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# Primary Hyperoxaluria: Case Reports and Review of Literature

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#### ABSTRACT

Primary hyperoxaluria type 1 (PH1) is a metabolic disorder that mainly affects the kidneys. It results from build-up of a substance called oxalate, which normally is filtered through the kidneys and excreted in the urine. In people with PH1, the accumulated oxalate is deposited in the kidneys and urinary tract. We report a series of 4 cases of different ages, grouping various clinical forms and presentations. Hydro-electrolyte disorders and renal insufficiency were present in all cases, genetic diagnosis was made in 2 cases. All patients were placed on supportive therapies and peritoneal dialysis. Additionally, a review of the literature for presentations, diagnosis, complications, and treatment of this rare genetic metabolic disease were included.

Keywords: Primary hyperoxaluria, Calcium oxalate, Nephrocalcinosis, Urinary stones, Oxalosis

## INTRODUCTION

Primary hyperoxaluria type 1 (PH1) is a metabolic disease that mainly affects the kidneys. It results from build-up of a substance called oxalate, which normally is filtered and excreted in the urine. In people with PH1, the accumulated oxalate is deposited in the kidneys and urinary tract. It is due to mutations in a gene called AGXT. Inheritance is autosomal recessive [1].

Signs and symptoms may include recurrent kidney stones; haematuria; and urinary tract infections. Left untreated, PH1 can result in end-stage renal disease, which is life-threatening [1,2].

## CASE REPORTS

Two males including one 4-year-old and a 13-year-old male were referred to our hospital due to acute urinary retention, occurring during their admission to another hospital for low abundant haematuria. There was no history of urinary symptoms or pain in the 2 cases.

In the first case, laboratory test results were as follows, sodium 132 mEq/L (normal range: 135 to 148), potassium 5.1 mEq/L (normal range: 3.7 to 5.6), blood urea nitrogen 0.43 g/L (normal range: 0.15 to 0.55), creatinine 12.3 mg/L (normal range: 5.7 to 12.5), calcium 98 mg/L (normal range: 84 to 102), phosphorus 41 mg/L (normal range: 23 to 47). Complete blood count (CBC) showed haemoglobin 11.9 g/dL (normal range: 9.5 to 13.5), mean corpuscular volume (MCV): 83 fL (normal range: 74 to 108), MCHC 33.2 g/dL (normal range: 30 to 36), and platelet 289.000/µL (normal range: 150.000 to 400.000). Urinalysis revealed: pH: 5, protein: negative and there was no infection.

The test for determination of urine oxalate level showed hyperoxaluria at 0.63 mmol/L, hypocitraturia at 0.02 mmol/L, with an Oxalate/Creatinine ratio at 0.21.

In the second case, blood tests were as follows, sodium 136 mEq/L, potassium 4.3 mEq/L, blood urea nitrogen 0.51 g/L, creatinine 11.7 mg/L, calcium 92 mg/L, phosphorus 52 mg/L. Complete blood count showed haemoglobin 12.6 g/dL, mean corpuscular volume: 81.5 fL, MCHC 33.7 g/dL, and platelet 304.000/L. Urinalysis revealed: pH: 5.5, protein: negative and pyelonephritis treated by antibiotherapy.

The test for determination of urine oxalate level showed hyperoxaluria at 0.72 mmol/L, hypocitraturia at 0.04 mmol/L, with an Oxalate/Creatinine ratio at 0.26.



In both cases, there was no other localization of the deposit of stones, ultrasound showed increased echo pattern and differentiation of both kidneys, associated with calcification of medullary papilla (nephrocalcinosis) (Figures 1 and 2).

Figure 1 Nephrocalcinosis and multiple stones in the urinary tract



Figure 2 Calcification of medullary papilla of the left kidney

The analysis of the urine calculation (composition and morphology) showed a pure calcium oxalate monohydrate and the genetic tests found the p.Ile244Thr mutation.

Despite supportive therapies and correction of fluid and electrolyte abnormalities, the cases gradually became oliguric progressing to anuria, and were placed on peritoneal dialysis.

A 6-month-old male was admitted to our hospital with vomiting, rapid breathing, poor feeding, and seizure. The baby was delivered via caesarean section from monoamniotic twin pregnancy, the parents were first cousins and his twin brother was healthy and asymptomatic. The elder brother was dead in the same context of respiratory distress. On admission, his body weight and length were normal for his age. Physical examination revealed agitation, and dyspnoea. Arterial blood pressure was 85/60 mmHg and his pulse was 152 beats/min.

Laboratory tests revealed haemoglobin 6.2 g/dL, blood urea 92 mg/dL, creatinine 13.8 mg/dL, bicarbonate 12 mmol/L, sodium 128 mmol/L, potassium 5.1 mmol/L, chloride 87 mmol/L, total protein 51 g/L, albumin 32 g/L, phosphate 102 mg/L and uric acid 112 mg/L. Urine analysis revealed protein and microscopic haematuria. Renal ultrasonography showed homogeneous normal-sized kidneys, with no cortico-medullar differentiation and massive nephrocalcinosis (Figure 3). Plasma oxalate concentration was 45  $\mu$ mol/L (normal <33  $\mu$ mol/L) and Urine oxalate was 0.6 mmol/m<sup>2</sup>/24 h (normal <0.5).



Figure 3 Multiples calcifications of both kidneys

The eye examination revealed oxalate retinopathy and bilateral macular yellow deposits. Correction of hydroelectrolytic disorders and peritoneal dialysis were initiated, the genetic test was not performed for this patient and systematic screening for the twin brother allowed early diagnosis of hyperoxaluria.

## DISCUSSION

Primary Hyperoxaluria are rare autosomal recessive diseases secondary to defects in glyoxylate metabolism, characterized by systemic oxalosis, highly elevated urinary oxalate, resulting in recurrent urolithiasis, progressive nephrocalcinosis that causes end-stage renal disease [3].

The epidemiology of PH1 in Morocco is rarely documented compared to neighbouring countries (Tunisia and Algeria), the estimated prevalence of PH1 in Morocco is from 1/7267 to 1/6264 [4].

Primary Hyperoxaluria type I is the most common and severe form of PH, it is due to mutations in the AGXT gene leading to deficiency of the liver enzyme called alanine-glyoxylate aminotransferase [5].

Different forms of PH1 are possible, the severe one is associated with the failure to thrive, high calcium levels in the kidneys, and kidney or urinary tract stones, they can cause a lot of symptoms including haematuria, abdominal pain, dysuria, and repeated urinary infections. PH type I causes progressive kidney damage and an early end-stage renal failure. When it appears during childhood or adolescence, the clinical features and the evolution are the same but less lightning [6,7].

Because of the decline of the kidney function, oxalate can also accumulate in different organs of the body particularly bone, skin, retinas, myocardium, blood vessels, and the central nervous system. Depending on the organ system affected, the clinical expression will be variable [8,9].

Several methods are possible for the diagnosis of PH1. The 24-hour urine collection oxalate measurement, the analysis of the composition of stones can be used. The genetic analysis allowed for the detection of the AGXT gene. Liver biopsy is used in patients in case of no identified mutation [10].

Dietary restriction of foods high in oxalate is essential; they include chocolate, rhubarb, and starfruit. Vitamin D and vitamin C should be avoided. They have also to avoid dehydration to prevent stone formation. Some individuals respond to supplementation with pyridoxine, it reduces oxalate levels.

Ureteroscopic laser lithotripsy can be used to remove stones may be after their destruction with a laser, but extracorporeal shock wave lithotripsy, is not recommended [10,11]

In case of advanced kidney disease or end stage renal disease, additional treatment will be recommended including dialysis, a liver transplant, a combined liver-kidney transplant. The therapy used will depend on specific requirements [12,13].

Gene therapy is a new for therapy, the defective gene will be replaced with a normal gene to enable the production of the deficient enzyme and prevent the disease. However, they remain some difficulties to resolve before declaring the gene therapy like an alternative [14].

Cell therapy is similar to gene therapy, in this technique hepatocytes are repopulated into the liver of the patient and will restore the activity of the enzyme alanine-glyoxylate aminotransferase [15].

#### CONCLUSION

PH1 had heterogeneous clinical presentations and can escape from the diagnosis until the disease is advanced. An early intervention can delay and prevent end-stage renal failure, combined liver and kidney transplantation is preferred in PH1.

**Core tip:** The manuscript draws the attention of readers to the importance of discussing this diagnosis in front of non-specific clinical signs at any age in order to preserve renal function before the stage of end-stage renal failure. The genetic diagnosis demonstrates the Mediterranean type mutation.

#### DECLARATIONS

#### Author contributions

All authors collected the patient's clinical data and wrote the paper.

#### **Conflict of interest**

The authors have disclosed no potential conflicts of interest, financial or otherwise.

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