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Acute Phosphate Nephropathy Successfully Treated with Hemodialysis: A Case Report and Literature Review

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Authors' contributions

This work was carried out in collaboration among all authors. Authors YHL, CHH and YJW collected and summarized the data of the patient. Authors YMC and CCS did the literature search and wrote the manuscript. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Acute phosphate nephropathy is a kind of acute kidney injury resulted from oral sodium phosphate solutions which are hyperosmotic purgatives used for bowel cleansing before colonoscopy, contains a large amount of phosphorus and causes calcium phosphate crystals precipitation in the renal tubule. Acute phosphate nephropathy seems less reversible than other forms of acute tubulopathy and might predispose patients to chronic kidney disease. We reported a 53-year-old woman without underlying kidney disease developed acute phosphate nephropathy with a seizure after taking oral sodium phosphate solutions 45 ml per day for 4 days. A session of 4-hour hemodialysis was undertaken emergently for the symptomatic hypocalcemia and severe

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hyperphosphatemia, resulted in a prompt resolution of seizure. Her serum calcium and phosphate level, as well as a renal function also returned to normal ranges after supportive management for days. This case reminds physicians of risk factors and complications of acute phosphate nephropathy. Early hemodialysis may play a role in preventing untoward consequences.

Keywords: Acute phosphate nephropathy; hemodialysis; hypocalcemia; hyperphosphatemia; oral sodium phosphate solutions.

1. INTRODUCTION

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

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

2. CASE REPORT

A 53-year-old woman with type 2 diabetes mellitus and hypertension was admitted to the orthopedic ward in Luodong Saint Mary's Hospital for dislocation of the 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 an enema. However, a seizure attacked after four-day Fleet Phospho-soda® ingestion (total amounts: 180 ml) 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 completely while serum phosphate and calcium levels returned to 6.5 mg/dL and 7.2 mg/dL, respectively. Intravenous fluids with half saline 2000 mL per day were supplied continuously to decrease calcium phosphate deposits in the renal tubule. The blood biochemistries examed 2 days after the HD session were BUN of 37.6 mg/dL, creatinine 1.5 mg/dL, sodium 151 mEq/L, potassium 3.2 mEq/L, calcium 7.3 mg/dL, and phosphate 3.4 mg/dL. The patient was discharged on the 13th admission day with completely recovered renal function and serum electrolytes (Table 1), followed by an uneventful course during the 2-year follow-up period until now.

3. DISCUSSION

We reported a case of APhN diagnosed by the history of OSPS intake, AKI, hyperphosphatemia, and hyperphosphaturia. It is noteworthy that hyperphosphatemia and hypocalcemia can develop in renal failure from any etiologies, however, hyperphosphaturia only occurs in the situation of excess exogenous phosphate (eg. OSPS) or endogenous phosphate from the intracellular compartment (eg. rhabdomyolysis and tumor lysis syndrome). The seizure was caused by hypocalcemia that was associated

with severe hyperphosphatemia. The hyperphosphatemia and hyperphosphaturia are attributed to excess phosphorus ingestion over a short period of time, as well as the impaired gastrointestinal motility which increases the time for phosphorus absorption in the intestine. Hypernatremia 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.

3.1 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 osmolality 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 [5]. Our patients ingested total 180 ml of OSPS (45 ml daily for 4 days) which contain 71.2 g of phosphate (22.5 g of elemental 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].

Table 1. Summary of laboratory data

	Day -90 baseline	Day 1 admission	Day 5 hemodialysis	Day 6	Day 7	Day 13 discharge	Day 60 post-discharge	Reference 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					
PCO2, mmHg			39.7					
PO2, mmHg			77.1					
SatO2, %			95.5					
HCO3, 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

Abbreviations: BUN, blood urea nitrogen; Cr, creatinine; Ca, calcium; P, phosphate; Na, sodium; K, potassium; PTH, parathyroid hormone; FEP, fractional excretion of phosphate.
Note: FEP=[(uirne P÷serum P) / (urine Cr÷serum Cr)] ×100%;
Day 1 denotes admission day. ∗denotes arterial blood gas under O2 mask with O2 flow of 10 liters/min

3.2 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 acute renal failure within hours to days of OSPS ingestion, but the kidney injury is usually reversible [6-9]. 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 [4,10]. High-dose OSPS and a 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.

3.3 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 administrated 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 by hemodialysis might contribute to a quick recovery in our patient. Besides, intravenous fluids should be given continuous*ly* to prevent further calcium phosphate precipitation and rectify residual hyperphosphatemia. Recommendations for volume repletion vary from 0.7 to 2.2 liters (at least 36 ounces with each 45 ml Fleet Phospho-soda administration), but the optimal amount may exceed 3.7 liters [11]. However, the benefits of increased oral hydration should be balanced against the risk of hyponatremia. It is unknown whether electrolyte-containing oral solutions are safer than water.

4. CONCLUSION

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

CONSENT

All authors declare that ‘written informed consent’ was obtained from the patient for publication of this paper.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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