

1 **Acute phosphate nephropathy successfully treated with hemodialysis:**
2 **a case report and literature review**

3 **Abstract**

4 Acute phosphate nephropathy (APhN) is a kind of acute kidney injury resulted from
5 oral sodium phosphate solutions (OSPS). OSPS, a hyperosmotic purgative used in
6 bowel cleansing before colonoscopy, contains a large amount of phosphorus and
7 causes calcium phosphate crystals precipitation in the renal tubule. APhN seems less
8 reversible than other forms of acute tubulopathy and might predispose patients to
9 chronic kidney disease. We reported a 53 year-old woman without underlying kidney
10 disease developed APhN with seizure after taking OSPS 45 ml per day for 4 days. A
11 session of 4-hour hemodialysis was undertaken emergently for the symptomatic
12 hypocalcemia and severe hyperphosphatemia, resulted in a prompt resolution of
13 seizure. Her serum calcium and phosphate level, as well as renal function also
14 returned to normal ranges after supportive management for days. This case reminds
15 physicians of risk factors and complications of APhN. Early hemodialysis may play a
16 role in preventing untoward consequences.

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18 **Key words:** Acute phosphate nephropathy, Hemodialysis, Hypocalcemia,
19 Hyperphosphatemia, Oral sodium phosphate solutions

20

21 **Introduction**

22 Acute phosphate nephropathy (APhN), previously termed acute nephrocalcinosis,
23 is a kind of crystal nephropathy caused by oral sodium phosphate solutions (OSPS)
24 [1,2]. While OSPS-related phosphorus loading results in severe hyperphosphatemia
25 and hyperphosphaturia, calcium.phosphate crystals deposit in the renal tubule and
26 acute kidney injury (AKI) occurs. Hyperphosphatemia is less commonly seen in the
27 absence of renal failure, however, OSPS can cause hyperphosphatemia even in
28 patients without underlying renal insufficiency.

29 OSPS (Fleet Phospho-soda), a hyperosmotic purgative with good efficacy in
30 bowel cleansing, was used for colonoscopy preparation since 1990 and reported for
31 the first time to cause APhN in 2003 [2,3]. Subsequent studies showed that 1-4% of
32 relatively healthy individuals developed some degree of renal failure after OSPS use
33 [4]. Although Fleet Phospho-soda had been withdrawn from the market of United
34 States after the warning statement of Food and Drug Administration in 2008, OSPS is
35 still used in some areas. Herein, we reported a case of APhN which was successfully
36 treated with hemodialysis (HD).

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Case report

A 53-year-old woman with type 2 diabetes mellitus and hypertension was admitted to our orthopedic ward for dislocation of right hip prosthesis which was implanted due to right femoral neck fracture 3 months earlier. At admission, constipation with ileus was noticed. Thus she was made nothing by mouth with intravenous fluid supplementation, and Fleet Phospho-soda® 45 ml daily was later prescribed for stool impaction unresponsive to enema. However, seizure attacked after four-day Fleet Phospho-soda® ingestion on the 5th admission day. No evidence of intracranial lesion disease was found. The seizure was not well controlled despite intravenous diazepam and phenytoin. The state blood tests revealed blood urea nitrogen (BUN) of 51.3 (8-25) mg/dL, creatinine of 2.3 (0.5-1.4) mg/dL, sodium of 157 (135-144) mEq/L, potassium of 1.7 (3.5-5.0) mEq/L, phosphate of 18.6 (2.5-4.5) mg/dL, total calcium of 4.2 (8.6-10.3) mg/dL, and albumin of 2.6 (3.6-5.0) g/dL. No other nephrotoxic agents were used and no clinical signs of volume depletion were noted. Whereas spot urine biochemistry examinations disclosed hypocalciuria and hyperphosphaturia with increased fractional excretion of phosphate. Besides, elevated serum parathyroid hormone level was also found. (Table 1).

By nephrology consultation, the diagnosis of APhN was established and an emergent HD was performed. After one session of 4-hour HD, the seizure subsided

57 completely while serum phosphate and calcium levels returned to 6.5 mg/dL and 7.2
58 mg/dL, respectively. Intravenous fluids with half saline 2000 mL per day were
59 supplied continuously to decrease calcium phosphate deposits in the renal tubule. The
60 blood biochemistries examined 2 days after the HD session were BUN of 37.6 mg/dL,
61 creatinine 1.5 mg/dL, sodium 151 mEq/L, potassium 3.2 mEq/L, calcium 7.3 mg/dL,
62 and phosphate 3.4 mg/dL. The patient was discharge on the 13th admission day with
63 completely recovered renal function and serum electrolytes (Table 1), followed by a
64 uneventful course during the 2-year follow-up period until now.

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66 **Discussion:**

67 We reported a case of APhN diagnosed by the history of OSPS intake, AKI,
68 hyperphosphatemia and hyperphosphaturia. It is noteworthy that hyperphosphatemia
69 and hypocalcemia can develop in renal failure from any etiologies, however,
70 hyperphosphaturia only occur in the situation of excess exogenous phosphate (eg.
71 OSPS) or endogenous phosphate from intracellular compartment (eg. rhabdomyolysis
72 and tumor lysis syndrome). The seizure was caused by hypocalcemia that was
73 associated with severe hyperphosphatemia. The hyperphosphatemia and
74 hyperphosphaturia are attributed to excess phosphorus ingestion over a short period of
75 time, as well as the impaired gastrointestinal motility which increases time for

phosphorus absorption in the intestine. Hyponatremia and hypokalemia occurred due to OSPS-related sodium loading and diarrhea. Parathyroid hormone increased in response to hypocalcemia and hyperphosphatemia but hyperparathyroidism further exacerbated hyperphosphaturia which resulted in calcium phosphate precipitation in the renal tubule. However, renal biopsy was not undergone because the patient refused.

APhN: pathophysiology and pathology

Although nephrocalcinosis by calcium precipitates with either oxalate or phosphate is usually gradual-onset, acute nephrocalcinosis may occur while extremely high phosphate is loaded. A bottle of 45-ml of Fleet Phospho-soda contains 5 g of sodium and 17.8 g of phosphate, yielding a solution with an osmolarity of 16622 mOsm/L (748 mOsm /45 ml). By taking this OSPS according to the instruction, 45 ml taken twice with 10 to 12 hours apart, the total amount of elemental phosphorus is 11.5 g, approximately 7- to 8- fold of normal daily dietary phosphorus.

After intake of OSPS, the phosphate reabsorption of renal proximal tubular decreases and the phosphate delivery to the distal tubule increases. High phosphate delivery to the distal tubule and collecting duct leads to calcium phosphate deposits which lead to kidney injury [1]. Hypovolemia from diarrhea and inadequate hydration

causes avid salt and water reabsorption in the proximal tubule, resulting in higher calcium phosphate product concentration in the distal tubule. Hypovolemia may also precondition the distal tubular epithelium which creates a ripe environment for calcium phosphate crystal adherence.

Pathological findings in APhN varied depending on the time interval between OSPS exposure and kidney biopsy. Acute tubular necrosis and chronic tubulointerstitial nephritis would be predominant in the case within and after 3 weeks of OSPS ingestion, respectively [4].

APhN: clinical manifestations and risk factors

Intake of OSPS can lead to hyperphosphatemia, hypocalcemia, hypokalemia, anion-gap metabolic acidosis, and hypernatremia or hyponatremia, as well as renal failure. Whereas the clinical features of APhN include low-grade proteinuria, a bland urine sediment and renal failure without other explanations. OSPS-induced kidney injury can be symptomatic or insidious. The symptomatic form presents with hypocalcemia-induced tetany, severe hyperphosphatemia and reversible renal failure within hours to days of OSPS ingestion. While the insidious form is generally onset after days to months but might predispose patients to chronic kidney disease.

The risk factors of APhN include advanced age, female gender, chronic kidney

disease, hypertension, diabetes mellitus, dehydration, ileus (increased phosphate absorptive time), the use of angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, diuretics and non-steroidal anti-inflammatory drugs [4,5]. High-dose OSPS and short interval between OSPS are also critical factors. Thus, OSPS should be contraindicated in patient with congestive heart failure, renal failure, ascites and gastrointestinal obstruction because of massive sodium and phosphate loading. Risk factors in the present case included female gender, ileus, hypertension and diabetes mellitus.

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123 ***APhN: Treatment***

Patients with APhN require rapid correction of abnormal electrolytes and aggressive fluid resuscitation. Urine alkalization is contraindicated because it promotes calcium phosphate crystal formation in the setting of severe hyperphosphatemia, and further decreases plasma ionized calcium concentration by the administration of sodium bicarbonate. Calcium supplementation should be administered with caution because high serum levels of calcium phosphate products will lead to metastatic calcification [2].

HD is indicated in the case with extreme hyperphosphatemia, hypocalcemia-related seizure, or severe renal failure. Immediate phosphate removal

133 by hemodialysis might contribute to a quick recovery in our patient. Besides,
 134 intravenous fluids should be given continuously to prevent further calcium phosphate
 135 precipitation and rectify residual hyperphosphatemia. Recommendations for volume
 136 repletion vary from 0.7 to 2.2 liters (at least 36 ounces with each 45 ml Fleet
 137 Phospho-soda administration), but the optimal amount may exceed 3.7 liters [6].
 138 However, the benefits of increased oral hydration should be balanced against the risk
 139 of hyponatremia. It is unknown whether electrolyte-containing oral solutions are safer
 140 than water.

141

142 ***Conclusion***

143 In summary, we reported a case of APhN presenting with seizure which subsided
 144 dramatically after a session of 4-hour HD. Her serum electrolytes levels and renal
 145 function also returned to normal ranges after supportive management for days.
 146 Despite of appropriate treatment, APhN may progress to chronic renal failure in some
 147 patients without underlying kidney disease. This case reminds physicians of the
 148 iatrogenic nephropathy and associated complications. High awareness of the risk
 149 factors for APhN, early recognition and prompt therapy could prevent untoward
 150 consequences.

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171 **Table 1. Summary of laboratory data.**

	Day -90	Day 1	Day 5	Day 6	Day 7	Day 13	Day 60	Reference
	Baseline	Admission	Hemodialysis			Discharge	Post-discharge	values
Blood tests								
BUN, mg/dL	23.0	28.4	51.3		37.6	21.1		8-25
Cr, mg/dL	0.7	0.8	2.3		1.5	0.9	0.9	0.5-1.4
Ca, mg/dL			4.1	7.2	7.3	7.6		8.6-10.3
P, mg/dL			18.6	6.5	3.4			2.5-4.5
Na, mEq/L	139	129	157		151	143	139	135-144
K, mEq/L	4.9	3.7	2.7		3.2	4.1	4.1	3.5-5.02.9
Albumin, g/dL			2.6			2.9		3.6-5.0

PTH, pg/ml	317	15-65
Arterial gas*		
pH	7.42	
PCO ₂ , mmHg	39.7	
PO ₂ , mmHg	77.1	
SatO ₂ , %	95.5	
HCO ₃ , mmol/L	25.1	
Urine tests		
Urine P/Cr	4.02	0.4-1.3
Urine Ca/Cr	0.025	0.1-1.2
FEP, %	49.7	10-15

172 **Abbreviations :**

173 BUN, blood urea nitrogen; Cr, creatinine; Ca, calcium; P, phosphate; Na, sodium; K, potassium; PTH, parathyroid hormone; FEP, fractional
174 excretion of phosphate.

175 **Note :** $FEP = [(urine\ P \div serum\ P) / (urine\ Cr \div serum\ Cr)] \times 100\%$;

176 Day 1 denotes admission day. * denotes arterial blood gas under O₂ mask 10 liters/min

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