.

The second patient was a 87-year old woman (Fig. 2). She was diagnosed with diabetes mellitus 4 years ago when fasting blood sugar was 248mg/dl, HbA1C was 5.8% and Hb was 13.4g/dl, and had been treated with oral anti-diabetic agents. However, recently Hb decreased to 6.8g/dl with spherocytosis and

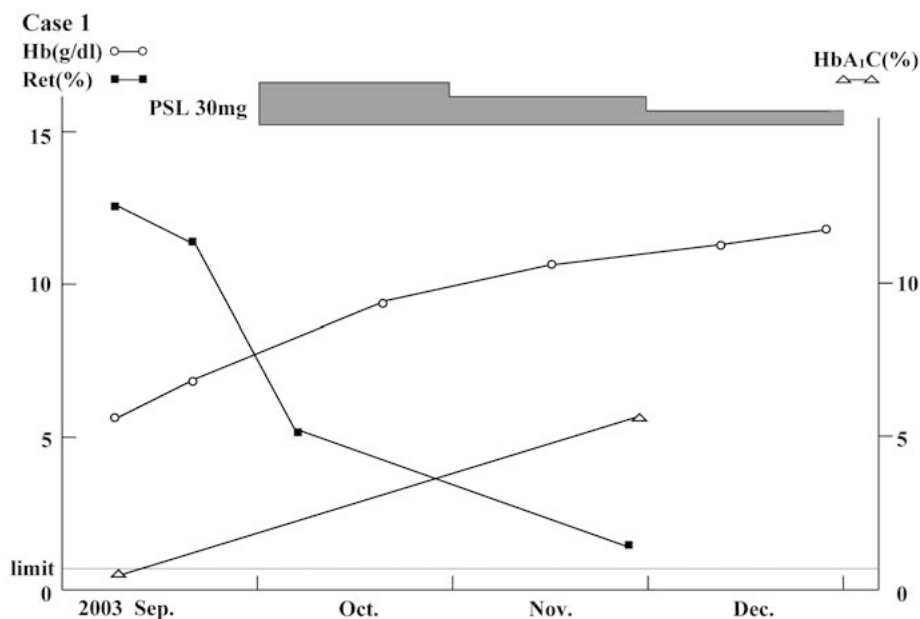


Fig. 1 Clinical course of the first patient.

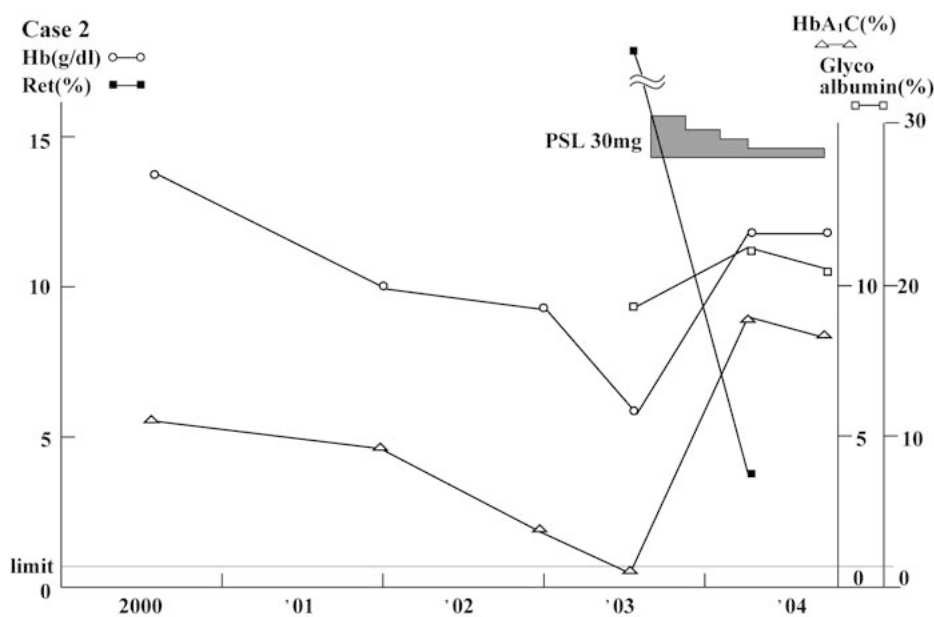


Fig. 2 Clinical course of the second patient.

reticulocytosis of 26%. Direct Coombs test was negative and indirect test was positive, haptoglobin was decreased and screening for hemoglobinopathy was negative. At that time, HbA₁C measured by immunoassay was below the detectable level, but glycosylated albumin was elevated to 20.7% (normal value 12.4-16.3%). Coombs-negative AIHA was diagnosed. The findings of the other autoimmune disorders were not observed. Anemia improved rapidly and reticulocyte count drop-

ed responding to the administration of prednisolone of 30mg/day, and Hb A₁C became measurable at 7.9%.

Discussion

Abnormal hemoglobinopathies, including variant hemoglobins, sickle cell disease, homozygous HbC disease, HbSC disease, and β -thalassemia, frequently show the abnormal chromatographic elution pattern or increased

amounts of minor Hb species, i.e., HbA2 and HbF, which interfere with some glycosylated hemoglobin measurement methods.¹⁾ The other interfering condition is uremia, whereby chemically modified carbamylated Hb has an isoelectric point similar to HbA1C resulting in falsely high HbA1C level by chromatographic method.¹⁾

The premature destruction of red cells as in autoimmune hemolytic anemia and hereditary spherocytosis with the consequence of shortened red cell life span results in a concomitant decrease in the exposure time of hemoglobin to glucose, leading to a low percentage of HbA1C.¹⁻³⁾ However, the cases with undetectable HbA1C levels as in our patients had been rarely reported, suggesting the extremely shortened and rapid turnover of red cells as evidenced with severe anemia and high reticulocyte count in our patients.

Measurement of glycosylated albumin or fructosamine has been favored over HbA1C in hemolytic anemias and hemoglobinopathies, since they are not affected by hemoglobin variants or increased RBC turnover rate.¹⁾³⁾

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