Case Report

A Case Report of Thiamine-responsive Megaloblastic Anemia Misdiagnosis in a Male Child With Diabetic Ketoacidosis and Glucose-6-phosphate Dehydrogenase Deficiency

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ABSTRACT

Background: Type 1 diabetes mellitus (T1DM) is one of the most common chronic diseases in childhood and may present acutely with diabetic ketoacidosis (DKA). Since both infection and DKA can trigger anemia in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency, failure to properly evaluate such anemia may lead to diagnostic confusion with other conditions such as thiamine-responsive megaloblastic anemia (TRMA). This study reported a case of TRMA misdiagnosis in a male child with DKA and G6PD deficiency.

Case Presentation: The case was a 5-year-old boy admitted to the emergency department of a hospital in Bushehr, south of Iran, with lethargy, polydipsia, polyuria, and Kussmaul breathing. Based on laboratory findings (pH=7.12, HCO_3^-=2, blood glucose=738 mg/dL), he was diagnosed with DKA, and treatment with insulin and intravenous fluids was initiated. Due to the presence of fever, abnormal lung findings on examination, and chest X-ray results, antibiotic therapy was also started for presumed pneumonia. One week after discharge, during outpatient follow-up, macrocytic anemia was diagnosed (Hb=6.8, MCV=95). Given the type of anemia in a diabetic child, a diagnosis of TRMA was made, and treatment with thiamine (100 mg twice daily) was initiated, and insulin was discontinued. As this decision coincided with the honeymoon phase of T1DM, the child remained stable for a few weeks. However, after exiting the honeymoon phase, he was readmitted with another episode of DKA. Further clinical assessment and detailed history revealed that the diagnosis of TRMA was incorrect, and the anemia was actually due to hemolysis associated with G6PD deficiency (favism), triggered by the initial DKA episode.

Conclusions: This case report highlights the importance of considering a broad differential diagnosis for anemia in children with diabetes. The overlapping clinical features of G6PD deficiency and TRMA, particularly in the context of DKA and the honeymoon phase of diabetes, can lead to misdiagnosis and inappropriate management. Careful follow-up, comprehensive hematologic evaluation, and consideration of genetic backgrounds are essential for accurate diagnosis and effective treatment planning.

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Introduction

Type 1 diabetes mellitus (T1DM) is one of the most common chronic diseases in childhood, resulting from autoimmune destruction of pancreatic β-cells, leading to reduced or absent insulin secretion. The classical triad of diabetes symptoms includes polyuria, polydipsia, and polyphagia [1, 2]. In addition to clinical findings, specialized laboratory tests also play an important role in confirming the diagnosis of T1DM. Among the most significant evaluations are diabetes-related autoantibodies, such as anti–glutamic acid decarboxylase (GAD) and islet cell antibodies (ICA), which are recognized as key markers of pancreatic autoimmunity [3]. According to studies, diabetic ketoacidosis (DKA), a life-threatening medical emergency, may be the initial presentation in 15-80% of children with newly diagnosed T1DM [4-6]. During the treatment of DKA, blood glucose control in some patients, especially those with glucose-6-phosphate dehydrogenase (G6PD) deficiency, can predispose to hemolytic anemia. G6PD deficiency is the most common enzymatic disorder in humans, which increases red blood cell susceptibility to oxidative stress and may lead to premature hemolysis in situations such as DKA correction [4, 7]. However, most individuals with G6PD deficiency remain asymptomatic until exposed to triggering factors such as fava bean (Broad Bean) ingestion, certain medications, severe infections, renal failure, or DKA [8].

On the other hand, the co-occurrence of macrocytic anemia and diabetes may raise suspicion for thiamine-responsive megaloblastic anemia (TRMA), a rare genetic disorder caused by mutations in the *SLC19A2* gene and characterized by the classic triad of megaloblastic anemia, diabetes mellitus, and progressive sensorineural hearing loss [9, 10]. This diagnosis may appear more plausible when a patient enters the honeymoon phase of T1DM, during which insulin requirements decrease. This phenomenon might be misinterpreted as a favorable response to thiamine therapy [9, 11]. Discontinuation of insulin therapy in such cases may lead to recurrence of DKA symptoms, including polyuria, polydipsia, weight loss, fatigue, and respiratory distress [2, 12]. In this study, we report a rare case of a child with newly diagnosed T1DM presenting with DKA who developed anemia due to G6PD deficiency-induced hemolysis but was initially misdiagnosed with TRMA and managed accordingly, eventually leading to the recurrence of DKA symptoms and re-hospitalization.

Case Presentation

The case was a 5-year, 2-month, and 9-day-old boy who was admitted to a hospital in Bushehr, south of Iran, with symptoms of fever, Kussmaul respirations, weakness, lethargy, fatigue, anorexia, polydipsia, polyuria, nausea, vomiting, abdominal pain, decreased level of consciousness, and moderate dehydration. Approximately five days before admission, he had developed fever and cough in the context of an upper respiratory tract infection, during which he was twice evaluated by physicians and treated with intravenous fluids and medications. However, symptoms such as anorexia, polydipsia, and polyuria had been present a few weeks earlier. At the time of admission, the child was toxic and presented with respiratory distress. On lung auscultation, wheezing and crackles were heard, particularly in the right lung.

Patient background

He was the second child in the family, with a birth weight of approximately 3800 grams. His growth and developmental indicators were within normal limits. There was no prior history of hospitalization, medication use, or surgical procedures. In the neonatal period, he had prolonged jaundice, which, although potentially indicative of G6PD deficiency (favism), had not been investigated at the time. His older sibling (16 years old) was healthy with only a history of febrile seizures. Their parents were distantly related. There was no family history of diabetes mellitus, but maternal relatives had a history of thyroid disorders.

First hospital admission

Upon admission to the hospital, the patient was diagnosed with DKA based on clinical findings and laboratory results (Tables 1, 2 and 3). Treatment was promptly initiated, including fluid therapy that started with a bolus of normal saline (20 cc/kg over the first hour), followed by half-normal saline (0.45% NaCl), calculated based on maintenance requirements and a 10% dehydration correction. Regular insulin infusion was started at a dose of 0.1 unit/kg/hr. Supportive care and monitoring of electrolytes, serum composition, and insulin dose adjustments were made according to laboratory parameters and clinical evolution (Table 1). Given the history of fever, intravenous antibiotic therapy (ceftriaxone at 75 mg/kg/day divided into two doses) was administered. Due to a decreased level of consciousness at the 18th hour of hospitalization, cerebral edema was suspected, and the patient received two doses of intravenous mannitol at 1 g/kg. On the second day of hospitalization, he was referred to another hospital in Bushehr.

Table 1. Laboratory results at the time of admission to the first hospital

Test	Day 1	Normal Range
WBC diff (10^3/µL)	14.3	4-10
Neut (%)	83.3	-
Lymph (%)	11.2	25-65
RBC (10^6/µL)	5.39	4.6-4.8
Hb (g/dL)	14.2	13-18
HCT (%)	41.7	42-49
MCV (fL)	77.4	80-96
MCH (pg)	26.3	26-33
MCHC (g/dL)	34.1	30-36
Plat (10^3/µL)	245	139-450
ESR-1 hr (mm/h)	7	0-10
AST (IU/L)	19	<38
ALT (IU/L)	17	<41
ALP (IU/L)	569	180-1200
BUN (mg/dL)	21	5-20
Cr (mg/dL)	1.16	0.6-1.4
Na (mEq/L)	130	136-143
K (mEq/L)	5.8	3.8-4.9
BS (mg/dL)	738	<140

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Abbreviations: WBC diff: White blood cell differential; Neut%: Neutrophil%; Lymph%: Lymphocyte%; RBC: Red blood cell; Hb: Hemoglobin; HCT: Hematocrit; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; Plat: Platelet; ESR-1 hr: Erythrocyte sedimentation rate in 1 hour; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; BUN: Blood urea nitrogen; Cr: Creatinine; Na: Sodium; K: Potassium; BS: Blood sugar.

First admission to the referred hospital

On the second day of treatment, the patient was transferred to the referred hospital. Upon admission, the patient's vital signs were as follows: Blood pressure: 90/60 mm Hg, pulse rate: 117 bpm, respiratory rate: 28 breaths/min, temperature: 38.5 °C, blood sugar: 263 mg/dL, pH: 7.218, HCO_3^-: 11.6 mmol/L, PCO_2: 28.2 mm Hg. The patient was alert, with a body weight of 14 kg at arrival.

In the emergency department, clinical and laboratory findings (Table 4) confirmed a diagnosis of new-onset T1DM. Given the fever, abnormal lung examination findings, and chest radiography, pneumonia was also diagnosed. Accordingly, in addition to intravenous ceftriaxone, clindamycin was initiated, along with supportive treatments including normal saline infusion, Apotel, 3% NaCl nebulization, and Ventolin nebulization. DKA management was continued until resolution of the acute phase. Upon completion of DKA treatment, subcutaneous insulin therapy with Novorapid and Lantus was initiated. During hospitalization, the patient received ongoing supportive care, including nebulized therapy, intravenous fluids, and antibiotic therapy. Capillary blood glucose was monitored before and two hours after each meal, and insulin doses were adjusted accordingly to maintain glycemic control. With clinical improvement and resolution of pneumo-

Table 2. Urinalysis results at the time of admission to the first hospital

Color	Yellow
Appearance	Semi clear
PH	Acid
Specific gravity	1.034
Protein	Positive (+)
Glucose	Positive (+++)
Keton	Positive (+++)
Blood	Negative
Nitrite	Negative
Urobilinogen	Normal
Bilirubin	Negative
WBC/h.p.f	0–1
RBC/h.p.f	1–2
Ep cells/h.p.f	0–1
Bacteria	Negative
Mucus	Negative
Crystals	Negative
Casts/h.p.f	Granular=25-30

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Abbreviations: PH: Potential hydrogen; Ep: Epithelial; h.p.f: High power field; WBC: White blood cell; RBC: Red blood cell.

nia, clindamycin was discontinued on day 5, and ceftriaxone was stopped on day 6 of hospitalization. Finally, on day 6, the patient was discharged in good overall condition, with outpatient follow-up. Before discharge, the patient's parents received comprehensive education on insulin administration and home blood glucose monitoring.

Table 3. VBG results related to DKA diagnosis

Test	1st Hospital Admission	1st Admission to the Referred Hospital	2nd Admission to the Referred Hospital
PH	7.407 → 7.126	7.218	7.393 → 7.238
PCO_2 (mm Hg)	17.6 → 18.7	28.2	35.1 → 28.7
PO_2 (mm Hg)	37.7 → 20.8	36.2	34.0 → 52.4
BE (mmol/L)	-	-	-3.4 → -13.8
BEecf (mmol/L)	-13 → -23.6	-16.4	-4.2 → -15.4
$H3O_3$(mmol/L)	2 → 11.9	11.6	20.7 → 11.9

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Abbreviations: VBG: Venous blood gas; PH: Potential of hydrogen; PCO_2: Partial pressure of carbon dioxide; PO_2: Partial pressure of oxygen; BE: Base excess; BEecf: Base excess in extracellular fluid; HCO_3: Bicarbonate.

Diagnosis of thiamine-responsive megaloblastic anemia after discharge

Approximately one week after discharge, the patient was referred to the hospital for follow-up of blood glucose levels. Given the acceptable glycemic profile and several episodes of hypoglycemia in the preceding days, insulin dosage was reduced under the assumption that the patient had entered the honeymoon phase of T1DM. During the clinical evaluation, the child appeared significantly weak, pale, and lethargic, with impaired mobility due to profound fatigue. Consequently, a new set of laboratory tests was ordered (Table 5). The results showed a hemoglobin level of 8.6 g/dL, red blood cell (RBC) count of 4.2 million/µL, and mean corpuscular volume (MCV) of 95 fL. Because of the anemia, a hematology consultation was requested for further diagnostic evaluation. According to the results of the requested laboratory tests (Table 5) and considering the presence of macrocytic anemia concurrently with diabetes, the possibility of TRMA was considered as the initial diagnosis. Accordingly, treatment with oral thiamine (100 mg twice daily) and folic acid (5 mg once daily) was initiated. At the same time, insulin therapy was discontinued, coinciding with the beginning of the honeymoon phase of T1DM, a period during which insulin requirements temporarily decline, and normoglycemia may be maintained without insulin. Reassured by the new diagnosis, the child's family decided to discontinue insulin therapy and cease diabetes-related follow-up. This continued until the child exited the honeymoon phase, at which point hyperglycemia recurred, and he was readmitted to the referred hospital with a second episode of DKA.

Table 4. Laboratory results at the time of first admission to the referred hospital

Test	Unit	Day 1	Normal Range
WBC diff	(10^3/µL)	8.9	4.8-10.8
Neut%	(%)	70.1	-
Lymph%	(%)	24.7	20-40
RBC	(10^6/µL)	3.98	4.5-6.5
Hb	(g/dL)	0.1	13.5-18
HCT	(%)	29.3	31-41
MCV	(fL)	73.6	81-98
MCH	(pg)	25.1	27-32
MCHC	(g/dL)	34.1	32-36
Plat	(10^3/µL)	114	150-450
ESR	(mm/h)	14	0-15
CRP	(mg/L)	0.1	0-10
BUN	(mg/dL)	8.3	6-23
Cr	(mg/dL)	0.48	0.6-1.4
Na	(mEq/L)	138	136-145
K	(mEq/L)	4	3.5-5.5
BS	(mg/dL)	263	<140

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Abbreviations: WBC diff: White blood cell differential; Neut%: Neutrophil%; Lymph%: Lymphocyte%; RBC: Red blood cell; Hb: Hemoglobin; HCT: Hematocrit; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; Plat: Platelet; ESR-1 hr: Erythrocyte sedimentation rate in 1 hour; CRP: C-reactive protein; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; BUN: Blood urea nitrogen; Cr: Creatinine; Na: Sodium; K: Potassium; BS: Blood sugar.

Table 5. Follow-up laboratory results after discharge

Test	7 Days After Discharge	10 Days After Discharge	2 Months After Discharge
WBC (10^3/µL)	9.4	6.8	6.11
RBC (10^6/µL)	2.4	2.74	4.76
Hb (g/dL)	6.8	7.5	12.8
HCT (%)	22.9	25.9	38.7
MCV (fL)	95	94.5	81.3
MCH (Pg)	28	27.4	26.9
MCHC (g/dL)	30	29	33.1
Plat (10^3/µL)	438	303	256
RDW-CV (%)	16.7	21.4	14.5
MPV (fL)	-	8.9	11.3
Reticulocytes (%)	-	9.6	-
G6PD (qualitative)	-	Severely deficient	-
Hb-A1c (%)	6.4	4.5	6.4
IgA (mg/dL)	159	-	-
Anti-tissue transglutaminase Ab (IgA) (U/mL)	1.89	-	-
FBS (mg/dL)	67	-	114
BS 2 hr-PP (mg/dL)	69	110	105
Total Bilirubin (mg/dL)	-	0.89	-
Direct bilirubin (mg/dL)	-	0.28	-
Indirect bilirubin (mg/dL)	-	0.6	-
LDH (U/L)	-	427	-
ESR-1 h (mm/h)	-	53	-
CRP quantitive	-	10.3	-
Hb A (%)	-	97.3	-
Hb A2 (%)	-	2.7	-
TSH (mIU/L)	2	2.81	-
Ferritin (ng/mL)	116.12	132	-
Vitamin D3 (25-OH) (ng/mL)	22.86	-	-
Ca (mg/dL)	9.2	-	-
P (mg/dL)	5.5	-	-
Folic acid (ng/mL)	-	9.15	-
Vitamin B12 (pg/mL)	-	574.6	-

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Abbreviations: RDW-CV: Red cell distribution width – coefficient of variation; MPV: Mean platelet volume; G6PD: Glucose-6-phosphate dehydrogenase; Hb-A1c: Hemoglobin A1c; IgA: Immunoglobulin A; Ab: Antibody; FBS: Fasting blood sugar; BS 2 hr-PP: Blood sugar 2 hours postprandial; LDH: Lactate dehydrogenase; Hb A: Hemoglobin A; Hb A2: Hemoglobin A2; TSH: Thyroid stimulating hormone; Ca: Calcium; P: Phosphate.

Table 6. Laboratory results at the time of second admission to the referred hospital

Test	Day 1	Normal Range
WBC diff (10^3/µL)	6.1	4.8-10.8
Neut (%)	52	-
Lymph (%)	42.6	20-40
RBC (10^6/µL)	4.75	4.5-6.5
Hb (g/dL)	12.1	13.5-18
HCT (%)	37.6	31-41
MCV (fL)	79.2	81-98
MCH (pg)	25.5	27-32
MCHC (g/dL)	32.2	32-36
Plat (10^3/µL)	255	150-450
ESR (m.m/h)	4	0-15
CRP (mg/L)	0.15	0-10
AST (IU/L)	22	2-37
ALT (IU/L)	39	2-41
ALP (IU/L)	526	180-1200
BUN (mg/dL)	12.5	6-23
Cr (mg/dL)	0.53	0.6-1.4
Na (mEq/L)	140 → 139 → 135	136-145
K (mEq/L)	4.1 → 4.1 → 4.6	3.5-5.5
BS (mg/dL)	352	<140

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Abbreviations: WBC diff: White blood cell differential; Neut%: Neutrophil%; Lymph%: Lymphocyte%; RBC: Red blood cell; Hb: Hemoglobin; HCT: Hematocrit; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; Plat: Platelet; ESR-1 hr: Erythrocyte sedimentation rate in 1 hour; CRP: C-reactive protein; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; BUN: Blood urea nitrogen; Cr: Creatinine; Na: Sodium; K: Potassium; BS: Blood sugar.

Second admission to the referred hospital

Three months after the initial diagnosis of T1DM, the patient was readmitted to the referred hospital with symptoms of fatigue, lethargy, constipation, polyuria, and polydipsia. At the time of admission, his vital signs were as follows: Blood pressure: 95/55 mm Hg, pulse rate: 103 bpm, respiratory rate: 20 breaths/min, temperature: 37.2 °C. A home blood glucose measurement prior to admission was 320 mg/dL. The patient was alert and weighed 13.5 kg upon arrival. Based on laboratory findings (Hb: 12.1 g/dL, blood sugar: 352 mg/dL, pH: 7.238, HCO_3^-: 11.9 mmol/L, PCO_2: 28.7 mm Hg), a second diagnosis of DKA was established (Tables 3, 6 and 7), and the standard treatment for DKA was initiated.

During hospitalization and further investigations, it was determined that the previous diagnosis of TRMA was incorrect, and the patient's anemia was actually related to G6PD deficiency. Consequently, treatment with thiamine was discontinued, and insulin therapy was restarted. The patient was discharged after clinical stabilization, with an appropriate diet and insulin treatment plan. At discharge, subcutaneous insulin therapy with Lantus and Novorapid was reinitiated, thiamine tablets were discontinued, and folic acid (5 mg once daily) was

Table 7. Urinalysis results at the time of second admission to the referred hospital

Color	Yellow
Appearance	Clear
PH	Acid
Specific gravity	1.02
Protein	Positive (trace)
Glucose	Positive (++)
Keton	Positive (++)
Blood	Positive (trace)
Nitrite	Negative
Bilirubin	Negative
WBC/h.p.f	1-3
RBC/h.p.f	0-1
Ep Cells/h.p.f	0-1
Bacteria	Negative
Mucus	Negative
Crystals	Negative
Casts/h.p.f	Granular cast: 2-4

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Abbreviations: PH: Potential hydrogen; Ep: Epithelial; h.p.f: High power field; WBC: White blood cell; RBC: Red blood cell.

continued. The family was advised to strictly avoid fava beans and foods high in vitamin C, to limit prolonged physical activity, and to ensure adequate intake of iron, folic acid, and foods rich in vitamin E and selenium. They were also instructed to avoid medications such as aspirin and ciprofloxacin. Most importantly, the family was strongly advised to inform the healthcare team of the patient's G6PD deficiency (favism) before initiating any medical intervention.

Follow-up

The latest follow-up was conducted when the patient was 5 years and 6 months old, approximately four months after the initial diagnosis of T1DM. At this time, the patient had appropriate weight gain, reaching 18 kilograms. Blood glucose levels were well controlled, and HbA1c was within the acceptable range. The patient showed no signs of anemia, and the CBC revealed normal parameters related to anemia, as shown in Table 8. Currently, the patient is in stable condition and continues to receive regular insulin therapy.

Discussion

In this study, we presented a 5-year-old child with T1DM and G6PD deficiency who developed DKA and hemolysis during treatment. Insulin-dependent T1DM is the most common form of diabetes in children, and up to 40% of cases may initially present with DKA. This condition often results from a lack of attention to classic diabetes symptoms [2, 5, 6, 13, 14]. According to the European Society for Pediatric Endocrinology and the Lawson Wilkins Pediatric Endocrine Society (ESPE/LWPES) consensus statement, hyperglycemia (blood sugar ≥200 mg/dL) in the presence of metabolic acidosis (pH <7.3, HCO_3 <18) and moderate to severe ketonemia or ketonuria are biochemical criteria for diagnosing DKA. Clinical manifestations include dehydration, Kussmaul respiration, weakness, lethargy, decreased consciousness level, and in severe cases, coma. Predisposing factors include delayed diagnosis, resulting in late initiation of treatment, as well as the presence of concurrent infections. A history of recent febrile illness or common cold has been reported to be associated with approximately

Table 8. Laboratory results 4 months after diagnosis of diabetes

Test	Result	Normal Range
WBC (10^3/µL)	7.47	4-11
RBC (10^6/µL)	4.6	4.3-5.5
Hb (g/dL)	12.1	11.4-14.5
HCT (%)	36.3	33-43.5
MCV (fL)	78.1	80-100
MCH (pg)	26	26-34
MCHC (g/dL)	33.2	30-36
Plat (10^3/µL)	285	140-450
RDW-CV (%)	12.9	11.6-14.5
MPV (fL)	10.7	7-11
Hb-A1c (%)	7.6	Normal: <5.7 Diabetic: ≥6.5
FBS (mg/dL)	213	70-100
Anti-tissue transglutaminase Ab (IgA) (U/mL)	9.7	Normal: <20 U/mL Elevated: >20 U/mL
T4 (µg/dL)	7.76	5.1-14.1
AST (IU/L)	20	>52
ALT (IU/L)	11	>39
TSH (mIU/L)	3.58	0.5-6.6
Ferritin (ng/mL)	57.77	30-400
Vitamin D3 (25-OH) (ng/mL)	23.9	Insufficient: 20-29 Sufficient: 30-100

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Abbreviations WBC: White blood cell; RBC: Red blood cell; Hb: Hemoglobin; HCT: Hematocrit; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; Plat: Platelet; RDW-CV: Red cell distribution width – coefficient of variation; MPV: Mean platelet volume; FBS: Fasting blood sugar; TSH: Thyroid stimulating hormone.

a tenfold increase in the number of children with T1DM and DKA at the time of diagnosis [15-17]. In our patient, both predisposing factors were relevant, despite the presence of polyuria and polydipsia several weeks earlier. Due to family neglect and delayed diagnosis at outpatient centers, the child presented to the emergency department with dehydration, decreased consciousness, blood glucose of 738 mg/dL, pH=7.12, and HCO_3 < 5 mmol/L, leading to hospitalization.

G6PD is an X-linked enzyme that protects RBCs from oxidative stress. Deficiency of this enzyme in the presence of oxidative triggers such as certain foods (e.g. fava beans), drugs (antimalarials, anticonvulsants, vitamin C), infections, and metabolic stresses (such as DKA) can result in acute hemolytic episodes. Clinical manifestations of hemolysis due to this deficiency may include weakness, pallor, lethargy, and urine discoloration [12, 18, 19]. Furthermore, in the early stages of G6PD deficiency-related hemolysis, thrombocytosis or mild microcytic anemia may be observed; however, during the recovery phase, reticulocytosis leads to increased MCV and a macrocytic anemia picture [19-22]. In our patient, the two main hemolytic triggers were acute pulmonary infection (pneumonia) and DKA. However, during hospitalization, hemolytic symptoms such as urine discoloration were not clinically significant, and urinalysis showed no clear findings. The severity of anemia at admission (hemoglobin 10 g/dL) also did not warrant urgent evaluation. Therefore, the treatment team fo-

cused on managing pneumonia, adjusting insulin doses, controlling blood glucose, and educating the family on post-discharge diabetic care. Given the high prevalence of G6PD deficiency in Iran (10–14% according to the World Health Organization) and in its southern cities like Bushehr, this diagnosis should be considered in all cases of symptomatic acute anemia, especially when accompanied by urine discoloration, although our patient did not have classic clinical features of G6PD deficiency [23]. Therefore, further investigations were conducted after his discharge to determine the cause of anemia.

Since the simultaneous occurrence of macrocytic anemia and diabetes can raise suspicion for TRMA, this diagnosis was considered based on the laboratory results (Hb=6.8 and MCV=95). TRMA is a rare genetic disorder in which thiamine administration can improve macrocytic anemia and reduce insulin requirements, although it may not significantly affect other manifestations of the syndrome, such as sensorineural hearing loss. Therefore, audiological evaluation with audiometry is considered an important part of the diagnostic workup for patients suspected of TRMA [9, 10, 24]. However, in our case, audiometric evaluation was not performed early. Nevertheless, thiamine was administered at a dose of 100 mg twice daily, and a partial improvement in clinical status was observed, which was initially interpreted as a response to thiamine treatment. This continued until the patient exited the "honeymoon" phase, with a subsequent rise in blood glucose and a second DKA episode requiring hospital readmission.

It became clear that although the healthcare team requested initial investigations for anemia, the diagnosis of TRMA was premature. It would have been more appropriate to consider all differential diagnoses one by one and wait for the results of initial tests. A more thorough history-taking, along with a detailed evaluation of the patient's symptoms and the trend of CBCs before and during hospitalization, should have been conducted. The possibility of the "honeymoon" phase as the cause of transient hypoglycemia should have been considered from the outset. Even if clinical doubt persisted, a gradual tapering of the insulin dose would have been more appropriate than abrupt discontinuation, especially given the family's reluctance to accept a permanent diabetes diagnosis. Therefore, other potential causes of macrocytic anemia in a diabetic child, including vitamin B12 and folate deficiency, hypothyroidism, malabsorption syndromes such as celiac disease, and liver disease, were evaluated. Normal thyroid function tests (TSH: 2.81), liver enzymes (AST: 19, ALP: 569, ALT: 17), and negative gluten sensitivity excluded these conditions [25, 26].

Finally, considering that reticulocytosis can cause increased MCV alongside anemia, and that various hemolytic anemias, including G6PD deficiency-related hemolysis, can present similarly, it was determined that the diagnosis of TRMA was made prematurely, and in fact, the anemia resulted from RBC lysis due to G6PD deficiency (favism) in the context of DKA and infection.

Conclusion

The coexistence of G6PD deficiency and the possible honeymoon phase of T1DM led to misdiagnosis of TRMA in a male child. This highlights the importance of step-by-step differential diagnosis, accurate interpretation of laboratory results, and avoiding hasty clinical decisions. Moreover, even when the diagnosis of TRMA is accurate, insulin therapy must be discontinued gradually and with close blood glucose monitoring. This is crucial, as in some TRMA cases, diabetes does not respond to thiamine and insulin therapy remains necessary. Therefore, proper family education and emphasis on regular follow-up play a vital role in preventing complications.

Ethical Considerations

Compliance with ethical guidelines

Ethics approval for this case report was obtained from the Ethics Committee of Bushehr University of Medical Sciences, Bushehr, Iran (Code: IR.BPUMS.REC.1404.407). Written informed consent was obtained from the patient's legal guardian.

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Authors contributions

Supervision: Seyedeh Tahereh Mousavi, Roqayeh Gashmard, and Farkhondeh Mehboodi; Data collection: Mohammad Reza Vahidi, Reyhaneh Sadat Mousavi, and Gholamreza Abdollahi; Clinical case management and clinical interpretation: Seyedeh Tahereh Mousavi; Writing the original draft: Gholamreza Abdollahi, Reyhaneh Sadat Mousavi, Mohammad Reza Vahidi, and Seyedeh Tahereh Mousavi; Final approval: All authors.

Conflicts of interest

The authors declared no conflict of interest.

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