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Case Report

Hemolysis During Diabetic Ketoacidosis Revealing Glucose-6-Phosphate Dehydrogenase Deficiency in New-Onset Type 1 Diabetes Mellitus: A Case Report

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Abstract

Background: Type 1 diabetes mellitus (T1DM) frequently presents in childhood with diabetic ketoacidosis (DKA), a potentially life-threatening complication. Hemolysis during DKA treatment is uncommon but may indicate an underlying condition such as glucose-6-phosphate dehydrogenase (G6PD) deficiency—a genetic enzymatic disorder that predisposes red blood cells to oxidative stress.

Case presentation: We report the case of a previously healthy 16-year-old male from Curaçao who presented with a one-week history of malaise, vomiting, polydipsia, polyuria, weight loss, and hematuria. He exhibited severe dehydration and Kussmaul respiration. Laboratory findings revealed marked hyperglycemia (394.5 mg/dL), severe metabolic acidosis and ketonuria, consistent with a diagnosis of new-onset T1DM with severe DKA. He was admitted to the Pediatric Intensive Care Unit and managed with intravenous fluids and insulin. Within 24 hours, ketosis had resolved, allowing transition to a subcutaneous insulin regimen (Degludec and Aspart). During admission, he developed progressive jaundice with laboratory findings of unconjugated hyperbilirubinemia, falling hemoglobin levels, and positive hemolysis markers. G6PD deficiency was confirmed through additional testing.

Conclusion: This case highlights the importance of considering G6PD deficiency in pediatric patients with DKA who develop unexplained hemolysis or jaundice. Early recognition can help guide supportive care and avoid exposure to oxidative triggers during diabetes management.

Keywords: *Type 1 Diabetes Mellitus, Glucose-6-Phosphate Dehydrogenase Deficiency, Diabetes Ketoacidosis, Hemolysis.*

Introduction

Type 1 diabetes mellitus (T1DM) is a prevalent autoimmune endocrinopathy in children and adolescents, often presenting with diabetic ketoacidosis (DKA) as an acute and potentially life-threatening metabolic complication (2,10). While the proportion of newly diagnosed patients presenting with DKA generally ranges from 30% to 40%, some cohorts report rates up to 47%, highlighting its ongoing clinical relevance.

Glucose-6-phosphate dehydrogenase (G6PD) deficiency, an X-linked enzymopathy and the most common human enzyme defect, affects an estimated 400 million individuals worldwide, particularly among populations in Africa, the Mediterranean region, the Middle East, and Asia (5).

Although most affected individuals remain asymptomatic, exposure to oxidative stressors—such as infections, certain medications, metabolic derangements including DKA, or rapid correction of hyperglycemia—can precipitate acute hemolytic anemia (5).

Although coexistence of T1DM and G6PD deficiency is rare, case reports describe hemolysis emerging during treatment or recovery, even in the absence of DKA (2,6). For example, Onyiriuka et al. reported a Nigerian adolescent with newly diagnosed T1DM who developed hemoglobinuria secondary to unrecognized G6PD deficiency despite no evidence of ketoacidosis (6). Similarly, pediatric patients have been described to develop delayed hemolysis following initiation of insulin therapy, coinciding with normalization of blood glucose levels (2). In adult populations, DKA has also been reported to unmask latent G6PD deficiency, with hemolysis typically occurring several days after metabolic stabilization (4).

Although the exact pathophysiological mechanisms remain incompletely understood, chronic hyperglycemia has been hypothesized to transiently increase G6PD activity, thereby masking enzymatic deficiency. Subsequent rapid metabolic correction may reduce the availability of nicotinamide adenine dinucleotide phosphate (NADPH), impairing erythrocyte antioxidant defense and predisposing to oxidative hemolysis (4, 7, 8).

We present a 16-year-old adolescent male with new-onset T1DM and DKA who developed hemolysis due to previously unrecognized G6PD deficiency during treatment. The diagnosis was confirmed according to established criteria, including quantitative measurement of enzyme activity below the reference range and assessment of the G6PD-to-pyruvate kinase ratio.

Case Presentation

We describe the case of a 16-year-old male from Curaçao who presented with a one-week history of generalized malaise, persistent vomiting, polydipsia, polyuria, unintended weight loss, and visible hematuria. He had no significant past medical history and was not taking any regular medications. He is the oldest child of non-consanguineous parents of Antillean descent, with no known family history of type 1 diabetes mellitus, hemolytic disorders, or other relevant medical conditions.

On physical examination, the patient was markedly dehydrated and exhibited Kussmaul respirations. Initial laboratory investigations revealed a significantly elevated blood glucose level of 394.5 mg/dL. Venous blood gas analysis demonstrated severe metabolic acidosis with a pH of 6.97 (reference: 7.35–7.45), bicarbonate of 5.5 mmol/L (reference: 22–28 mmol/L), and a base deficit of –25 mmol/L (reference: –3 to +3 mmol/L). Urinalysis showed high levels of ketones. These findings were consistent with a diagnosis of new-onset diabetes mellitus (DM) presenting with severe diabetic ketoacidosis (DKA). Type 1 diabetes mellitus (DMT1) was later confirmed by the presence of glutamic acid decarboxylase (GAD) antibodies.

The patient was admitted to the Pediatric Intensive Care Unit (PICU), where he received intravenous fluid resuscitation and insulin therapy. Within 24 hours of admission, ketonemia had nearly resolved, allowing a transition to subcutaneous insulin therapy. He was initiated on a basal-bolus regimen consisting of insulin Degludec (Tresiba) and rapid-acting insulin Aspart (Novorapid). Although glucose levels initially remained elevated, they subsequently stabilized under this regimen.

The patient presented with progressive jaundice. Laboratory tests revealed isolated unconjugated hyperbilirubinemia (total bilirubin 120 µmol/L), declining hemoglobin, and evidence of hemolysis. G6PD deficiency was confirmed, with enzyme levels of 0.6 and 0.5 U/g Hb, and G6PD-to-pyruvate kinase ratios of 0.04 and 0.03, supporting the diagnosis.

Table 1. Comparison of Published Case Reports: Type 1 Diabetes Mellitus and G6PD Deficiency.

Authors / Year	Age / Gender	Nationality	Presentation	G6PD Status	Hemolysis Trigger	Notes
Onyiriuka et al., 2021	16 y/o male	Nigeria	New-onset T1DM without DKA, hemoglobinuria	Confirmed	Initial hyperglycemia (not DKA)	First presentation of diabetes; hematuria noted
Govindarajan et al., 2022	10 y/o male	Iraq	New-onset T1DM, without DKA, jaundice during follow-up	Genetically confirmed	Subsequent to diagnosis	Mutation confirmed via gene sequencing
Acta Endocrinologica, 2023	15 y/o male	Unspecified	New-onset T1DM without DKA, developed hemolytic anemia	Confirmed	Insulin therapy and glucose normalization	Osmolality stable
Orman et al., 2023	Not specified	Turkey	New-onset T1DM, hemolytic anemia post glucose correction	Genetic variant identified	Rapid glucose correction	Genetic mutation: c.653C>T (p.Ser218Phe)
Allied Academies, 2015	10 y/o female	Unspecified	Moderate DKA, hemolysis, hemoglobinuria	Double heterozygous mutation	DKA and treatment	Mutations: c.1376G>T and c.1388G>A
Alzaki & Alalawi, 2019	17 y/o male	Bahrain	T1DM with DKA, hemolysis and methemoglobinemia	Confirmed	DKA-related oxidative stress	Methemoglobin 8.1%

Discussion

This case highlights the rare but clinically significant coexistence of type 1 diabetes mellitus (T1DM) and glucose-6-phosphate dehydrogenase (G6PD) deficiency in an adolescent male, with hemolysis occurring during the acute management of diabetic ketoacidosis (DKA). Although DKA is a common initial manifestation of T1DM, the development of acute hemolysis during or shortly after metabolic correction is uncommon and should prompt evaluation for underlying red blood cell enzymopathies such as G6PD deficiency.

G6PD plays a crucial role in maintaining erythrocyte redox homeostasis through the generation of nicotinamide adenine dinucleotide phosphate in its reduced form (NADPH), which is required to preserve glutathione in its reduced state. In G6PD-deficient individuals, impaired NADPH production limits the ability of erythrocytes to neutralize reactive oxygen species, rendering them highly susceptible to oxidative injury, membrane instability, and premature destruction.

The pathophysiological relationship between DKA treatment and hemolysis in G6PD deficiency remains incompletely understood; however, several mechanisms have been proposed. Chronic hyperglycemia has been suggested to transiently increase G6PD activity, potentially masking clinical manifestations of the deficiency. During DKA management, rapid normalization of blood glucose levels and metabolic shifts induced by insulin therapy may lead to a relative decline in functional antioxidant capacity within erythrocytes. This reduction in redox buffering may precipitate oxidative damage, particularly in the context of systemic inflammation, acidosis, and increased production of reactive oxygen species characteristic of DKA.

Furthermore, metabolic acidosis and osmotic stress may contribute to erythrocyte membrane fragility, amplifying the risk of hemolysis in susceptible patients. The combination of oxidative imbalance, abrupt metabolic correction, and underlying enzymatic vulnerability may therefore explain the temporal association between DKA treatment and hemolytic episodes observed in this and previously reported cases (9).

Our patient's clinical course is consistent with prior reported cases in which hemolysis did not occur at presentation but rather during the recovery phase of diabetic ketoacidosis (DKA). This delayed hemolytic manifestation highlights the importance of close monitoring during metabolic correction, particularly in populations with a high prevalence of glucose-6-phosphate dehydrogenase (G6PD) deficiency, including individuals of African, Mediterranean, or Caribbean ancestry. In this case, G6PD deficiency was only identified after the onset of visible hematuria, jaundice, and laboratory evidence of hemolysis, underscoring the need to consider this diagnosis early when unexplained hematologic abnormalities arise during DKA management.

Several case reports support a temporal association between metabolic stabilization in DKA and hemolysis in previously unrecognized G6PD-deficient patients. In these reports, hemolytic episodes were observed following insulin therapy and normalization of hyperglycemia, suggesting that rapid metabolic shifts may unmask an underlying impairment in erythrocyte antioxidant defense. Systemic inflammation, oxidative stress, osmotic changes, and metabolic acidosis associated with DKA further contribute to erythrocyte membrane instability, promoting hemolysis in vulnerable individuals. Although insulin therapy and intravenous fluids are not direct hemolytic triggers, the profound biochemical and oxidative changes accompanying DKA resolution may precipitate red blood cell destruction in patients with enzymatic defects.

Early recognition of G6PD deficiency facilitates appropriate monitoring, avoidance of additional oxidative stressors, and timely diagnostic confirmation. Notably, G6PD deficiency is highly prevalent in Latin America and the Caribbean. Despite this, few case reports have described patients from this region. To our knowledge, this is the first reported case of an association between G6PD deficiency and DKA-related hemolysis, despite the high prevalence of the deficiency in Latin America and the Caribbean, emphasizing the need for increased awareness of this condition in clinical practice in the region. (2,6).

Conclusion

This case highlights the rare but clinically relevant coexistence of glucose-6-phosphate dehydrogenase (G6PD) deficiency and newly diagnosed type 1 diabetes mellitus presenting with diabetic ketoacidosis, in which hemolysis developed during metabolic recovery. It emphasizes the importance of maintaining clinical vigilance for hemolytic complications in patients undergoing treatment for DKA, particularly in populations with a higher prevalence of G6PD deficiency. Early recognition of this association may facilitate timely diagnostic evaluation, appropriate monitoring, and avoidance of additional oxidative stressors, ultimately improving patient outcomes. Greater awareness of this potential complication may also support consideration of targeted screening strategies in selected high-risk clinical settings.

Conflict of Interest

The authors declare there is no conflict of interest.

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None.

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