Erciyes Med J 2022; 44(1): 102–5 • DOI: 10.14744/etd.2021.92489
CASE REPORT – OPEN ACCESS

Management of Acute Kidney Injury in a Patient with Diabetic Ketoacidosis and Multiple Autoimmune Diseases

Emre Sarıkaya[1], Gül Direk[1], Serkan Özsoylu[2], İsmail Dursun[3], Nihal Hatipoğlu[1]

ABSTRACT

Background: Type 1 diabetes mellitus (DM) is an autoimmune disease caused by the failure of pancreatic beta cells to secrete sufficient insulin. Several other autoimmune diseases that involve the endocrine glands may accompany type 1 DM. Prerenal acute kidney injury due to dehydration occurring during diabetic ketoacidosis (DKA) is a common condition that usually improves with appropriate fluid therapy management.

Case Report: A 9-year-old child presented with DKA and renal failure that was resistant to treatment. Other autoimmune conditions potentially accompanying the DM were investigated and it was determined that the patient had severe hypothyroidism due to Hashimoto's thyroiditis. The hypothyroidism was the cause of the treatment-resistant renal failure, which regressed within days of starting levothyroxine treatment.

Conclusion: In addition to classic causes of renal failure in patients with diabetes, it is important to remember the potential effects of other underlying autoimmune events, such as hypothyroidism.

Keywords: Acute kidney injury, autoimmunity, diabetic ketoacidosis, Hashimoto's thyroiditis

Cite this article as: Sarıkaya E, Direk G, Özsoylu S, Dursun İ, Hatipoğlu N. Management of Acute Kidney Injury in a Patient with Diabetic Ketoacidosis and Multiple Autoimmune Diseases. Erciyes Med J 2022; 44(1): 102-5.

[1]Department of Pediatric Endocrinology, Erciyes University Faculty of Medicine, Kayseri, Turkey
[2]Department of Pediatric Intensive Care, Erciyes University Faculty of Medicine, Kayseri, Turkey
[3]Department of Pediatric Nephrology, Erciyes University Faculty of Medicine, Kayseri, Turkey

Submitted 03.11.2020
Accepted 22.01.2021
Available Online 16.12.2021

Correspondence Nihal Hatipoğlu, Erciyes University Faculty of Medicine, Department of Pediatric Endocrinology, Kayseri, Turkey
Phone: +90 352 207 66 66/ 25474
e-mail: nihalhatipoglu@yahoo.com

INTRODUCTION

Type 1 diabetes mellitus (DM), the most common form of diabetes among children, is an autoimmune disease caused by the failure of pancreatic beta cells to secrete sufficient insulin (1). Although the etiology of type 1 DM is related to organ-specific autoimmunity, accompanying autoimmune conditions targeting other organs may co-exist or develop in the future. Anti-thyroid antibodies have been reported in more than 25% of type 1 DM patients, transglutaminase antibodies in 10%, and anti-adrenal antibodies in 1.7% (2).

A patient presented with diabetic ketoacidosis (DKA) and renal failure that was resistant to treatment. Other associated autoimmune diseases were evaluated as a potential cause of the treatment-resistance. This report is a description of a rare case, the treatment management difficulties, and ultimate successful result.

CASE REPORT

A 9-year-old girl was referred from another center with the diagnoses of DKA and acute kidney injury (AKI) with complaints of weakness, weight loss, polydipsia, and polyuria. Her medical history revealed that she had been born in the 26th gestational week due to preeclampsia with a birth weight of 1100 g and remained in the neonatal unit for 9 weeks. Her parents were not consanguineous and there was no known autoimmune disease or chronic kidney disease in the family. Severe dehydration findings, such as tachycardia, hypotension, dry mouth, decreased skin turgor, and Kussmaul respiration, were observed at the time of presentation. Her weight was recorded as 26.5 kg (25–50%), height was measured as 128 cm (10–25%), and she had not yet entered puberty. All of the other systemic examination findings were normal. The laboratory findings on admission were consistent with moderate DKA (Table 1). Appropriate fluid and insulin infusion therapy were administered. The levels of blood urea nitrogen (BUN) of 23.1 mg/dL (7–18 mg/dL) and creatinine (Cr) of 1.38 mg/dL (0.31–0.88 mg/dL) seen at admission increased to BUN: 58.4 mg/dL and Cr: 3.12 mg/dL on the fourth day of hospitalization. Hemodialysis was performed twice due to resistance acidosis and renal failure. A diabetic evaluation revealed the following values: glycated hemoglobin: 12.5% (4–5.6%), C-peptide: 0.379 ng/mL (1.1–4.4 ng/mL), anti-pancreatic islet cell antibody: negative, glutamic acid decarboxylase antibody: 53 IU/mL (0–10 IU/mL). A routine evaluation for other autoimmune conditions accompanying diabetes revealed these measurements: thyroid-stimulating hormone: >100 mIU/mL (0.60–4.68 mIU/mL), free thyroxine: 0.47 ng/dL (0.97–1.67 ng/dL), free

Table 1. The laboratory values and response to treatment management during follow-up

	Day 1	Day 2	Day 3	Day 4	Day 6	Day 8	Day 13	Outpatient control 1 week after discharge
pH	7.17	7.19	7.27	7.44	7.41	7.38		7.35
HCO_3 (mmol/L)	6	5.8	9.1	17	21.6	17.9		21.2
Glucose (mg/dL)	515	373	218	225	100	108	130	88
BUN (mg/dL)	23.1	33.5	32.2	58.4	54.3	45.2	30.1	20.2
Cr (mg/dL)	1.38	2.58	3.12	2.09	2.1	1.54	0.84	0.45
Na (mmol/L)	144	147	149	133	136	134	136	141
K (mmol/L)	3.4	3.5	3.9	4.8	3.7	3.8	3.6	4.8
Cl (mmol/L)	125	120	124	102	99	93	97	102
Ca (mg/dL)	10.2	9.6	8.3	7.73	8.55	9.2	9.2	9.9
P (mg/dL)	2.6	6.1	5.1	4.8	5.4	4.3	4.3	5.3
Hb (g/dL)	10.7	9.3	8.6	8.5		8.9	8.5	9.9
WBC (10^3/µL)	16.3	11.9	12.4	8.2		5.45	8.49	5.47
PLT (10^3/µL)	272	236	176	163	178	329	566	490
TSH (µU/mL)				>100		>100		6.11
FT4 (ng/mL)				0.472		0.911		1.91
PTH (pg/mL) (15–65)				43.5				
ACTH (pg/mL)						11. 4		
Cortisol (µg/dl)						15.7		
HbA1C (4.8–5.9%)			12.5					
C-peptide (ng/mL) (1.1–4.4)			0.379					
Management and Treatment		Hemodialysis was performed		Levothyroxine 50 mcg/day started			IVIG was given	

ACTH: Adrenocorticotropic hormone; BUN: Blood urea nitrogen; HbA1c: Glycated hemoglobin; Ca: Calcium; Cr: Creatinine; FT4: Free thyroxine; Hb: Hemoglobin; HCO_3: Bicarbonate; IVIG: Intravenous immune globulin; K: Potassium; Cl: Chlorine; Na: Sodium; P: Phosphorus; PLT: Platelet; PTH: Parathyroid hormone; TSH: Thyroid-stimulating hormone; WBC: White blood cell

triiodothyronine): 1.55 pg/mL (2.53–5.22 pg/mL), anti-thyroid-peroxidase: 184 U/mL (0–34 U/mL). It was determined that the patient had severe hypothyroidism due to Hashimoto's thyroiditis, and levothyroxine treatment was initiated. A progressive decrease in the BUN and Cr values was observed beginning on the fourth day of treatment.

Anti-endomysium immunoglobulin A testing for celiac disease yielded a result of >200 IU/mL (0–1 IU/mL). Adrenal insufficiency and hypoparathyroidism were ruled out with the appropriate laboratory tests. A hemoglobin (Hb) value of 10.7 g/dL (12–15 g/dL) and a mean corpuscular volume (MCV) value of 78.1 fL (78–95 fL) were recorded at admission, however, on the fifth day of hospitalization, the values of both Hb and MCV decreased to 8.1 g/dL and 81.8 fL, respectively. Iron deficiency and pernicious anemia were ruled out with more detailed laboratory testing. Autoimmune hemolytic anemia was diagnosed based on findings of reticulocytosis and a positive direct Coombs test. The patient's anemia responded to intravenous immune globulin (IVIG) therapy. The laboratory values and response to treatment management during the patient's follow-up are summarized in Table 1.

The patient was discharged with multiple-dose insulin and levothyroxine treatment and a re-evaluation was performed 1 week later (Table 1). The results of renal function tests and a complete urinalysis were normal. The improvement in hemoglobin count also continued. Follow-up was planned with the pediatric nephrology department for kidney function and the pediatric gastroenterology department for celiac disease.

DISCUSSION

Type 1 diabetes is an autoimmune condition, and prerenal renal failure is a common complication seen in severe clinical conditions such as DKA, that can be quickly resolved with appropriate fluid therapy (3, 4). Hashimoto's thyroiditis and celiac disease are common autoimmune diseases that may accompany diabetes (2). However, as in the present case, renal failure due to hypothyroidism and concomitant autoimmune hemolytic anemia are not frequently expected pathologies with type 1 DM. Acute kidney injury can develop in 64% of patients presenting with ketoacidosis. High serum glucose, high serum protein, low serum bicarbonate, and high serum chlorine levels for 24 hours have been associated with increased risk of kidney damage. In more than half of these patients, renal failure decreases within the first 24 hours using rehydration alone, and rarely, hemodialysis is required (3, 4). The difficulty in managing the DKA treatment of our case was the development of progressive renal failure despite the hydration treatment. Although the patient was hydrated and her blood sugar and ketosis improved, acidosis persisted, and her BUN and Cr values progressively increased. Therefore, hemodialysis was performed. The acidosis and hyperchloremia improved after dialysis, but the BUN and Cr values continued to increase. The severe hypothyroidism detected in further evaluation was thought to be the cause of resistance renal failure.

Although renal dysfunction due to hypothyroidism is rare, it is a well-known condition. Rhabdomyolysis and kidney damage may occur in patients with a late diagnosis of Hashimoto's thyroiditis or those who have not received treatment for an extended period. In such cases, the elevation of BUN and serum Cr typically improves within days of levothyroxine treatment (5, 6).

Thyroid function should also be evaluated in routine controls of patients with acute renal failure (5). In this patient, acute renal failure, initially thought to be related to DKA, continued despite hydration and hemodialysis treatment. Once hypothyroidism was diagnosed and levothyroxine treatment was administered, the signs of renal failure regressed within days. Although the precise physiopathology of kidney disease secondary to hypothyroidism is not known, decreased kidney mass, decreased peripheral vascular resistance, decreased cardiac output-related kidney blood supply, renin-angiotensin-aldosterone system overactivity, decreased response to sympathetic activation, and rhabdomyolysis are considered possible causes of the development of AKI (6). In our patient, no signs of renal parenchymal disease, such as hematuria or proteinuria, or obstruction were detected that might explain the AKI. Furthermore, there was no explanatory feature in complete urine analysis findings. Her kidney-urinary tract and bladder ultrasonography findings were unremarkable for congenital abnormalities of the kidney and urinary tract, and her renal and urinary system ultrasonography findings were normal. She also had normal transaminase levels and showed good response to thyroid hormone replacement therapy. Therefore, hypothyroidism was thought to be the likely cause of AKI.

The coexistence of autoimmune hemolytic anemia and hypothyroidism has been reported in only a few cases in the literature. These cases were diagnosed as systemic lupus erythematosus and Evans syndrome and were accompanied by thrombocytopenia (7). In addition, a few cases of a combination of atypical hemolytic syndrome and DKA have been described (8, 9). In this case, thrombocytopenia was not observed in the clinical follow-up, as shown in Table 1.

In this case of a patient presenting with DKA, there was involvement of >1 endocrine gland. The patient was first evaluated for autoimmune polyglandular syndrome (APS). In APS type 3, hypothyroidism and insulin-dependent diabetes are often associated with other autoimmune diseases without adrenal insufficiency or hypoparathyroidism. Although the literature suggests that APS type 3 is the most common autoimmune polyendocrinopathy seen in the child and adolescent age groups, there are not enough studies to fully determine the clinical spectrum (10).

There were no indications of alopecia areata, vitiligo, or ectodermal candidiasis in this case. Since adrenal insufficiency and hypoparathyroidism were not observed, APS types 1 and 2 were ruled out and it was determined that the patient had type 1 DM and autoimmune thyroiditis in accordance with type 3 APS. Celiac antibody positivity was also observed. In addition, anemia was present in our patient. However, contrary to the expected pernicious anemia seen in APS type 3, only autoimmune hemolytic anemia was observed in this patient, which resolved with IVIG treatment (10). This suggested a severe autoimmune reaction.

In this case, a severe autoimmune reaction and hypothyroidism led to progressive deterioration and renal failure after DKA treatment, which caused difficulties in the treatment management. This case illustrates the importance of examining the possibility of other underlying autoimmune causes, such as hypothyroidism, in addition to classical causes of renal failure in patients with diabetes.

Informed Consent: A written consent form was obtained from the patient's parent.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – GD; Design – İD; Supervision – NH; Materials – SÖ; Data Collection and/or Processing – ES; Analysis and/or Interpretation – ES; Literature Search – NH; Writing – ES; Critical Reviews – NH.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Norris JM, Johnson RK, Stene LC. Type 1 diabetes-early life origins and changing epidemiology. Lancet Diabetes Endocrinol 2020; 8(3): 226–38. [CrossRef]
2. Yang W, Sheng F. Factors associated with thyroid dysfunction in children with newly diagnosed type 1 diabetes mellitus. Minerva Pediatr (Torino) 2021; 73(4): 324–9. [CrossRef]
3. Baalaaji M, Jayashree M, Nallasamy K, Singhi S, Bansal A. Predictors and outcome of acute kidney injury in children with diabetic ketoacidosis. Indian Pediatr 2018; 55(4): 311–4. [CrossRef]
4. Hursh BE, Ronsley R, Islam N, Mammen C, Panagiotopoulos C. Acute kidney injury in children with type 1 diabetes hospitalized for diabetic ketoacidosis. JAMA Pediatr 2017; 171(5): e170020. [CrossRef]
5. Choy J, Yaxley J, Yaxley W. A Rare case of renal impairment caused by primary hypothyroidism. Korean J Fam Med 2018; 39(3): 204–6.

6. Peringat J, Manappallil RG, Karadan U. Rhabdomyolysis: a rare complication of Hashimoto's thyroiditis precipitated by statin therapy. BMJ Case Rep 2018; 2018: bcr2017223229. [CrossRef]
7. Lin H, Wu K, Zhang W, Lin G, Cai C. Evans syndrome with acute kidney injury. Arch Iran Med 2019; 22(6): 336–9.
8. Zhu Z, Chen H, Gill R, Wang J, Spitalewitz S, Gotlieb V. Diabetic ketoacidosis presenting with atypical hemolytic uremic syndrome associated with a variant of complement factor B in an adult: a case report. J Med Case Rep 2016; 10: 38. [CrossRef]
9. Alizadeh F, O'Halloran A, Alghamdi A, Chen C, Trissal M, Traum A, et al. Toddler with new onset diabetes and atypical hemolytic-uremic syndrome in the setting of COVID-19. Pediatrics 2021; 147(2): e2020016774. [CrossRef]
10. Valenzise M, Aversa T, Saccomanno A, De Luca F, Salzano G. Epidemiological and clinical peculiarities of polyglandular syndrome type 3 in pediatric age. Ital J Pediatr 2017; 43(1): 69. [CrossRef]