Milk of Calcium Renal Stone in a Patient with Acute Promyelocytic Leukemia

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A case of milk of calcium renal stone is reported. This is a rare disease in which a suspension of calcium salts is formed within a renal cyst. The pathognomonic sign is a fluid level seen in a standing position and an oval density seen in a supine position. In the present case, the milk of calcium was found to develop in a hydronephrotic kidney during the course of acute promyelocytic leukemia and this condition was suggested to be a complication of infection.

Key words: Staghorn calculus, Hydronephrosis, Renal cyst, Infection

Milk of calcium renal stone is a rare condition in which there is a suspension of calcium salts within a renal cystic lesion. The term was first applied radiologically by Howell in 1959 (1), since it resembled milk of calcium bile (limy bile), a particular form of calcium salt deposition within the gallbladder. Roentgenography reveals a mobile calcification within a cystic lesion, which shows a hemispherical calcium fluid level in a standing position, and a spherical radio-dense deposit in a supine position. Therefore, the diagnosis of this entity depends upon the demonstration of a change in the shape of the calcific density between supine and standing position.

We report here an unusual case of this disease in a hydronephrotic kidney obliterated with staghorn calculus observed in a leukemic patient, which was confirmed by postmortem examination with mineral analysis of the fluid content.

CASE REPORT

A 69-year-old Japanese male was initially admitted in September 1985 because of fever and a bleeding tendency, and he was diagnosed as having acute promyelocytic leukemia (APL) on the basis of hematological findings. Cholecystectomy for cholecystolithiasis had been performed 19 years previously, and the patient's family history was not contributory. Complete remission of APL was obtained with combination chemotherapy and he was discharged in February 1986. Five months later, APL relapsed, but a second remission was achieved and the patient was discharged in November 1986. At the first and second admissions, calculi were seen in the right renal shadow on X-ray films, but no milk of calcium sign was apparent on either occasion. Whenever myelosuppressive agents were administered, he always suffered from macroscopic hematuria and right abdominal pain with fever.

On March 20, 1987, he was re-hospitalized because of a second relapse of APL, this being the third admission. On physical examination, no bleeding tendency was noted. The right upper quadrant was tender to direct pressure but no masses were palpable.

Hematological findings on the third admission were as follows: red blood cells $4.66 \times 10^{12}$/l, hemoglobin 14.8 g/dl, platelets $29 \times 10^9$/l, white...
blood cells $1.1 \times 10^9/l$. Differential leukocyte count showed 4% band-forms, 42% segmented neutrophils, 2% monocytes and 52% lymphocytes, but there was no indication of APL cells in the peripheral blood. Bone marrow examination revealed a nucleated cell count of $75 \times 10^9/l$ with 77% leukemic promyelocytes. The erythrocyte sedimentation rate was 7 mm per the first hour, and the level of serum fibrin degradation products (FDP) was 40 $\mu$g/ml.

Blood chemistry showed the following results: GOT 68 U/ml, GPT 95 U/ml, ALP 121 U/ml, BUN 19 mg/dl, serum creatinine 1.0 mg/dl, uric acid 9.6 mg/dl. Serum Ca was 9.4 mg/dl and phosphorus was 3.0 mg/dl. Creatinine clearance was 41.7 ml/min. C-reactive protein (CRP) was negative. Serum immunoglobulin and complement levels were normal. Urinalysis revealed macroscopic hematuria, positivity for protein and a pH of 6.0. Urinary excretion of Ca was 198 mg/day and that of phosphorus was 532 mg/day. Urine culture revealed no bacterial strains.

Based on these findings, the patient was diagnosed as suffering from relapse of APL and was treated with a combination chemotherapy including aclurubicin, vindesine, neocarzinostatin, cytarabine and prednisolone, and the third remission was obtained. When leukopenia and thrombocytopenia occurred due to the chemotherapy, he suffered from right abdominal pain with high fever and macroscopic hematuria, but no bacteria were isolated from the urine, probably due to the use of antibiotics.

A plain X-ray film at the third admission revealed that one of the right renal calculi showed a peculiar rosette-shaped calcification (Figs. 1, 2), and also a round opaque shadow 4.5 cm in diameter was evident in the right hypochondrium. The shape of this round calcified shadow was found to change when the patient shifted his body position, i.e.; a spherical shape in the supine position (Fig. 1), and a half-moon shadow in the standing position (Fig. 2). From these findings, milk of calcium in the renal cyst in the middle portion of the right kidney was suggested. Ultrasonography (US) showed a cystic lesion in the middle portion of the right kidney, with mobile fluid levels as the patient’s position was changed (Fig. 3). Drip infusion pyelography (DIP)
showed an opaque density in the right side of the abdomen, and fluoroscopy 15 minutes after infusion confirmed that a well circumscribed mass was associated with the middle portion of the right kidney (Fig. 4). This lesion appeared to communicate with the ureter, suggestive of obliteratorative hydronephrosis. A few calculi were also noted in the left kidney, but the left renal outlines and pelvocalyceal systems were normal. From the time of the patient's first admission, no calculi had been passed in the urine.

After the third remission was obtained with intensive chemotherapy, the patient was discharged on July 24, 1987. Unfortunately, however, on October 23, 1987, he was admitted by ambulance because of dyspnea and consciousness loss. At this time hematocrit showed only 8% and a severe bleeding tendency was noted. Despite intensive therapy he died four hours later.

Postmortem examination was carried out. Invasion of leukemic promyelocytes was noted in the bone marrow, spleen and liver. The right kidney showed renal cysts with a separated wall, and milk of calcium was removed as a slightly reddish brown turbid fluid. It precipitated innumerable minute granular particles as well as a few 3-mm stones. Also, staghorn calculus incarcerated in the right calyx was isolated (Figs. 5, 6). Histologically, the cyst wall consisted of transitional epithelium and fibrous tissue, suggesting a pyelogenic origin. The milk of calcium renal stone was analyzed by infrared
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Fig. 6. Isolated staghorn calculus.

Fig. 7. Infrared spectrum of milk of calcium. The absorption band at 1,050 cm⁻¹ is identified as calcium phosphate, and those at 1,620 cm⁻¹, 1,320 cm⁻¹ and 780 cm⁻¹ are identified as calcium oxalate.

spectrometry as described previously (2), and was found to be composed of 82% calcium oxalate and 18% calcium phosphate (Fig. 7).

DISCUSSION

This is an unusual case in which milk of calcium developed in a hydronephrotic kidney obliterated with staghorn calculus during the course of acute promyelocytic leukemia (APL). The chemical composition of this milk of calcium was also disclosed.

Milk of calcium renal stone is a rare condition characterized by fluid opacity which consists of a colloid-like sediment of innumerable minute calcific granules. This material, showing a mobile shadow, is a sludge of concretions and is altered according to a change in body position because its specific gravity is greater than that of the non-opaque contents of the cystic lesion. The milk of calcium is observed radiologically as a characteristic crescent shadow with a fluid-calcium level in a standing position, and as a spherical radio-dense deposit in a supine position (1, 3). Therefore, plain films of the abdomen in various positions are important for diagnosis.

It has been proposed that this is an acquired condition because it does not occur in childhood and the youngest patient yet described was 21 years old (4). Furthermore, the composition of milk of calcium suggests secondary rather than hereditary urolithiasis (5−7). There are three distinct types of renal milk of calcium (8), i.e., the diverticular type (D-type) formed in a calyceal diverticulum (9), the cystic type (C-type) formed in a renal cyst (10), and the hydronephrotic type (H-type) associated with hydronephrosis (11). The present case corresponds to the H-type.

The mechanism of formation of milk of calcium is not definitely known, and it is possible that the term milk of calcium renal stone was given to one particular type of radiological entity and that the above types fall into other categories. Obstruction or infection has been speculated to be the cause of the D-type or the C- and H-types, respectively. In the D-type, the communicating sinus to the pyelocalyceal system is obliterated with stasis of its content and calculi may be formed (12). Infection is suggested to be a factor in the formation of milk of calcium renal stone in both C- and H-types (13, 14). This is, however, not the entire picture, since very few among the vast number of patients with obstruction or infection develop this disorder. Regarding the present case, bacterial infection in the pyelogenic cyst may have provided a milieu in which this disorder was able to occur. On the other hand, drug-induced urolithiases are known. Particularly, adrenocorticosteroid hormone-induced urolithiasis
via the increase in the urinary excretion of calcium has been well recognized (15). In our patient, combination chemotherapy including prednisolone (PSL) had been administered through the course. Therefore, PSL may also be responsible for stone formation. Moreover, some constitutional factor for urolithiasis is also speculated, because a few renal calculi were seen at the first admission.

This disease may be asymptomatic, but as seen in the present case, symptoms such as pain, hematuria, pyuria and fever can occur in the presence of urinary tract infection (8-10). In our patient, fever and right abdominal pain were seen simultaneously when the leukocyte count fell due to chemotherapy for APL. In addition, hematuria due to the bleeding tendency in APL with the presence of calculi led to massive bleeding.

For differential diagnosis from limy bile of the gallbladder, DIP is essential, although cholecystography should also be performed. However, the common characteristic of the H-type is that it is associated with renal dysfunction (8), and thus DIP is not always necessary in such cases. Recently, findings of “milk of calcium sign” have been reported using ultrasonography (US) (16), computed tomography (CT) (17) and magnetic resonance imaging (MRI) (18). These imaging modalities would be acceptable for diagnosis even in patients with renal dysfunction. In particular the use of US with different body positions is recommended as well as other essential diagnostic methods for this disease.

REFERENCES