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Ammonium Urate Urinary Stones

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Summary. Until the last century, ammonium urate stones were quite common in preindustrial Europe. In contemporary practice these stones are found in developing countries, and are associated with uric acid and ammonium-enriched urine. Such conditions may occur with a) urealytic infection, resulting in mixed ammonium urate/magnesium ammonium phosphate precipitates and b) urinary phosphate deficiency of alimentary origin, resulting in precipitates free of magnesium ammonium phosphate, in sterile urine. The latter situation is closely related to a diet poor in phosphate and to a low fluid intake common in endemic lithiasis areas. Ammonium urate and uric acid have different solubility patterns dependent on pH, and consequently treatment will be different in each case.

Key words: Urolithiasis, Ammonium urate, Epidemiology, Deficient diet, Urinary phosphate.

Introduction

Ammonium urate urolithiasis is a rare condition in industrial countries. We present a case report together with a discussion of the epidemiology, etiology and treatment of the condition.

Materials and Methods

A 34-year-old Spanish housemaid presented with symptoms of bilateral renal colic. Her mother had also suffered from renal stone disease. During the year preceding her admission, she had followed a diet, loosing more than 30 kgs in a few months. Her food intake was composed of vegetables and carbohydrate-rich foods, and was almost devoid of meat, fish and dairy products. Fluid intake was limited to a few deciliters of carbonated soda.

Blood chemistry was within normal limits (hematocrite: 37.9%; hemoglobine: 12.6 g%; leucocytes: 9,700/ml; urates: 189 μmol/l; creatinine: 74 μmol/l; calcium: 2.46 mmol/l). Urinary pH varied between 5 and 6.4; urine cultures were sterile.

Intravenous urography showed radiolucent stones in the right renal pelvis and in the middle third of the left ureter.

Following surgical removal, the two dark brown-red stones, about 10 mm in diameter, were air and alcohol-dried, then halved with a low-speed isomet saw; one half served to prepare ground sections, the other was ground and sieved to 200 mesh. Infrared spectra were recorded with a Perkin-Elmer 683 spectometer. The technique employed was that of KBr disks (1 mg sample and 250 mg KBr). X-Ray diffraction patterns were obtained from samples by means of a Guinier camera with monochromator and focalization.

Results

Morphological observation of the ground sections by means of the polarizing microscope showed spheruliths (about 30 microns in diameter) aggregates and layered chunks of ammonium urate crystals (Fig. 1).

X-ray diffraction patterns (Table 1) and infrared spectra showed that the stones were composed of pure ammonium urate. The most characteristic infrared band of this substance is found at 598 cm^{-1} [20].

Discussion

Historic and Epidemiologic Background of Ammonium Urate Lithiasis

In the early nineteenth century, ammonium urate was a common component of urinary stones in Europe. At present it accounts for only about 0.2% of lithiasis in industrial countries. However, in some developing countries the condition remains endemic (Table 2). Improvement in nutrition in industrial countries has caused the virtual disappearance of this form of endemic lithiasis [1, 3, 18, 23].

Armbruster [2] reported a series including 15 ammonium urate stones observed in the Ruhr area. Of these, 2 stones were from German adults with urinary tract infection. The other 13 were from children of Turkish migrant

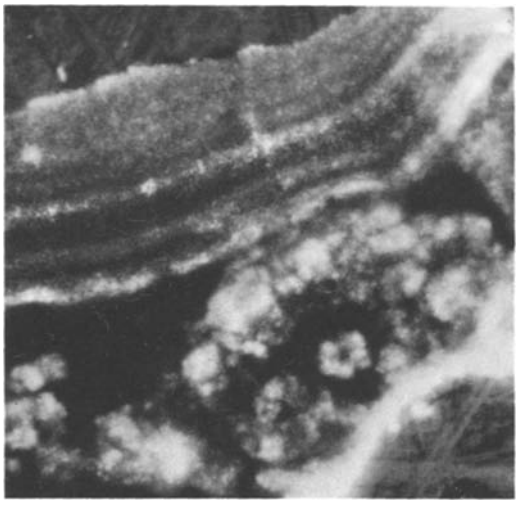

Fig. 1. Polarized light micrograph of a ground section, displaying spherulite aggregates and layered chunks of ammonium urate crystals

Table 1. X-ray diffraction pattern of the concretions

Observed d(A)	Ammonium urate [22]	
	d(A)	I/I_1
9.7	9.68	10
–	9.2	1
8.6	8.57	15
5.65	5.64	60
–	5.10	2
4.87	4.88	8
–	4.59	8
–	4.3	2
3.65	3.63	8
3.45	3.46	100
3.35	3.35	3
–	3.32	3
3.25	3.25	17
3.16	3.16	12
3.02	3.01	40
2.95	2.93	8

workers, some born in Turkey, some born in Germany. Comparative clinical examinations, blood and urine analysis of Turkish and German children failed to show any difference. Armbruster relates the tendency of the Turkish children to develop this type of stone to socio-economic factors such as nutrition and hygiene.

Etiology and Precipitation Conditions

Ammonium urate stones can be separated in two morphological types [6].

Type 1 Stones. Crystals are large, yellowish, have a needle-like configuration and a disordered disposition, mixed with magnesium ammonium phosphate crystals. This type is often associated with urealytic infection.

Ammonium urate precipitation may begin only when urine is oversaturated by both uric acid and ammonium ions (pH in the neutral to alkaline range) [11, 24]. Normal urine submitted to in vitro urealytic infection gives rise to magnesium-ammonium phosphate precipitates, whereas normal urine previously oversaturated with uric acid and subsequently submitted to urealytic infection results in mixed magnesium-ammonium phosphate/ammonium urate

Table 2. Ammonium urate-containing stones in percent of total number of urinary calculi

Source	Period	Origin	Localization and age	% Ammonium urate	
Lonsdale (1968)	1773–1800	Norwich (GB)	Bladder, <19 years	77%	
Lonsdale (1968)	1773–1800	Norwich (GB)	Bladder, >19 years	46%	
Lonsdale (1966)	1932–1961	Norwich (GB)	Bladder, Ureter, Kidney	2.5%	
Schubert (1983)	1971–1982	Berlin (Germany)	Bladder, Ureter, Kidney	0.75%	Industrial
Herring (1962)	1959–1962	USA	Bladder, Ureter, Kidney	0.32%	
Otnes (1983)	1975–1980	Oslo (Norway)	Kidney, Ureter	0.2%	Countries
Otnes (1983)	1975–1980	Olso (Norway)	Bladder	2%	
Unni Moopan (1979)	Recent	Brooklyn (USA)	Bladder, Ureter, Kidney	0.76%	
Armbruster (1979)	Recent	Essen (Germany)	Bladder, Ureter, Kidney	8.8%	
Lonsdale (1966)	1965	Turkey	Bladder, 2–15 years	42%	
Lonsdale (1966)	1965	Turkey	Kidney, 2–14 years	34%	Developing
Shahjehan (1971)	Recent	Karachi (Pakistan)	Bladder	69%	
Shahjehan (1971)	Recent	Karachi (Pakistan)	Ureter, Kidney	47%	Countries
Shahjehan (1971)	Recent	Karachi (Pakistan)	Bladder, Ureter, Kidney	60%	
Hsu (1966)	Recent	Taiwan	Bladder, Ureter, Kidney	18%	
Hazarika (1974)	1970–1972	India	Adults: Ureter, Kidney	9.4%	

precipitates [24]. These precipitates correspond to morphological type 1 stones. Large, disorganized crystals are thought to originate if precipitation takes place rapidly in a strongly alkaline environment [6].

In this context it is interesting to note that dalmatian dogs with urinary infection are known to form ammonium urate-rich stones. This breed of dogs is affected by a congenital deficiency in tubular reabsorption of uric acid, which may result in high peak concentrations of uric acid in the urine.

Type 2 Stones. Crystals are small and organized into spheruliths. Sometimes they are associated with calcium oxalate monohydrate (whewellite) crystals. Type 2 stones are formed in aseptic urines. This type of stone is that found in endemic lithiasis.

In a study on urolithiasis in Karachi (Pakistan), Shahjehan [21] indicated that, by comparison to a healthy control group, the stone-forming group had a diet deficient in calories, proteins, vitamin A and phosphorus. Phosphaturia in children, who tend to form bladder stones, was below normal. Similar reports are available for Thailand endemic stone areas [9]. Epidemiologic surveys of endemic bladder lithiasis showed an absence of urinary tract infection in most of these cases.

A purine-rich diet combined with low liquid intake may be one of the factors resulting in urinary uric acid oversaturation. This situation is common in regions of endemic vesical lithiasis and in underprivileged social environments [5].

Andersen [1] and Robertson [18] suggest a correlation between an improvement in standards of living and the decreasing frequency of ammonium urate stones. The diet poor in milk and rich in cereals eaten by children in certain underdeveloped areas could be lithogenic. This diet is acidic and phosphate-poor. (Some dietary forms of organic phosphate esters such as the phytic acid of cereals and seeds are not readily available to man, since the human intestine is relatively deficient in the enzyme phytase, essential for its hydrolysis [7]). Urinary phosphates are one of the main H^+ excretion buffers; in phosphate deficiency, ammonium will be mobilized as a buffer resulting in increased endogenous NH_3 production. In the tubular lumen, NH_3 reacts with free H^+ to give ammonium ion. Thus, urinary ammonium is increased [18].

Borden and Dean [5] studied three cases of ammonium urate lithiasis in young Navajo indians from New Mexico. All had upper urinary tract stones. One suffered urinary infection. Navajo diet is based on purine-rich Pinto beans, and their usual drink is carbonated soda. Generation of these upper urinary tract stones seems to be similar to endemic bladder lithiasis, their location in the upper urinary tract being related to low urinary flow. Ammonium urate was more frequently found in the core of vesical and renal stones than in their periphery [9, 23]. The stones may originate in the upper urinary tract and later migrate to the bladder. There, they are subject to further ammonium urate and calcium oxalate accretion.

Urates may remain soluble even in oversaturated solutions. However, once precipitation starts, it can continue even with reduced levels of urate and ammonium concentration [4]. A recent report [12] showed that in the rat, ammonium urate stone formation was initiated by portocaval shunt, which raised urinary pH, uric acid, citrate and ammonium excretion. The mean relative supersaturation product of urine with the ammonium urate phase was quite low.

Chemical dissolution of ammonium urate calculi is not possible in vivo. With decreasing pH ammonium urate solubility increases, but the risk of uric acid precipitation is also increased. At high pH, urate salts are stabilized [4].

The stones found in our case were of type 2 morphology. The cause for their formation was certainly due to voluntary dietary restriction of proteins and of dairy products, which was associated with a low fluid intake. Subsequently our patient developed anorexia. This could have been, at least partially, secondary to the phosphate deficiency [7]. Her diet remained phosphate-poor, and she suffered recurrent bilateral stones necessitating further endoscopic removal eight months later.

Treatment

Stone clearance must be achieved. Further prevention of lithogenesis is most important. Borden and Dean [5] recommend a purine-poor regimen with adequate animal protein and liquid intake, allopurinol and urinary acidification. However, in view of the metabolic conditions leading to lithogenesis, the latter suggestion does not appear to be appropriate: the increased renal ammonium production is caused by a lack of the phosphate buffer. An additional acid load should therefore be avoided, at least until phosphate metabolism is corrected.

Conclusion

Ammonium urate upper urinary tract stones were observed in a patient with sterile urine. Ammonium urate stones are commonly found in children from certain regions in developing countries. In industrial countries they are occasionally found in lower socio-economic groups (migrant workers) with similar dietary habits. Solubility of ammonium urate is very different from uric acid stone solubility, since ammonium urate salts are stabilized at high pH. Hence, it is not possible to dissolve these calculi by urinary acidification or alkalinization. Since the origin of ammonium urate in sterile-urine stones is a deficient diet (particularly in phosphates) treatment must be orientated towards prevention: adequate nutrition and the administration of allopurinol.

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