

[CASE REPORT]

A Diagnostic Blind Spot in Pseudo-Bartter Syndrome: Aberrant Renin-angiotensin-aldosterone System Activation from Focal Renal Scarring

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Abstract:

A 40-year-old woman presented with intermittent limb weakness, edema, and persistent hypokalemia. She had a history of recurrent urinary tract infections, but no diuretic or laxative use. Laboratory findings revealed metabolic alkalosis with elevated plasma renin activity and aldosterone levels. The urinary electrolyte response to fluid administration suggested pseudo-Bartter syndrome due to the volume depletion. Abdominal imaging revealed renal scarring, suggesting focal renin release from the ischemic regions. This case highlights the importance of recognizing secondary systemic renin-angiotensin-aldosterone system (RAAS) activation driven by focal renin release in renal scarring. This also illustrates a paradox in which salt and water restriction may worsen RAAS-driven hypokalemia.

Key words: hypokalemia, pseudo-Bartter syndrome, renal scarring, renin-angiotensin-aldosterone system, urinary tract infection

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Introduction

Bartter syndrome (BS) is a rare inherited renal tubular disorder characterized by hypokalemia, metabolic alkalosis, and hyperreninemia, with normal to low blood pressure (1, 2). BS results from mutations affecting ion transporters involved in salt reabsorption in the thick ascending limb of Henle's loop (3). In contrast, pseudo-Bartter syndrome (pseudo-BS) presents with similar biochemical features but occurs secondary to acquired conditions, such as chronic vomiting, diuretic or laxative abuse, cystic fibrosis, or eating disorders, such as anorexia nervosa.

Pseudo-BS without an apparent external cause presents a diagnostic challenge, particularly when signs of volume depletion are subtle. An under-recognized mechanism involves localized renal ischemia due to focal scarring, often a sequela of recurrent urinary tract infections (UTIs). Such scarring may provoke localized renin release and subsequent ac-

tivation of the intrarenal renin-angiotensin system, leading to elevation of aldosterone levels, even when systemic blood pressure remains preserved.

We herein report a middle-aged woman with persistent hypokalemia, intermittent edema, and a history of recurrent UTIs. Abdominal imaging showed focal renal scarring consistent with localized ischemia and inappropriate renin-angiotensin-aldosterone system (RAAS) activation. This case highlights a diagnostic blind spot, pseudo-BS, driven by aberrant RAAS activation secondary to renal scarring. It also illustrates a clinical paradox, wherein restricting salt and water to prevent edema may paradoxically worsen the condition by enhancing RAAS activity.

Case Report

A 40-year-old Japanese woman was referred for the evaluation of persistent hypokalemia, bilateral lower extremity edema, and episodic limb weakness. She had no history

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of developmental delays or familial electrolyte disturbances. Her body weight had gradually declined from 53 kg (body mass index; BMI 22 kg/m²) in her 20s to 42 kg (BMI 17.6 kg/m²) at presentation, following a 10-kg postpartum loss and ongoing undernutrition. She reported frequent nocturnal vomiting and generalized fatigue throughout her 30s and had a long-standing history of recurrent UTIs since childhood. These episodes had been untreated during her early years, and no urological evaluation had been conducted. She denied any use of diuretics, laxatives, or weight loss agents, including over-the-counter supplements. Her diet was chronically low in animal proteins and fish, and she had minimal sun exposure. As a physical therapist, she frequently experienced orthostatic dizziness during work.

Approximately four years prior to admission, she had been diagnosed with dyslipidemia and was started on statin therapy. Routine follow-up laboratory tests subsequently revealed persistent hypokalemia (1.9-2.6 mmol/L), particularly during warmer months, which was accompanied by fatigue and muscle weakness. Although potassium chloride was prescribed, poor palatability resulted in poor adherence and suboptimal correction. Three years before admission, she visited a general hospital, where testing revealed markedly elevated plasma renin activity (PRA ≥ 20 ng/mL/h) and plasma aldosterone concentration (PAC 325 pg/mL) despite consistently low blood pressure (e.g. 95/54 mmHg). Owing to the difficulty in tolerating potassium chloride, multiple mineralocorticoid receptor antagonists (MRAs) were prescribed sequentially; however, hypokalemia persisted along with sustained urinary potassium wasting. In addition, the patient reported occasionally skipping doses of MRAs around the time of her menstrual period because of low blood pressure symptoms.

The patient was admitted to our hospital for a further evaluation. On admission, her BMI was 17.3 kg/m², indicating underweight status; however, there was no evidence of limb muscle weakness or peripheral edema, and no calluses on the dorsum of the hand ("Russell's sign") suggestive of habitual vomiting were observed. Laboratory data revealed profound hypokalemia (K 2.4 mmol/L), low serum chloride (Cl 90 mmol/L), alkalemia (pH 7.46), and elevated bicarbonate (HCO₃⁻ 39.8 mmol/L) and PCO₂ (56.5 mmHg), indicating metabolic alkalosis with concurrent respiratory acidosis (Table 1). Despite these abnormalities, serum sodium, calcium, and magnesium levels were within the normal range, and there was no evidence of hypomagnesemia or hypocalciuria, suggestive of Gitelman syndrome (GS). The renal function was preserved, with a creatinine-based estimated glomerular filtration rate (eGFR) of 81.0 mL/min/1.73 m² and a cystatin C-based eGFR of 76.0 mL/min/1.73 m². Urinary electrolyte analysis revealed inappropriately high renal potassium wasting, with a fractional excretion of potassium (FEK) of 30.3%. A urinary chloride concentration greater than 20 mmol/L argued against extrarenal chloride loss, such as vomiting, and instead suggested a renal cause of salt wasting, as seen in BS or pseudo-BS states. PRA and

PAC levels were persistently elevated at 16.7 ng/mL/h and 232 pg/mL, respectively. The patient also demonstrated hyperuricemia (UA 10.1 mg/dL), suggesting possible volume depletion.

Nutritional and endocrine assessments revealed markedly low levels of insulin-like growth factor-1 (IGF-1, 34 ng/mL; reference range: 98-245 ng/mL), vitamin D deficiency, and secondary hyperparathyroidism, consistent with chronic catabolic stress. Abdominal computed tomography demonstrated cortical irregularity and focal atrophy of the right kidney (Fig. 1A, arrowhead). Since patient consent could not be obtained, contrast-enhanced computed tomography (CT) was not performed, preventing the direct evaluation of regional perfusion defects. Given these findings, additional morphological and functional assessments of the kidneys are warranted. Therefore, radionuclide renography was performed. Technetium-99m dimercaptosuccinic acid (^{99m}Tc-DMSA) scintigraphy revealed a decreased cortical uptake in the corresponding region of the right kidney. This finding was most evident in the right posterior oblique (RPO) view, focusing on the right kidney (arrowheads in Fig. 1B). Quantitative analysis demonstrated a total relative uptake of 53.46% in the left kidney and 46.54% in the right kidney, which is consistent with localized cortical dysfunction. Technetium-99m diethylenetriaminepentaacetic acid (^{99m}Tc-DTPA) renography showed preserved perfusion and glomerular filtration without evidence of obstruction (left GFR: 45.4 mL/min; right GFR: 38.1 mL/min; Fig. 1C), suggesting focal ischemia rather than global renal dysfunction.

To assess volume responsiveness, isotonic saline infusion (1 L/day for 3 consecutive days) was administered. As shown in Table 2, this resulted in a gradual correction of electrolyte and acid-base disturbances, with serum chloride increasing from 94 to 107 mmol/L, potassium from 2.4 to 3.1 mmol/L, and uric acid from 11.6 to 6.1 mg/dL. Metabolic alkalosis also improved, with venous pH decreasing from 7.436 to 7.388 and bicarbonate from 36.2 to 28.1 mmol/L. These changes, along with the normalization of FEK, indicated that chronic hypovolemia contributed significantly to RAAS activation. Furthermore, to assess RAAS responsiveness, furosemide stimulation and captopril suppression tests were performed (Table 3). The furosemide test revealed a modest increase in PRA (<0.2 → 1.1 ng/mL/h) accompanied by a marked elevation in PAC (25.3 → 318 pg/mL). This disproportionate aldosterone response relative to the minimal rise in renin suggests enhanced adrenal sensitivity to the renin-angiotensin axis. In contrast, the captopril challenge test demonstrated an appropriate suppression of PAC (98.4 → 27.8 pg/mL), indicating preserved feedback regulation of aldosterone secretion. Meanwhile, PRA showed only a modest increase (0.5 → 1.4 ng/mL/h) without the marked renin surge typically observed in renovascular hypertension. These findings argue against significant renal artery stenosis as the underlying cause of the RAAS activation in this case.

Taken together, this patient presented with pseudo-BS

Table 1. Admission Laboratory Data.

Parameter	Value	Unit	Reference range	Parameter	Value	Unit	Reference range
pH	7.462		7.35-7.45	Na	140	mmol/L	138-145
PCO ₂	21.9	mmHg	35-45	K	2.4	mmol/L	3.6-4.8
HCO ₃ ⁻	39.8	mmol/L	20-26	Cl	90	mmol/L	101-108
WBC	7,450	/μL	3,300-8,600	Ca	9.4	mg/dL	8.8-10.1
RBC	4.22×10 ⁶	/μL	3.86-4.92×10 ⁶	P	3.1	mg/dL	2.7-4.6
Hb	12.6	g/dL	11.6-14.8	Mg	1.8	mg/dL	1.8-2.4
Ht	37.6	%	35.1-44.4	GH	0.3	ng/mL	<3.0
PLT	483×10 ³	/μL	158-348×10 ³	IGF-1	34	ng/mL	98-245
TP	7.8	g/dL	6.6-8.1	ACTH	8.6	pg/mL	7.7-63.1
Alb	4.3	g/dL	4.1-5.1	Cortisol	10.6	μg/dL	2-18
T-Bil	0.6	mg/dL	0.4-1.5	PRL	13.2	ng/mL	4.1-28.9
AST	27	U/L	13-30	LH	6.1	mIU/mL	1.7-13.3
ALT	16	U/L	7-23	FSH	4.0	mIU/mL	4.5-11.0
LDH	182	U/L	124-222	E2	275.4	pg/mL	15.6-297.1
ALP	75	U/L	38-113	FT ₃	2.7	pg/mL	2.1-3.8
γ-GTP	16	U/L	9-32	FT ₄	1.4	ng/dL	0.8-1.5
ChE	317	U/L	201-421	TSH	4.202	mU/L	0.61-4.23
CK	95	U/L	41-153	PAC	232	pg/mL	4.0-82.1
Amylase	64	U/L	44-132	PRA	16.7	ng/mL/h	0.2-2.3
TG	251	mg/dL	30-149	U-Na	60	mmol/L	
HDL-C	59	mg/dL	40-103	U-K	16	mmol/L	
LDL-C	178	mg/dL	65-139	U-Cl	64	mmol/L	
UA	10.1	mg/dL	2.6-5.5	U-Ca	5.7	mg/dL	
BUN	6.9	mg/dL	8.0-22.0	U-Cre	14.1	mg/dL	
Cre	0.64	mg/dL	0.46-0.79	U-Ca/Cre	0.4		
eGFRcre	81	mL/min/1.73 m ²		U-NAG	12.6	U/L	0.7-11.2
CysC	0.98	mg/L	0.56-0.87	U-β2MG	69.2	μg/L	30-240
eGFRcys	76	mL/min/1.73 m ²					
PG	88	mg/dL	73-109				
HbA1c	5.3	%	4.9-6.0				

IGF-1 reference values are age- and sex-specific. pH: potential of hydrogen, PCO₂: partial pressure of carbon dioxide, HCO₃⁻: bicarbonate, Na: sodium, K: potassium, Cl: chloride, Ca: calcium, Mg: magnesium, P: phosphate, BUN: blood urea nitrogen, Cre: serum creatinine, eGFR: estimated glomerular filtration rate, CysC: cystatin C, UA: uric acid, PG: plasma glucose, HbA1c: hemoglobin A1c, WBC: white blood cell, RBC: red blood cell, Hb: hemoglobin, Ht: hematocrit, PLT: platelet, TP: total protein, Alb: albumin, T-Bil: total bilirubin, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, ALP: alkaline phosphatase, γ-GTP: gamma-glutamyl transpeptidase, ChE: cholinesterase, CK: creatine kinase, TG: triglyceride, HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, GH: growth hormone, IGF-1: insulin-like growth factor 1, ACTH: adrenocorticotrophic hormone, Cortisol: serum cortisol, PRL: prolactin, LH: luteinizing hormone, FSH: follicle-stimulating hormone, E2: estradiol, FT₃: free triiodothyronine, FT₄: free thyroxine, TSH: thyroid-stimulating hormone, PAC: plasma aldosterone concentration, PRA: plasma renin activity, U-Na: urinary sodium, U-K: urinary potassium, U-Cl: urinary chloride, U-Ca: urinary calcium, U-Mg: urinary magnesium, U-Cre: urinary creatinine, U-Ca/Cre: urinary calcium-to-creatinine ratio, U-NAG: urinary N-acetyl-β-D-glucosaminidase, U-β2MG: urinary beta-2 microglobulin

characterized by renal potassium wasting and chronic volume depletion despite the absence of diuretic use or ongoing vomiting. The pathophysiology appeared to involve focal renin release and activation driven by ischemia in scarred regions of the right kidney under conditions of volume contraction. Genetic testing for hereditary tubulopathies (e.g. SLC12A3 and CLCNKB) was performed in view of the acquired nature of her condition and favorable response to supportive therapy. MRA therapy was discontinued owing to orthostatic intolerance. Oral potassium chloride (16 mEq/day) was resumed with improved adherence, and nutritional

counseling was provided.

The patient's clinical course is summarized in Fig. 2, showing gradual normalization of potassium, bicarbonate, PRA, and PAC levels. Intermittent limb muscle weakness improved with potassium supplementation. On admission, no peripheral edema was evident, although she had previously experienced mild intermittent swelling of the face and legs. These episodes were not simply due to habitual excessive salt or water intakes. RAAS hyperactivation associated with hypovolemia was often accompanied by orthostatic dizziness or transient limb weakness, and edema was presumed

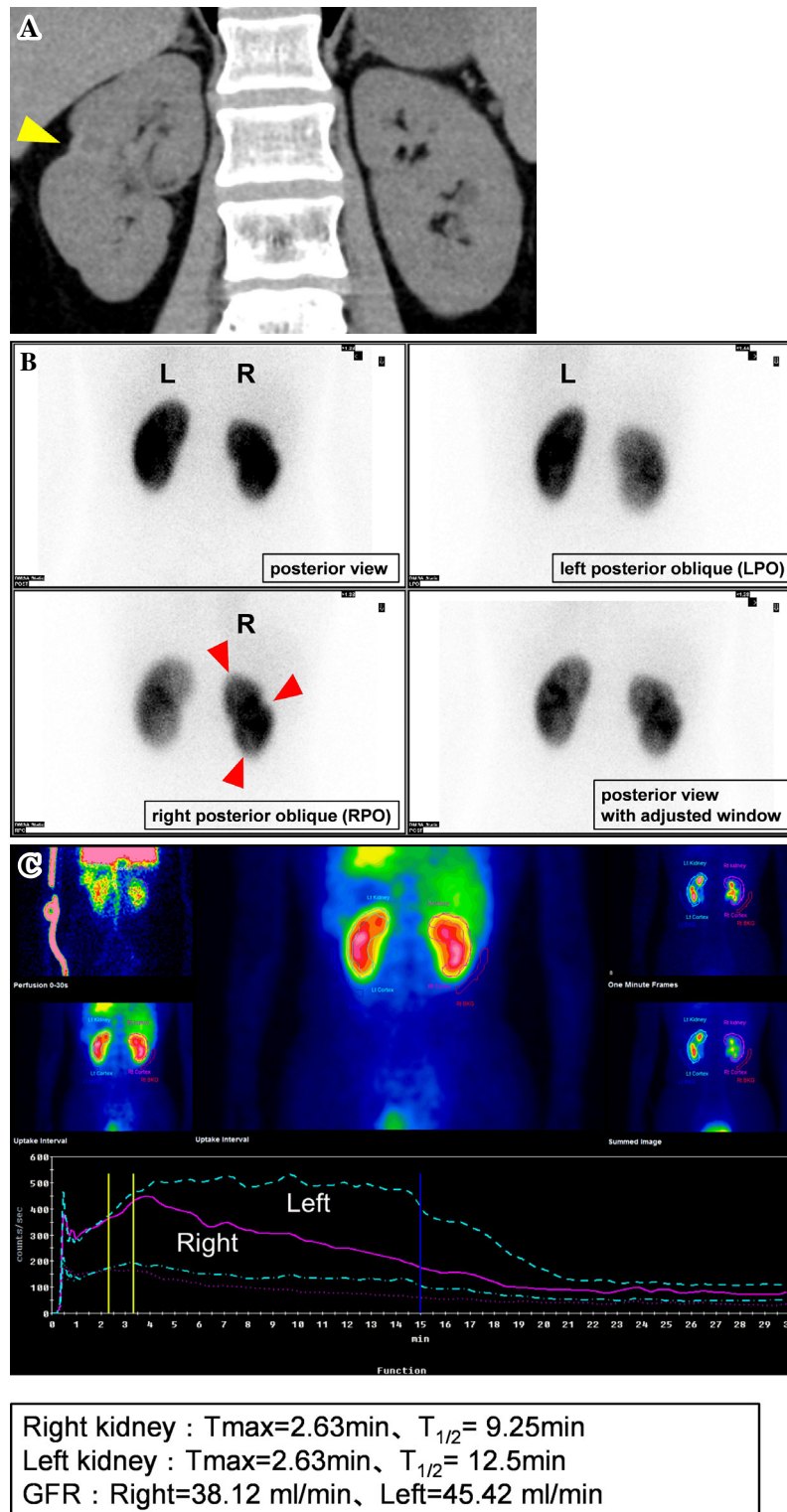


Figure 1. Abdominal CT and renal scintigraphy findings indicating right renal scarring and functional impairment. (A) Non-contrast axial abdominal CT showing cortical thinning and irregular scarring in the right kidney (arrowhead). (B) Technetium-99m dimercaptosuccinic acid (^{99m}Tc -DMSA) scintigraphy of the kidneys. Four views are shown: posterior (upper left), left posterior oblique (LPO, upper right), right posterior oblique (RPO, lower left), and posterior with adjusted window to enhance contrast (lower right). Arrowheads indicate the region of decreased cortical uptake in the right kidney. A quantitative analysis showed a total relative uptake of 53.46% in the left kidney and 46.54% in the right kidney. (C) Technetium-99m diethylenetriaminepentaacetic acid (^{99m}Tc -DTPA) renography showing a symmetrical uptake with slightly prolonged excretion in both kidneys. A split renal function analysis showing a right GFR of 38.1 mL/min and left GFR of 45.4 mL/min.

Table 2. Time Course of Laboratory Parameters before and after Saline Infusion.

Data	Day 1	Day 2	Day 4 (Pre-infusion)	Day 7 (Post-infusion)	Day 8	Day 10	Day 30 (Post-discharge)
Venous Blood Gas							
pH	7.462	7.465	7.436	7.388	7.38	7.371	7.33
PCO ₂ (mmHg)	56.5	54.5	54.7	47.7	46.4	41.2	50.9
HCO ₃ ⁻ (mmol/L)	39.8	38.7	36.2	28.1	26.8	23.3	23.1
Serum							
Na (mmol/L)	140	138	139	143	145	142	140
K (mmol/L)	2.4	2.2	2.4	3.1	2.9	3.4	4.4
Cl (mmol/L)	90	91	94	107	109	110	106
Mg (mg/dL)	1.8	1.9	2.3	2	1.9	1.9	1.9
BUN (mg/dL)	6.9	NA	7.4	3.6	4.4	4.1	3.3
Cre (mg/dL)	0.64	0.63	0.52	0.46	0.51	0.45	0.51
UA (mg/dL)	NA	10.1	11.6	6.1	5.6	5.5	3.2
Urine							
U-Na (mmol/L)	60	32	<10	28	38	62	41
U-K (mmol/L)	16	24.5	15.5	23.5	20.1	10.8	105.7
U-Cl (mmol/L)	64	31	21	29	40	47	118
U-Mg (mg/dL)	NA	3.3	10.9	3.6	5.5	7.1	6.8
U-Ca (mg/dL)	5.7	7.3	1.6	1	1.1	1.5	0.9
U-Cre (mg/dL)	14.1	52.4	81.5	102.6	91.1	60.9	90
Fractional excretion							
Na (%)	1.95	0.28	NA	0.09	0.15	0.32	0.17
K (%)	30.26	13.39	4.12	3.40	3.88	2.35	13.61
Cl (%)	3.23	0.41	0.14	0.12	0.21	0.32	0.63
Mg (%)	NA	2.09	3.02	0.81	1.62	2.76	2.03

Day 4 (Pre-infusion) and Day 7 (Post-infusion) represent laboratory values before and after intravenous isotonic saline administration, respectively. Day 30 corresponds to the outpatient follow-up visit after discharge. NA: not available (parameter not measured), pH: potential of hydrogen, PCO₂: partial pressure of carbon dioxide, HCO₃⁻: bicarbonate, Na: sodium, K: potassium, Cl: chloride, Mg: magnesium, BUN: blood urea nitrogen, Cre: serum creatinine, UA: uric acid, U-Na: urinary sodium, U-K: urinary potassium, U-Cl: urinary chloride, U-Mg: urinary magnesium, U-Ca: urinary calcium, U-Cre: urinary creatinine

to occur when the patient attempted to compensate for such situations by taking slightly excessive amounts of salt and water. During hospitalization, transient edema and mild elevation of brain natriuretic peptide (BNP) were observed after isotonic saline infusion, but both resolved spontaneously within several days as RAAS activity normalized. At discharge, the patient was instructed to continue potassium supplementation and to maintain adequate salt and water intake. While adherence was good, her electrolyte balance remained stable, and no recurrence of edema was observed. However, following a lapse in clinic visits during warm weather, she ran out of medication and experienced recurrence of hypokalemia and metabolic alkalosis. This clinical course reinforces the importance of sustained treatment adherence and volume maintenance in preventing relapse of pseudo-BS.

Discussion

Pseudo-Bartter or Gitelman syndrome (pseudo-BS/GS) is a diagnostically challenging but clinically important entity that mimics inherited tubulopathies. While most cases of hypokalemic metabolic alkalosis are attributable to gastrointestinal losses, diuretic abuse, or eating disorders (4), a subset

of patients lacks such antecedents, prompting consideration of acquired mimics of genetic disorders, such as BS/GS (5, 6). Notably, up to 50% of adult patients clinically diagnosed with Gitelman syndrome do not harbor mutations in known causative genes, suggesting an alternative etiology (7).

In our case, the patient exhibited persistent hypokalemia, metabolic alkalosis, elevated renin and aldosterone levels, and normotension, without diuretic use or overt volume loss. Imaging showed focal cortical atrophy of the right kidney with a reduced uptake on DMSA scintigraphy, suggestive of localized ischemia. Fluid therapy primarily corrected acute functional hypovolemia, thereby attenuating RAAS overactivity and improving markedly elevated renin activity observed at presentation. However, fluid therapy did not reverse the ischemic scarring. After discharge, when fluid intake was insufficient or during hot weather, the patient again demonstrated increased renin activity and disproportionate aldosterone responses. Thus, the pathophysiology appears to involve both systemic hypovolemia and focal renin activation within the scarred kidney, forming a vicious cycle in which volume depletion triggers further RAAS activation and clinical deterioration.

Table 3. Results of the Furosemide and Captopril Challenge Tests.

Furosemide test			
Parameter	Baseline	60min	120min
Plasma renin activity (ng/mL/h)	<0.2	1.1	0.8
Plasma aldosterone (pg/mL)	25.3	315	318
Na (mmol/L)	138	138	136
K (mmol/L)	4.6	4.2	4.4
FENa (%)	0.4	7.1	1.8
FEK (%)	5.1	29.0	21.0

Captopril challenge test			
Parameter	Baseline	60min	120min
Plasma renin activity (ng/mL/h)	0.5	1.1	1.4
Plasma aldosterone (pg/mL)	98.4	35.8	27.8

Furosemide (20 mg) was administered intravenously. After the injection, the patient remained in a seated position for 2 hours, and blood samples were collected at baseline, 1 hour, and 2 hours. Captopril (50 mg) was administered orally, and blood samples were collected at baseline, 1 hour, and 2 hours while the patient remained in a resting supine position. Na: sodium, K: potassium, FENa: fractional excretion of sodium, FEK: fractional excretion of potassium

Taken together, these findings suggest that the pathophysiology is acquired rather than genetic in nature. Although genetic testing was not performed, the diagnosis of true BS/GS was considered unlikely given the absence of a family history, reversibility of the biochemical abnormalities following isotonic saline infusion, and favorable clinical course.

Furthermore, previous studies have demonstrated that patients with BS/pseudo-BS exhibit blunted pressor responses to exogenous angiotensin II, attributed to chronic salt wasting, angiotensin II type 1 (AT1) receptor desensitization, prostaglandin E₂-mediated vasodilation, and hypokalemia-related vascular hyporeactivity (8, 9). This phenomenon, together with systemic hypovolemia, may explain the paradox of marked RAAS activation in the absence of hypertension.

While RAAS activation is classically attributed to systemic hypotension or volume depletion, local perfusion defects, such as those caused by infection-related renal scarring, may also independently trigger renin release and activate RAAS. Such focal renin activation, despite a preserved global renal function, has been reported in pediatric patients with urinary tract disease-associated renal scars, where renin-producing cells were enriched in fibrotic areas (10). Experimental studies further demonstrate that under homeostatic stress, such as a low sodium intake, hypotension, or angiotensin-converting enzyme inhibitor treatment, vascular smooth muscle cells and other renin-lineage descendants can de-differentiate and re-acquire renin-producing capacity (11), suggesting that chronic renal injury or fibrosis may promote focal renin release and reactivation via cellular reprogramming. In our case, focal renal ischemia likely served as a trigger for RAAS activation, while chronic undernutrition may have amplified its downstream effects, ultimately leading to potassium-wasting alkalosis and a biochemical profile resembling BS/GS.

Another noteworthy observation was the exaggerated aldosterone response during furosemide loading, which appeared disproportionate to the modest increase in PRA. This finding suggests a state of heightened adrenal sensitivity to angiotensin II (Ang II). Previous studies have shown that chronic sodium depletion can upregulate AT1 receptors in the adrenal zona glomerulosa, thereby augmenting aldosterone responsiveness (12, 13). In addition, chronic activation of the RAAS itself may also induce structural and functional remodeling of the adrenal cortex, leading to a hyper-responsive state. Prolonged Ang II stimulation has been shown to enhance aldosterone synthesis not only by upregulating CYP11B2 transcription but also by increasing cholesterol uptake from circulating lipoproteins, augmenting StAR protein expression, and enlarging zona glomerulosa cells. Furthermore, chronic Ang II exposure increases the expression of AT1 receptors in glomerulosa cells, thereby amplifying adrenal responsiveness to circulating stimuli (14). In our case, sustained Ang II stimulation resulting from chronic sodium deficiency may have promoted structural and functional remodeling of the adrenal zona glomerulosa, thereby inducing excessive aldosterone secretion and diminished responsiveness to potassium supplementation, despite normotension.

Nutritional and hormonal parameters further support the presence of chronic catabolic stress. The patient exhibited a low BMI and persistently reduced IGF-1 levels, vitamin D deficiency, and secondary hyperparathyroidism. A multicenter retrospective study from Japan reported that patients with pseudo-GS presented with a significantly lower BMI than genetically confirmed GS cases (18.7 ± 4.8 vs. 21.2 ± 3.5 kg/m², $p=0.02$), along with an older age at the diagnosis, female predominance, and lower eGFR (15). The marked reduction in the BMI in pseudo-GS is thought to reflect the

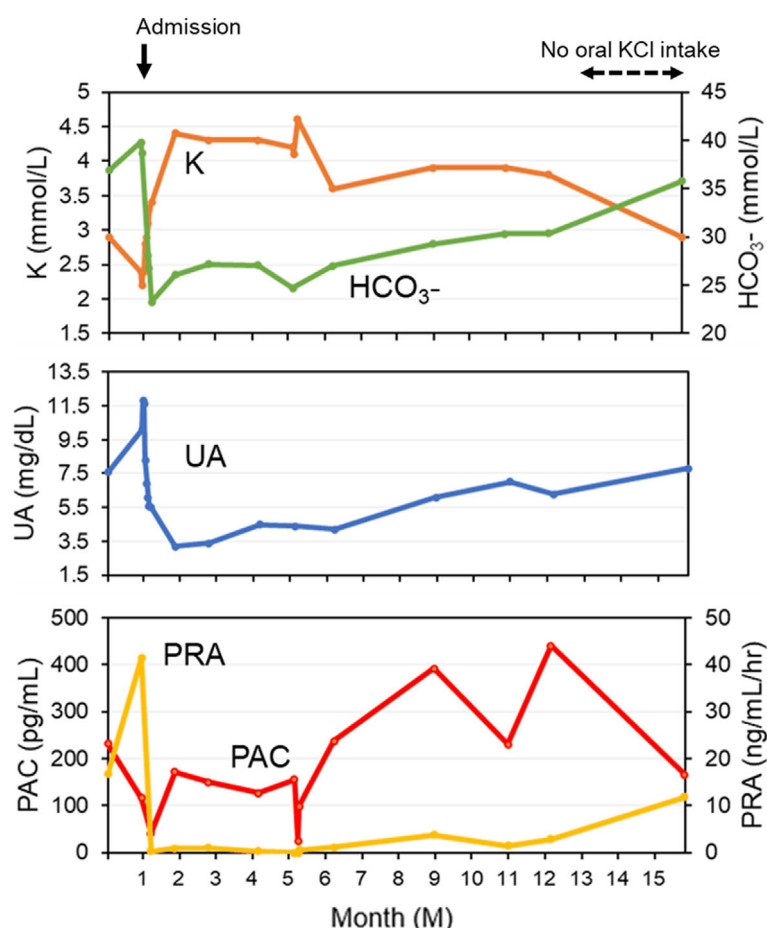


Figure 2. Clinical course and changes in laboratory parameters. Time course of serum potassium, bicarbonate, uric acid, plasma renin activity (PRA), and plasma aldosterone concentration (PAC) during hospitalization and follow-up. The arrows indicate the timing of isotonic saline infusion and key therapeutic interventions.

underlying chronic volume depletion and malnutrition, both of which may contribute to enhanced RAAS activity. In the present case, transient hyperuricemia that normalized rapidly after saline infusion further supports the presence of functional hypovolemia, distinguishing the presentation from true BS, in which serum urate typically remains unchanged despite the correction of metabolic abnormalities (16).

Catabolic stress and prolonged electrolyte imbalance can also affect skeletal muscle function. In our patient, although chronic hypokalemic myopathy could not be completely excluded, the absence of persistent weakness and normal creatine kinase levels argued against structural muscle damage, suggesting that the functional effects of hypokalemia were the main contributors to her muscle symptoms.

Importantly, in the present case, fluid and salt restriction in response to mild edema paradoxically exacerbated RAAS activation, hypokalemia, and metabolic alkalosis. This represents a key clinical pitfall of pseudo-BS/GS, in which conventional volume restriction may be counterproductive by reinforcing hypovolemic stimuli. Notably, even a small amount of isotonic saline administered after the furosemide loading test resulted in transient peripheral edema and elevated BNP levels, suggesting persistent aldosterone excess

and impaired sodium handling. A similar physiological mechanism has been described in patients with eating disorders, in whom delayed suppression of RAAS activity after the cessation of purging can lead to fluid retention and acute weight gain (17). This shared pathophysiological basis may also underlie the heightened fluid sensitivity observed in our case. In clinical practice, the presence of mild edema in such patients may reflect a transitional phase of recovery from RAAS hyperactivation, rather than simple overconsumption of salt and water. At this stage, maintaining an appropriate intake rather than imposing restrictions can stabilize the electrolyte balance without recurrence of edema, as shown by our patient's course. This consideration is particularly relevant when hypovolemia and compensatory behaviors coexist.

This case highlights several important clinical and conceptual implications. First, in patients presenting with RAAS-driven hypokalemia and metabolic alkalosis, clinicians should maintain a high index of suspicion for acquired mimics of hereditary tubulopathies, particularly in the absence of diuretic use, gastrointestinal loss, or genetic confirmation. Nutritional and imaging assessments may uncover overlooked contributors such as renal scarring, undernutri-

tion, or chronic catabolic stress. Radiographic imaging with DMSA has long been recognized as a sensitive modality for detecting focal cortical scarring, particularly in patients with a history of recurrent urinary tract infections (18).

Second, this case invites a re-examination of the current disease framework that dichotomizes BS/GS into strictly genetic versus acquired categories. Rather than being a binary distinction, these syndromes may exist on a functional spectrum of RAAS dysregulation, ranging from irreversible genetic defects to potentially reversible acquired states mediated by ischemia, inflammation, or nutritional factors. Recognizing this pathophysiological continuum may refine diagnostic accuracy and expand therapeutic approaches.

Third, the limitations of this study should be acknowledged. Genetic testing was not performed, and histopathological confirmation of focal renin activation within the scarred kidney was unavailable. Nevertheless, the diagnosis was inferred based on the clinical presentation, biochemical reversibility, and imaging findings. Rapid improvement with fluid and salt repletion strongly supports the proposed mechanism.

In conclusion, this case underscores the need for increased awareness of pseudo-BS/GS, particularly in cases driven by focal renal ischemia and nutritional stress. In patients with unexplained hypokalemic alkalosis, especially in women with a low BMI and a history of recurrent UTIs, clinicians should carefully consider focal renin activation within the scarred kidney as a potential contributor. Equally important, clinicians should avoid undue suspicion of diuretic abuse or eating disorders when encountering such patients because premature attribution may hinder an accurate diagnosis and appropriate management.

Written informed consent for publication of clinical details and clinical images was obtained from the patient. A copy of the consent form is available for review by an editor.

Author's disclosure of potential Conflicts of Interest (COI).

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