Case Reports

G-6-PD Deficiency-Induced Hemolysis in Diabetic Twins

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We report hemolysis due to glucose-6-phosphate dehydrogenase (G-6-PD) deficiency in two Egyptian monozygotic brothers, at the onset of diabetes type 1. Hemolysis occurred following the treatment of hyperglycemia and ketoacidosis (one twin). It was related to unknown G-6-PD deficiency. The fall in glucose availability after the treatment of hyperglycemia is proposed as a possible etiology for hemolysis.

Key words: *Glucose-6-phosphate dehydrogenase deficiency, Hemolysis, IgA, Type 1 diabetes.*

Type 1 diabetes mellitus is characterized by insulin deficiency resulting from immune-mediated pancreatic beta-cell destruction. It has been reported that the incidence of childhood type 1 diabetes mellitus has increased in recent years(1). Glucose-6-phosphate dehydrogenase (G-6-PD) is a cytoplasmic enzyme expressed in all tissues, that is essential for a cell's capacity to withstand oxidant stress. G-6-PD deficiency is the commonest enzymopathy of humans, affecting over 400million people worldwide and is one of the important causes of hemolytic anemia and neonatal jaundice(2,3). Blood glucose normalization-induced hemolysis in three adolescents with type 1 diabetes mellitus at onset associated with unknown G-6-PD deficiency has been reported(4). We report the occurrence of hemolysis due to G-6-PD deficiency in a pair of male twins following the control of hyperglycemia in DKA.

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Case Report

Case record: Twin 1

A 4-year-old boy was hospitalized in May 2002 for severe ketoacidosis (*Table I*). Two days after rehydration and treatment with continuous i.v. insulin infusion (0.05-0.1 IU/kg BW/h) ketoacidosis remission was easily obtained. He then received subcutaneous intensive insulin injection therapy (1.0 IU/kg BW/24-h: three regular times before meals and one intermediate before bedtime). Euglycemia was attained within 4 days with blood glucose concentrations ranging from 105-165 mg/dL. On day 7 he developed jaundice and pallor. Hematological evaluation at that time showed the following: hemoglobin level (Hb) 10.3 g/dL, reticulocytes 10%, direct bilirubin 1.77 mg/dL, increased urobilinogen in urine. The diagnosis of hemolytic anemia was considered. Causes for hemolytic anemia such as hereditary hemoglobinopathies, hereditary spherocytosis and autoimmune hemolytic anemia–due to drugs or infection–were excluded (normal Hb electrophoresis, normal red blood cell resistance, negative Coombs reaction and

TABLE I– *Hematological and Biochemical Findings on Admission.*

	Twin 1	Twin 2
Hb (g/dL)	13.4	12.5
WBCs	11300/mm^3	10400/mm^3
Glucose (mg/dL)	510	325
pH	7.1	7.2
HCO_3 (mEq/L)	3	20.5
Glucosuria	+ + + + +	+ + +
Ketonuria	+ + + +	+ +
CRP	< 0.35 mg/dL	< 0.35 mg/dL
IgG (mg/mL)	8.3	8.7
IgA (mg/mL)	1.3	0.26
IgM (mg/mL)	0.82	0.85

absence of cryoimmunoglobulins in the blood). Hemolytic anemia was due to G-6-PD deficiency (0 IU/101[2] erythrocytes, Sigma enzymatic quantitative method, normal values140-370). Hemolysis ceased spontaneously and hemoglobin increased gradually over next 3 weeks.

Case record: Twin 2

The twin brother of the patient above was hospitalized on the same admission day for polyuria. Hematological and biochemical examination on admission are shown in *Table I*. He received a 48 h subcutaneous intensive insulin injection therapy (1.0 IU/kg BW/ 24-h: three regular times before meals and one intermediate before bedtime). This was followed by subcutaneous 12 hourly injections of mixed insulin (regular and intermediate) at the same dose as above. Blood glucose concentrations became normal by the 4th day and ranged between 85 and 145 mg/dL. On the 7th day he also developed jaundice and pallor. Hematological assessment diagnosed hemolysis: Hb 8.1 g/dL, reticulocytes 12%, direct bilirubin 5.5 mg/dL. Causes for hemolytic anemia such as hereditary hemoglobinopathies, hereditary spherocytosis and autoimmune hemolytic anemia–due to drugs or infection–were excluded (normal Hb electrophoresis, normal red blood cell resistance, negative Coombs reaction and absence of cryoimmunoglobulins in the blood). Hemolytic anemia was due to G-6-PD deficiency. Hemolysis ceased spontaneously and hemoglobin increased gradually.

Discussion

The most interesting point in this report is the fact that both twins developed diabetes mellitus type 1 concurrently, and also the fact that they both had G-6-PD deficiency and developed a hemolytic syndrome. The concurrent manifestation of diabetes mellitus type 1 in these twins implies that the prenatal or early postnatal period during which the twins were exposed to the same environment may have played an important role in addition to their being genetically identical(5). A higher prevalence of G-6-PD deficiency is reported in patients with diabetes mellitus type 1 than in healthy population(6). An explanation has been put forward to explain why patients with diabetes type 1, who are more likely to have G-6-PD deficiency, are, therefore, prone to develop hemolysis under certain conditions, such as drug administration, food (fava beans), toxic agents (naphthalene) or infections. However, during the hemolytic episode, neither of the twins was exposed to any of the above agents. Hemolysis due to G-6-PD deficiency has been reported in patients with diabetes type 1 having hyperglycemia or hypoglycemia(7). Ketoacidosis as a cause of hemolysis in these patients is controversial(8). A report from Alexandria(8) supports the concept that the Mediterranean type variant of G-6-PD deficiency may be complicated by hemolysis in diabetes mellitus type 1. Hemolysis appeared when hyperglycemia

was corrected and relative euglycemia was obtained. It was speculated that the blood glucose normalization in diabetes induced a stressing glucose deprivation for the energy dependent functions of red blood cells similar to that which results from repeated episodes of hyperglycemia(8). There is a similarity of the hemolytic syndrome noticed by these twin brothers at the onset of diabetes mellitus type 1 to that reported in three Italian adolescents(4). There have been very few reports in the literature. It is a rare manifestation even in areas in which diabetes and G-6-PD deficiency are common such as Sardinia(4,9). The Mediterranean type variant of G-6-PD deficiency may be complicated by hemolytic crises in diabetes type 1 regardless of the severity of ketoacidosis. In conclusion, hemolysis may be attributed to relative hypoglycemia during hyperglycemia correction. G-6-PD should be assessed in diabetic type 1 patients and in case of deficiency one should be less aggressive in treating hyperglycemia to avoid rapidly induced euglycemia, which may cause hemolysis in these patients. If hemolysis does occur, however, the patient recovers spontaneously.

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