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Letter to Editor

Piperacillin-Tazobactam Induced Fanconi Syndrome

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To the Editor,

Proximal renal tubular acidosis (pRTA) is a rare condition characterized by impaired bicarbonate reabsorption in the proximal renal tubule, resulting in normal anion gap metabolic acidosis. Often occurring alongside Fanconi syndrome, it is marked by widespread proximal tubular dysfunction. Although genetic disorders and autoimmune conditions are known etiologies, medications have also been implicated (1). We report a unique case of piperacillin-tazobactam (Pip-Tazo) induced pRTA associated with Fanconi syndrome.

A 64-year-old female with hypertension and diabetes underwent surgical repair for a right hip fracture under spinal anesthesia with bupivacaine. Intravenous Pip-Tazo was initiated on postoperative day two for antibiotic prophylaxis and pneumonia treatment, alongside enoxaparin therapy. By postoperative day four, she exhibited polyuria and tachypnea. Laboratory tests indicated normal anion gap metabolic acidosis with hypokalemia and hypophosphatemia, consistent with proximal tubular dysfunction. Pip-Tazo was discontinued on day seven, and supplementation with sodium bicarbonate and potassium resulted in the gradual resolution of electrolyte abnormalities and metabolic acidosis over subsequent days. Laboratory values during follow-up confirmed these observations (Table 1). The temporal relationship between Pip-Tazo initiation and the resolution following its cessation strongly suggests causality. The role of bupivacaine was discounted, as spinal anesthetics generally do not enter systemic circulation.

Proximal RTA has previously been linked to several antimicrobials, including penicillin, cephalosporin, and aminoglycosides, but our literature search revealed no prior association with Pip-Tazo (2). Fanconi syndrome, characterized by increased urinary excretion and decreased plasma levels of substances usually reabsorbed by the proximal convoluted tubule (PCT),

Table 1. Laboratory values

Postoperative:	Day 2.	Day 4.	Day 12.
Plasma chemistry			
pH	7,40	7,32	7,54
HCO3 (mEq/L)	23,1	10,9	27,4
CO2 (mmHg)	41,1	11,6	31,9
Lactate (mEq/L)	0,9	1,0	1,0
Na (mEq/L)	134	126	131
Cl (mEq/L)	102	112	102
K (mEq/L)	4,30	2,58	4,07
Glycose (mg/dL)	277	304	189
Creatinine (mg/dL)	1,34	0,91	0,78
Urea (mg/dL)	67	45	41
P (mg/dL)	3,6	1,8	3,2
Ca (mg/dL)	8,06	7,64	8,64
Mg (mg/dL)	1,95	1,58	1,75
Urate (mg/dL)	6,5	2,5	2,9
Albumin (g/dL)	2,6	1,9	2,4
Protein (g/dL)	6,4	5,2	6,1
PTH (pg/mL)		102	
Vitamin D (ng/mL)		15	
Urine analysis			
pH	5	6	8
WBC (per hpf)	3	2	1
RBC (per hpf)	68	27	14
Glucose	pos	pos	neg
Ketone	neg	neg	neg
Protein	neg	pos	neg
K (mEq/L)		22,8	
Na (mEq/L)		126	
Cl (mEq/L)		33	
Creatinine (mg/dL)		18	

often coexists with proximal RTA in patients exposed to causative agents (3). Our patient's clinical profile, low plasma potassium, phosphorus, and bicarbonate despite replacement, normal anion gap metabolic acidosis, increased urinary anion gap, and urinary alkalosis, was consistent with Fanconi syndrome.

Glucosuria, typically indicative of Fanconi syndrome, might partially be explained by transient hyperglycemia, given the patient's glucose exceeded 300 mg/dL on the day glucosuria was detected (4). However, the concurrent hypophosphatemia, hypokalemia, non-anion gap metabolic acidosis, alkaline urine, positive urinary anion gap, and rapid biochemical improvement after Pip-Tazo discontinuation collectively supported a diagnosis of drug-induced Fanconi syndrome rather than isolated hyperglycemia-related glucosuria.

Technical limitations prevented analysis of fractional excretion of bicarbonate, phosphorus, uric acid, protein, and amino acids, markers sensitive to proximal tubulopathy. Diagnosis was thus reliant on clinical and biochemical improvement post-drug withdrawal.

Typically, Fanconi syndrome is suspected when proximal tubulopathy arises with medication use, confirmed by symptom resolution upon withdrawal. The temporal relationship is generally clear, though late presentations (months or years later) have been documented with drugs like tenofovir (5). However, Fanconi syndrome linked to Pip-Tazo use is absent from existing literature.

The rapid onset of symptoms within 2-3 days post-administration and resolution following discontinuation strongly supports Pip-Tazo as the cause. Nevertheless, Pip-Tazo's exact pathogenic mechanism remains unclear, particularly since some literature argues against its nephrotoxicity (6). Using the Naranjo Adverse Drug Reaction Probability Scale, we scored a 5 out of 13, indicating a 'probable' association based on timing, symptom resolution upon withdrawal, laboratory confirmation, and exclusion of alternate causes (7).

Clinicians should remain vigilant for Fanconi syndrome in patients receiving Pip-Tazo, especially in postoperative scenarios. Early recognition and medication discontinuation are vital for patient recovery.

Sincerely,

DECLERATIONS

Ethics committee approval: None

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We obtained written informed consent from the patient to publish this case report.

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