Telmisartan-induced type 4 renal tubular acidosis: a case report

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Abstract

Hyperkalemia is a common electrolyte disturbance in hospitalized patients, often caused by impaired renal potassium excretion due to hypoaldosteronism. Type 4 Renal Tubular Acidosis (RTA), commonly associated with diabetes mellitus and RAAS-inhibiting medications, is a significant consequence. We report a 56-year-old male with diabetes, hypertension, and coronary artery disease who developed type 4 RTA after starting telmisartan post-hip replacement. His course was complicated by pneumonia and worsening hyperkalemia, with arterial blood gas showing Normal Anion Gap Metabolic Acidosis (NAGMA) and a positive urinary anion gap. Discontinuing telmisartan and initiating hydrocortisone led to significant renal function improvement and potassium normalization. This case highlights the importance of caution when using RAAS inhibitors in high-risk patients and supports hydrocortisone as a viable alternative when fludrocortisone is unavailable.

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Case Report

A 56-year-old male patient was referred to our department following a complicated postoperative course. His medical history was significant for DM2, hypercholesterolemia, hypertension, and chronic stable coronary artery disease. His home medications included amlodipine and insulin; however, he reported poor adherence to his prescribed regimen. The patient had undergone right hip replacement surgery at the referring hospital, where the intraoperative course was uneventful. However, by postoperative day 7, his recovery was complicated by pneumonia associated with poorly controlled blood glucose levels and blood pressure, necessitating his transfer to our hospital for further management. Upon admission, he presented with mild dyspnea but remained hemodynamically stable.

Initial laboratory investigations revealed mild anemia, leukocytosis, and significantly elevated inflammatory markers, while other parameters were unremarkable. The patient had been receiving subcutaneous Low Molecular Weight Heparin (LMWH) 60 mg/day since the first postoperative day for Deep Vein Thrombosis (DVT) prophylaxis and was initiated on antibiotics for his pneumonia. Notably, he had no prior history of treatment with Angiotensin Receptor Blockers (ARBs), Angiotensin-Converting Enzyme inhibitors (ACE inhibitors), or Nonsteroidal Anti-Inflammatory Drugs (NSAIDs). Given his clinical status, telmisartan 40 mg once daily was introduced on postoperative day 8 to manage his hypertension (*Supplementary Materials, Table 1*). LMWH was discontinued on postoperative day 10 and replaced with aspirin. The patient remained clinically stable throughout his hospitalization. However, by postoperative day 10, his leukocyte count exhibited a gradual increase, peaking at 24.64 G/L on postoperative day 14 (Table 1). Concurrently, his platelet count increased from baseline, fluctuating between 511 and 636 G/L, likely reflecting reactive leukocytosis and thrombocytosis secondary to anemia. On postoperative day 12, a rise in serum potassium levels to 5.1 mmol/L was noted and was managed with intravenous furosemide (20 mg/day). However, by postoperative day 14, a marked increase in serum creatinine levels from a baseline of

approximately 1 mg/dl was observed, alongside a peak serum potassium level of 5.6 mmol/L. Pseudohyperkalemia secondary to thrombocytosis was ruled out by repeated serum and plasma potassium measurements.

Since the patient remained hemodynamically stable and euvolemic throughout hospitalization, prerenal acute kidney injury due to hypovolemia was ruled out. To further evaluate the acute decline in renal function and persistent hyperkalemia—which appeared disproportionate to the degree of renal impairment—an Arterial Blood Gas (ABG) analysis was performed, revealing a NAGMA. A spot urine electrolyte analysis on postoperative day 15 demonstrated a positive Urinary Anion Gap (UAG) of 54.7. Urinalysis findings were unremarkable, with a pH of 6.5 and no evidence of infection, proteinuria, or ketonuria; however, serial urine pH measurements demonstrated an acidic trend. Given that other non-renal tubular acidosis causes of NAGMA were excluded, these findings were consistent with type 4 RTA.

Due to the acute worsening of kidney function, refractory hyperkalemia, and suspected type 4 RTA, telmisartan was discontinued on postoperative day 15, and intravenous furosemide was continued to control hyperkalemia. Given the unavailability of fludrocortisone in our department, hydrocortisone (200 mg/day) was initiated as an alternative to manage the patient's tubular dysfunction. Following the discontinuation of telmisartan and the introduction of hydrocortisone, renal function improved significantly. By postoperative day 16, serum creatinine levels had returned to baseline (1.01 mg/dl), and serum potassium had decreased to 5.0 mmol/L. By postoperative day 17, potassium levels had further normalized to 4.1 mmol/L. The patient's NAGMA also improved, with normalization of serum HCO_4^+ and a mild reduction in the urine anion gap.

Given the patient's clinical improvement, they were discharged on postoperative day 17 with a 10-day course of oral hydrocortisone. A follow-up evaluation three weeks later confirmed a return to baseline creatinine levels (~1.01 mg/dl) and complete resolution of NAGMA and hyperkalemia.

Discussion

Hyperkalemia is one of the most frequently encountered electrolyte disturbances in hospitalized patients, with causes broadly classified into increased potassium intake, impaired renal excretion, transcellular shifts, or pseudohyperkalemia. When hyperkalemia persists in the absence of an obvious cause, hypoaldosteronism should be considered a primary etiology. Hypoaldosteronism may arise from either true aldosterone deficiency or aldosterone resistance, both of which impair renal potassium excretion. Type 4 RTA falls under this category and should be included in the initial diagnostic workup for unexplained hyperkalemia.

The pathophysiology of type 4 RTA is characterized by hyperkalemia and NAGMA, primarily due to hypoaldosteronism, which is more commonly observed than aldosterone resistance.[1] Hypoaldosteronism can be either acquired (secondary mineralocorticoid deficiency) or, less frequently, inherited (primary mineralocorticoid deficiency). The most prevalent cause of secondary mineralocorticoid deficiency is Hyporeninemic Hypoaldosteronism (HH), frequently associated with DM2 and certain medications that interfere with the RAAS.2 These include drugs that suppress renin synthesis, such as NSAIDs, nonselective beta-blockers, and calcineurin inhibitors, especially agents that directly inhibit aldosterone production, such as heparin, ACE inhibitors, ARBs, and renin inhibitors (*e.g.*, aliskiren).[3]-Although most patients with HH are asymptomatic and present with mild to moderate hyperkalemia, the condition may become clinically significant when additional precipitating factors further disrupt potassium homeostasis.2 These factors include acute kidney injury, salt restriction, or medications such as ACE inhibitors, ARBs, potassium-sparing diuretics, or heparin.[4] In this case report, we describe a male patient with DM2 who developed type 4 RTA following the initiation of Telmisartan, an ARB commonly used in clinical practice. Although type 4 RTA is a recognized side effect of RAAS inhibitors, detailed case reports specifically linking telmisartan to type 4 RTA are limited in the literature.

The pathophysiological basis of type 4 RTA involves impaired aldosterone activity, which leads to reduced sodium (Na^+) reabsorption in the distal nephron. This, in turn, diminishes the electrochemical gradient required for potassium (K^+) and hydrogen (H^+) excretion, resulting in hyperkalemia and metabolic acidosis. Additionally, hyperkalemia inhibits renal ammonium (NH_4^+) production in the proximal tubule, further impairing acid excretion and exacerbating acidosis.[5]

Key laboratory findings in this patient were consistent with a diagnosis of type 4 RTA. These included persistent hyperkalemia that was disproportionate to the degree of renal dysfunction and potassium intake, mildly reduced serum bicarbonate, NAGMA, and a positive UAG—all hallmark features of type 4 RTA.

In type 4 RTA, urine pH is often still acidic (<5.5) because H^+ secretion via ATP-dependent proton pumps in the distal nephron is partially preserved. However, the overall acid excretion is impaired due to reduced NH_4^+ production, which limits the kidney's ability to buffer and eliminate acid effectively. That said, some patients may initially present with a urine pH >5.5, especially early in the disease course. This can occur when H^+ secretion is transiently impaired, even though the mechanisms for acidification are intact. In our patient, the initial urine pH was 6.5, but with progression and treatment, subsequent measurements showed a clear acidification trend, with the urine pH ultimately decreasing to 5.5, which signifies the patient's ability to acidify urine.

Patients with diabetes mellitus are particularly vulnerable to type 4 RTA due to dysregulation of the RAAS, increasing their risk of hyperkalemia.[6] The introduction of RAAS inhibitors, such as ARBs, can further aggravate this imbalance, potentially triggering type 4 RTA, as observed in this case.

Notably, the patient achieved normokalemia and a return to baseline creatinine levels shortly after discontinuing Telmisartan and initiating hydrocortisone (200 mg/day). This outcome is particularly significant, as type 4 RTA is conventionally managed with fludrocortisone to correct aldosterone deficiency.[7] The successful use of hydrocortisone in this case suggests its potential role as a therapeutic alternative when fludrocortisone is unavailable.

The primary limitation of this case report is the inability to perform a more comprehensive diagnostic workup, such as measuring aldosterone levels or calculating the urine osmolal gap, due to temporary limitations in local laboratory resources.

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Online supplementary materials

Table 1. Changes in the laboratory values of the patient over 10 postoperative days (from day 7 to day 17). "N/A" denotes that the laboratory values were not available for a given day. Additionally, a selection of the patient's in-hospital medications is documented. The green bars indicate the duration during which the patient received the medications, while the white bars denote periods when the medications were either withheld or discontinued.