Cystinuria : Cause of Recurrent Renal Stones in a 4-Year-Old Girl

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Abstract

This paper presents the case report of a 4-year and 6-month old girl with cystinuria. She clinically presented with recurrent radiopaque renal stones since the age of 3 years. She received 2 subsequent operations of pyelolithotomy combined with ureterolithotomy at the age of 3 years 6 months, and pyelolithotomy alone at the age of 5 years. She was initially diagnosed as having cystinuria by the presence of hexagonal plate crystals in her acidified urine and positive for the urinary cyanide-nitroprusside test. The diagnosis was confirmed by urinary amino acid analysis using quantitative ion-exchange chromatography which revealed increased amounts of cystine and dibasic amino acids of lysine and ornithine. In spite of maintaining a high fluid intake and alkalinizing urine by giving potassium citrate after the first operation, recurrent renal stones were found. Therefore, after the second operation, D-penicillamine was additionally introduced. During the 18-month follow-up, although there were recurrent renal stones, the rate of stone formation was slower. To the authors' knowledge, this is the first case report in Thailand.

Key word : Recurrent Renal Stones, Cystinuria, D-Penicillamine, Alkalinization

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Cystinuria is an autosomal recessive genetic defect of transepithelial transport of cystine and the other dibasic amino acids in the kidney and intestine (1,2). The renal transport defect is expressed by the excessive urinary excretion of cystine, the least soluble amino acids, which results in cystine crystallization and subsequent formation of a cystine stone. Cystinuria is the cause of 1 per cent to 2 per cent of renal stones observed in adults(3,4) and about 6 per cent to 8 per cent of pediatric urinary calculi in Western countries(5,6). As the genetic transport defect exists since birth, stone formation begins in the first decade of life and continues life long. The majority of patients with cystinuria will suffer recurrent renal stone disease during their lifetime(7) with subsequent urinary tract obstruction, infection and possible renal insufficiency(7). Cystine stones are poorly fragmented by extracorporeal shock wave lithotripsy (ESWL) and hence operative lithotomy is often necessary. To prevent recurrent renal stone formation, regular medical treatment is of particular importance in affected patients(8).

CASE REPORT

A 4-year and 6-month-old girl was referred to the Pediatric Nephrology Unit, Ramathibodi Hospital for the management of recurrent renal stones. Her past medical history included recurrent abdominal pain and urinary tract infections at the age of 3 years. Her intravenous pyelography revealed bilateral hydronephrosis, right radiopaque renal stones and left distal ureteric stones. Right pyelolithotomy and lower left ureterolithotomy were successfully performed at the age of 3 years and 6 months. She had been doing well since the calculi were removed. One year post-operatively, she developed recurrent bilateral renal stones. Ultrasonography showed bilateral hydronephrosis, 2 small stones in the right upper and middle calices and a large one in the lower calyx, about 2.2 cm in diameter and a left lower pole renal stone, about 0.8 cm.

On physical examination, the patient was a healthy-looking child in no acute distress. The only abnormal finding was surgical scars on the right flank area and left lower abdomen. Laboratory studies revealed normal complete blood count ; blood urea nitrogen 11 mg/dl, serum creatinine 0.5 mg/dl, sodium 138 mmol/L, potassium 4.53 mmol/L, chloride 110 mmol/L, total CO_2 20.7 mmol/L, calcium 10.0 mg/dl,

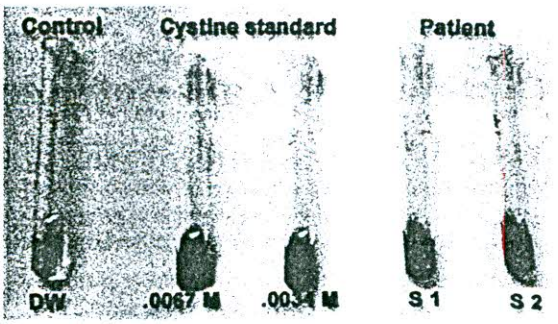

Fig. 1. The urine cyanide-nitroprusside test of the patient (S_1 and S_2) revealed magenta color compared with cystine standard and control using distilled water.

phosphate 4.8 mg/dl and uric acid 4.5 mg/dl. Urinalysis revealed yellowish color, pH 5, specific gravity 1.020, markedly positive blood, WBC 5-10/HPF, RBC >100/HPF, no casts and few hexagonal crystals. The 24-hour urine calcium was 0.19 mg/kg/day. The cystine test was performed on the patients fresh and first-morning-voided urine using cyanide-nitroprusside. After adding sodium cyanide and nitroprusside, a purple red or magenta color was revealed which was suggestive of the presence of cystine (Fig. 1). Subsequently, urinary amino acid analysis by quantitative ion-exchange chromatography revealed increased amounts of cystine and dibasic amino acids of lysine and ornithine (Table 1).

Her mother had also had a right ureteric stone which was removed at the age of 26 years. She has been doing well and no recurrence of renal stone was found during the 9-year follow-up. There was no family history of consanguinity. No other family member had history of renal stones. Laboratory findings for her mother including complete blood counts, serum electrolyte, blood urea nitrogen, serum creatinine, calcium, uric acid and urinalysis were within normal limits. The 24-hour urine calcium was 73 mg/day. Her urine cyanide-nitroprusside test was negative for cystine. There was no radiopaque stone on a recent abdominal radiograph. The urinary amino acid analysis of the mother revealed 25 per cent