Urol Res (1985) 13:301–304

Urological Research

Sodium Orthophosphate Hydrate ($NA_3PO_4 \cdot 12H_2O$): A New Type of Human Urinary Stone

K. M. Kim[1], H. B. Alpaugh[2], and F. B. Johnson[2]

[1] V. A. Medical Center and University of Maryland, Baltimore, and [2] Armed Forces Institute of Pathology, Washington, DC, USA

Accepted: April 30, 1985

Summary. In a series of electron microscopic studies of human urinary stones, a stone composed of sodium orthophosphate hydrate was identified. The stone was recovered from a patient who succumbed to advanced renal failure. A massive failure of the sodium pump, which cotransports phosphate across the brush border membrane of the proximal tubules is thought to be responsible for such an exceptional stone. This appears to be the first description of sodium phosphate crystal in a human urinary stone. Electron microscopy is a useful tool for stone analysis.

Key words: Electron microscopy, Urolith, Sodium phosphate, New stone component.

Introduction

Phosphate crystal deposition in humans, either physiological or pathological, occurs mainly as calcium salts with the exceptions of magnesium and ammonium magnesium phosphates in urinary stones [5]. In view of the high solubility, sodium phosphate crystals in human urine have been virtually unknown. In a series of electron microscopic studies of human urinary stones, a stone which consisted solely of sodium orthophosphate hydrate was encountered.

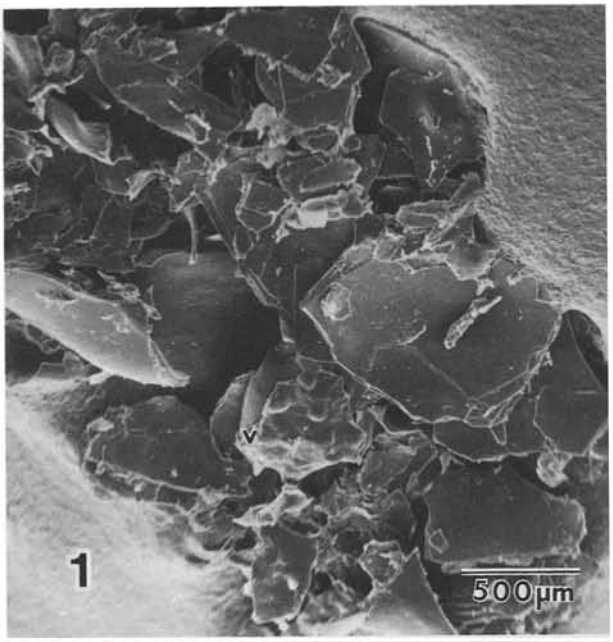
Materials and Methods

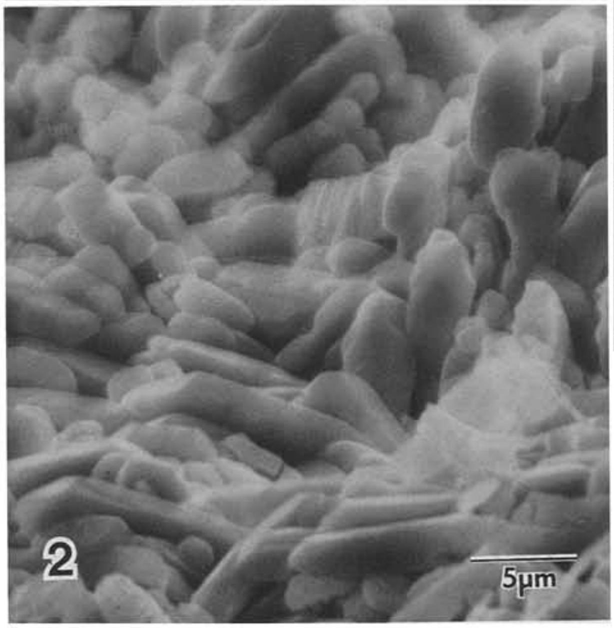
The patient was a 91-year-old black male who sufferred from chronic renal failure due to severe arteriolar nephrosclerosis associated with secondary hyperparathyroidism and hyperkalemia. He also had aortic stenosis, gout, adrenal cortical insufficiency and essential thrombocytosis. The patient remained comatose during his last hospital admission of 8 days duration. His blood urea nitrogen ranged from 85 to 175 mg/dl; potassium 6.5 to 8 mEq/l; calcium 8.6 to 6.5 mg/dl; inorganic phosphorus 7.1 to 7.9 mg/dl; HCO_3^- 10 to 17 mEq/l; and blood pH was 7.15. His urine electrolytes were measured once, revealing osmolality of 264 mOsm/kg H_2O, Na 57 mEq/l, K 11 mEq/l and Mg 2.3 mEq/l. Urine calcium and phosphate were not recorded. Despite vigorous treatment, the patient developed anuria 3 days after admission which improved only slightly with dopamine infusion. The patient expired from Klebsiella pneumonia following an episode of pulmonary edema. An oval grayish white stone measuring 1 x 0.5 cm in diameter was found in a mildly distended renal pelvis on autopsy.

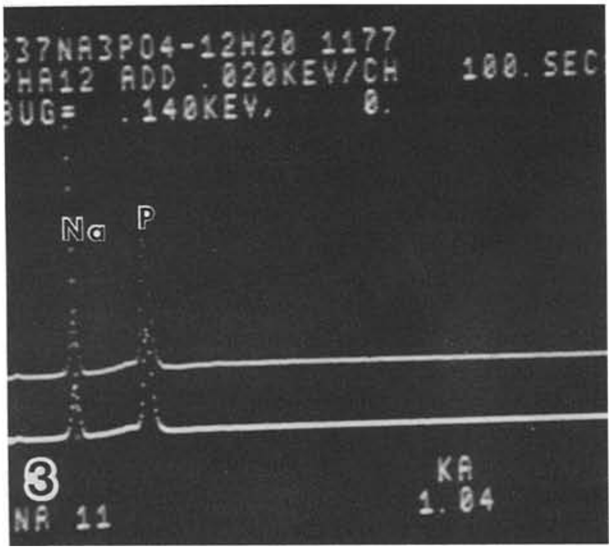
The stone crumbled into pieces when it was cracked with a razor blade and a hammer. Larger pieces were mounted on an aluminum stub with the fractured surface up, using carbon conductive glue. The mounted specimens were coated with either carbon or gold in a sputter coater and examined with an ETEC Autoscan scanning electron microscope (SEM) and energy dispersive x-ray microanalysis (XA). Representative portions of the stone were ground with a mortar and a pestle, mounted on formvar coated grids and an additional carbon coating was applied to stabilize the particles in an evaporator. Selected area electron diffraction was performed on the powdered stone using gold coated grid as a standard in a JEOL 100CX Analytic Electron Microscope. All the particles demonstrating unique morphology by transmission electron microscopy were subjected to electron diffraction at 80 KeV and camera length of 76 cm. X-ray diffraction was performed using a Debye-Scherrer diffraction camera. Infrared spectra were obtained with a Perkin-Elmer 727 Infrared Spectrometer using the KBr pellet technique.

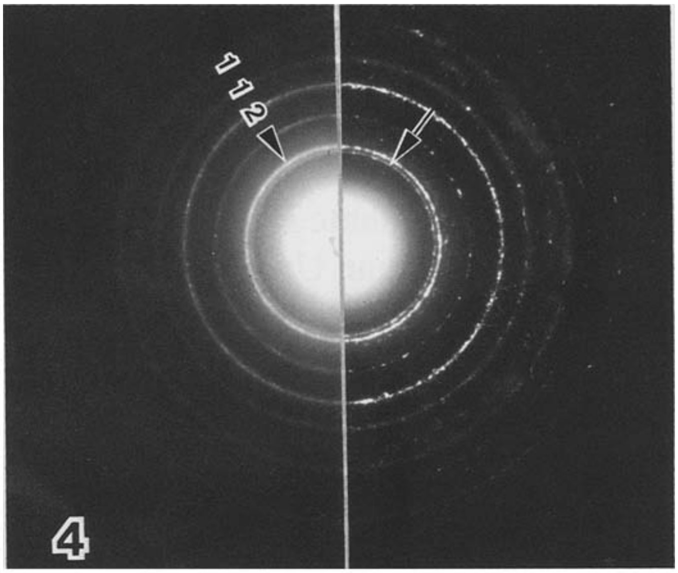
Results

SEM of the stone revealed an aggregate of spheroidal shells with empty centers (Fig. 1). The inner surface of the shell was smooth. The outer surface appeared granular with nodular protuberances. The fractured surface of the shell was conchoidal (smoothly curved) and the shell wall appeared to be formed by multiple layers of thin lamellar crystals. Amid the aggregate of the shells, there were occasional clusters of oval plates or spindle shaped particles (Fig. 2). XA of both the shells and the plates yielded exclusively the peaks of Na and P, which were similar in heights to those of the authentic $Na_3PO_4 \cdot 12H_2O$ (Fischer Scientific Co., Pittsburgh, Pa.) (Fig. 3). Electron and x-ray diffractions of both the shells and the plates produced the powder pattern most consistent with sodium orthophos-









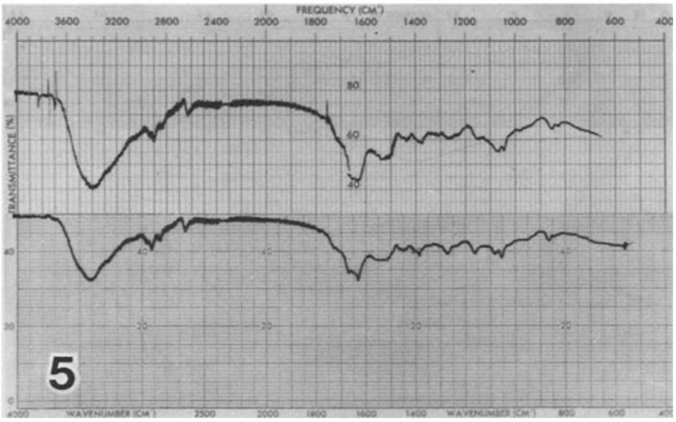


Fig. 1. The stone consisted mainly of an aggregate of spherical shells with empty centers

Fig. 2. A small amount of oval plate shaped crystals were seen in areas

Fig. 3. X-ray analysis of both the shells and the plates yielded *Na* and *P* (*upper spectrum*). The peaks are very similar to an authentic $Na_3PO_4 \cdot 12H_2O$ (*lower spectrum*) in heights

Fig. 4. Electron diffraction pattern of the stone (*left*) and the authentic $Na_3PO_4 \cdot 12H_2O$ (*right*) which show identical powder patterns. X-ray diffraction yielded similar patterns. Both patterns contain an extra d spacing (*arrow*) which is not listed in the JCPDS Powder. Diffraction file (see Table 1)

Fig. 5. Infrared spectrum of the stone (*upper*) and the reference $Na_3PO_4 \cdot 12H_2O$ (*lower spectrum*)

Table 1. Lattice spacings of the stone crystal compared with JCPDS standard measurements for $Na_3PO_4 \cdot 12H_2O$[a]

hkl	dA stone	dA $Na_3PO_4 \cdot 12H_2O$
002	6.35	6.34
102, 111	5.33	5.39
–	4.69	–[b]
112	4.34	4.34
212	3.30	3.32
104	3.00	3.03
204	2.71	2.702
214	2.45	2.461
323	2.06	2.065
315	1.89	1.896

[a] Powder Diffraction File No. 10–191, Joint Committee on Powder Diffraction Standards, Philadelphia

[b] The d spacing is not listed in the JCPDS standard measurements. However, authentic crystal of $Na_3PO_4 \cdot 12H_2O$ produced the same d spacing (see Fig. 4)

phate hydrate (Table 1). Furthermore, the diffraction pattern of the stone was identical to that of simultaneously diffracted authentic sodium orthophosphate hydrate crystal (Fig. 4). The pattern frequencies of the infrared spectra of the stone and the authentic $Na_3PO_4 \cdot 12H_2O$ were nearly identical (Fig. 5).

Discussion

Urinary stones have been analyzed by various methods, mainly x-ray diffraction and infrared spectroscopy [2, 3, 8, 9, 14, 18, 19]. Unfortunately, these methods are not without limitations in their sensitivity and reliability particularly in the detection of minor components of urinary stones [1, 9, 14, 16, 17]. There has recently been an increasing utilization of electron microscopy (EM) for the study of urinary stones [2, 6, 7, 11, 15] and its potential as a tool for stone analysis has recently been claimed [12]. The discovery of a new kind of stone by EM in a small series as described here further verifies the claim.

In view of an extra line in the electron and x-ray diffraction patterns, the presence of an additional phase of sodium phosphate was initially suspected. However, the same line appeared in the diffraction pattern of the authentic crystal. Deliberate heating of both the stone and authentic crystals at 100 °C overnight eliminated the extra line. The line thus appears to be related to unstable water molecules in the crystal.

Unfortunately, a detailed study of electrolytes in this patient's urine has not been performed. Nevertheless, formation of such an extraordinary stone indicates that an extreme state of high sodium and phosphate, and low calcium concentrations in urinary tract may occur in advanced renal failure. A five fold increase in phosphaturia occurs in advanced renal failure as a result of the secondary hyperparathyroidism and renal tubular adaptation to hyperphosphatemia [20]. Extracellular fluid expansion has been known to cause phosphaturia and natriuria secondary to a decrease in the renal tubular reabsorption of these ions [10]. Considerable evidence indicates that fluid expansion causes a release of natriuretic hormone, which has yet to be identified, into the circulation. The humoral factor is believed to inhibit Na^+-K^+-ATPase of the tubular epithelial cells [4]. Inasmuch as phosphate is cotransported by the powerful sodium pump across the brush border membrane, an extensive failure of the sodium pump in the proximal tubules would have accounted for the phosphaturia associated with natriuria. Acid base imbalance, adrenal cortical insufficiency and diuretics are known to cause phosphaturia as well [13]. Concurrent existence of all these phenomena may have led to such an exceptional stone formation in this patient.

In view of its large size, it is unlikely that the stone had formed during the terminal anuric phase of the patient. Interestingly, scanty but discrete precipitates containing sodium and phosphorus were seen in 2 out of 20 prostatic stones similarly studied by x-ray analysis (unpublished data). Failure of detecting sodium phosphate stone in the past may not be due entirely to its rarity. It is possible that stones recovered at postmortem may have been neglected.

References

1. Beeler MF, Veith DA, Morris RH, Biskind GR (1964) Analysis of urinary calculus. Comparison of methods. Am J Clin Pathol 41:553–560
2. Berg W, Szabo-Földvari E (1982) Das kristalline Harnsediment in seiner Bedeutung für die Atio-Pathogenese und Diagnostik des Harnsteinleidens. Jena, Friedrich-Schiller-Universität
3. Brien G, Schubert G, Bick C (1982) 10,000 analyses of urinary calculi using x-ray diffraction and polarization microscopy. Eur Urol 8:251–256
4. Buckalew VM Jr, Gruber KA (1984) Natriuretic hormone. Ann Rev Physiol 46:343–358
5. Carmona P, Bellanato J, Cifuentes-Delatte L (1980) Trimagnesium orthophosphate in renal calculi. Invest Urol 18:151–154
6. Dosch VW, Koester C (1975) Rastelelektronenmikroskopie von Harnsteinen. Z Urol 68:25–41
7. Cifuentes-Delatte L (1983) Crystalluria. In: Roth RA, Finlayson B (eds) Stones, clinical management of urolithiasis. Williams Wilkins, Baltimore, pp 8–20
8. Gault MH, Ahmed M, Kalra J, Senciall I, Cohen W, Churchill D (1980) Comparison of infrared and wet chemical analysis of urinary tract calculi. Clin Chim Acta 104:349–359
9. Herring LV (1962) Observation of the analysis of ten thousand urinary calculi. J Urol 38:545–562
10. Jahn HA, Rocha GM, Kondo M, Schohn DC, Schmitt RL (1980) Natriuresis and phosphaturia during extracellular volume expansion, blood volume expansion or stimulation of the intrathoracic volume receptors. Adv Exp Med Biol 128:93–105
11. Kim KM (1982) The stones. Scanning Electron Microsc IV: 1635–1660
12. Kim KM, Resau J, Chung J (1984) Scanning electron microscopy of urinary stones as a diagnostic tool. Scanning Electron Microsc IV:1819–1831

13. Knox FG, Greger F, Lang FC, Marchand GR (1977) Renal handling of phosphate: Update. Adv Exp Med Biol 82:3–14
14. Lagergren C (1956) Biophysical investigation of urinary calculi. Acta Radiol (Stockh) 133(Suppl):1–71
15. Leusmann DB (1983) Routine analysis of urinary calculi by scanning electron microscopy. Scanning Electron Microsc I: 387–396
16. Otnes B, Montgomery O (1980) Method and reliability of crystallographic stone analysis. Invest Urol 17:314–319
17. Pollack SS, Carlson GL (1969) A comparison of x-ray diffraction and infrared technics for identifying kidney stones. Am J Clin Pathol 52:656–660
18. Prien EL, Prien EL Jr (1968) Composition and structure of urinary stone. Am J Med 45:654–672
19. Sutor DJ, Wooley WE (1971) Composition of urinary calculi by x-ray diffraction: collected data from various localities. IX–XI. Br J Urol 43:268–272
20. Wong NLM, Quamme GA, Dirks JH, Sutton RAL (1980) Phosphate handling by the remnant dog kidney in the presence and absence of the contralateral normal kidney. Adv Exp Med Biol 128:117–124

Dr. K. M. Kim
Associate Professor of Pathology
University of Maryland
Veterans Admin. Medical Center
3900 Loch Raven Blvd.
Baltimore, MD 21218, USA