

Case Report

Always Look Beyond the Stones: Hyperoxaluria Overlooked

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ABSTRACT

We report a case of hyperoxaluria type I in a nine-year-old boy with nephrolithiasis. His initial management included multiple percutaneous nephrolithomies and lithotripsy. Metabolic screening was not undertaken initially. Hyperoxaluria was finally diagnosed by elevated urine oxalate (1.363 mmol/24h). A diagnosis of hyperoxaluria type I was confirmed by liver biopsy. His kidney function was nearly normal and he was started on

pyridoxine and crystallization inhibitors. He will require a liver transplant to cure his primary hyperoxaluria. Clinical clues of primary hyperoxaluria type I are positive family history or presentation with several renal stones. Irrespective of the above, all patients with first presentation of renal calculi should undergo metabolic screening including urinary oxalate level determination.

KEYWORDS: glomerular filtration rate, hyperoxaluria, renal stone

INTRODUCTION

Primary hyperoxaluria type I is an autosomal recessive inborn error of metabolism, which is the result of endogenous overproduction of oxalate and glycolate. The disease is due to low or absent activity of liver specific peroxisomal enzyme alanine glyoxylate aminotransferase (AGT). This leads to recurrent urolithiasis, nephrocalcinosis and accumulation of insoluble oxalate throughout the body. Although the clinical course is highly variable as to when and if end stage renal failure (ESRF) will result, about 50% of patients will reach ESRF before the age of 25 years.

A high degree of clinical suspicion coupled with elevated urinary oxalate, points strongly to this condition. Liver biopsy demonstrating AGT deficiency remains the diagnostic gold standard.

CASE REPORT

A 9-year old Kuwaiti boy presented at the age of three years with abdominal pain and retention of urine due to renal calculi and a bladder stone. Subsequently percutaneous lithotripsy and percutaneous nephrolithotomy were performed. He continues to pass stones per urethra on a regular basis, approximately one every one to two months. He has not had any further episodes of urinary obstruction. His parents are non-consanguineous and he has two older sisters (19 and 17 years old) who also pass stones in the urine but have good

kidney function. On examination, he looked well-grown and healthy without anemia or jaundice. His weight was 21.3 kg and height 119 centimeters. The pulse was 80 / minute regular and the blood pressure was 100 / 55 mmHg. Neither kidney was palpable. There was no hepatosplenomegaly. Initial laboratory studies revealed a serum Na 137 mmol/l, K 4.6 mmol/l, Cl 103 mmol/l, HCO₃ 21 mmol/l, serum creatinine 50 umol/l, Ca 2.41 mmol/l, phosphate 1.69 mmol/l, urate 222 mmol/l. The estimated GFR was 95 ml / minute / 1.73 m².

Plain abdominal X-ray showed multiple stones in both kidneys and bladder (Fig. 1).

Ultrasound of KUB revealed calcification of the cortico-medullary junction and renal calculi with mild bilateral renal pelvic and ureteric dilatation. The right kidney measured 7 cm and the left kidney 7.6 cm in length (Fig. 2).

The MAG3 scan showed marginal impairment of left sided renal function at 43% of total GFR but no evidence of urinary obstruction.

Further biochemical analysis showed urinary oxalate excretion 1.363 mmol / 24h (normal range = 0.1 - 0.46), urinary oxalate: creatinine ratio 340 (normal range = 1 - 38) and urine calcium 0.8 mmol /24h (normal range = 2.5 - 7.5 mmol / 24h). Stone analysis revealed calcium oxalate.

A liver biopsy showed normal liver but confirmed the diagnosis of primary oxaluria with a level of alanine glyoxylate aminotransferase (AGT)



Fig. 1: Abdominal X-Ray showing multiple stones in both kidneys and bladder

activity of 3.7 $\mu\text{mol/h/mg}$ protein (normal range = 19.1 - 47.9). Chromium EDTA GFR was mildly reduced at 81 $\text{mls} / \text{min} / 1.73 \text{m}^2$ (normal range = 80-130 $\text{mls}/\text{min}/1.73\text{m}^2$). He was commenced on pyridoxine 50 mg daily and polycitra (sodium + potassium citrate) 10 ml/bd . Flexible ureterorenoscopy was performed to remove all the stones within the collecting system. He was followed up in the pediatric department of Al Sabah Hospital since the age of four years. His current condition remains extremely stable but he will require a liver transplant to cure his primary hyperoxaluria.

DISCUSSION

Primary hyperoxaluria type I is an autosomal recessive inherited metabolic disease in which excessive oxalate is formed in the liver and excreted by the kidneys. It manifests as a wide spectrum of phenotypes ranging from renal failure in infancy to renal stones in adulthood. Medical treatment centers on high fluid intake and pyridoxine. Pyridoxal phosphate is an essential co-factor for alanine - glyoxalate aminotransferase (AGT) and at a dose of 5-20 $\text{mg}/\text{kg} / \text{day}$ can significantly decrease hyperoxaluria in 30% of those affected. Pyridoxine responsiveness may prevent or delay the progression to ESRF^[1]. The patients most likely to respond are those with residual AGT activity. Other measures are directed towards decreasing the formation of calcium oxalate crystals in urine with potassium citrate, magnesium and adequate



Fig. 2: Ultrasound of KUB showing multiple renal stones in both kidneys with bilateral renal pelvic and ureteric dilatation.

hydration^[2]. The natural history of the condition is such that a therapeutic window of opportunity exists only if the diagnosis is made before renal function deteriorates significantly. If treatment is delayed, deterioration of GFR inevitably leads to decreased urinary excretion of oxalate and accelerated increase of oxalate burden, even in the face of pyridoxine therapy. Neither hemodialysis nor peritoneal dialysis is able to keep pace with the endogenous production of oxalate in these patients^[3]. Survival on dialysis is poor, principally due to progressive tissue oxalate accumulation and deposition.

Isolated renal transplantation is complicated by acute oxalate nephropathy. Recurrent nephrocalcinosis and stone formation are expected, except among those who are pyridoxine responsive. The results of isolated cadaveric kidney transplant performed in Europe in the 1980s were very poor with 3 - year survival rate of 20% for grafts and 74% for patients. The cause of graft loss was related to rejection in 33% of patients and recurrence of stone disease in 31%^[4]. Isolated liver transplantation might be the first-choice treatment in selected patients before an advanced stage of chronic renal failure occurs, *i.e.*, while the GFR is between 60 $\text{mls}/\text{min}/1.73 \text{m}^2$ and 40 $\text{mls}/\text{min}/1.73 \text{m}^2$ ^[5]. Once significant renal insufficiency has developed, combined liver and renal transplants appear to offer the best chance for long term survival (*i.e.*, while GFR ranges between 20 - 40 $\text{mls}/\text{min} / 1.73 \text{m}^2$) because at this level oxalate retention increases rapidly^[6]. Survival rates of 80% for patients at five years with combined transplant have been reported. Despite the potential risks to the grafted kidney due to oxalate release from body stores, kidney survival is about 95% at three years after transplantation. Renal function

remained stable with a creatinine clearance of 40 - 60 mls/min/1.73m² after five years^[7]. Whatever the transplantation strategy, the kidney must be protected against the damage that can be induced by heavy oxalate load suddenly released from tissue. Forced fluid intake of 5 l/1.73 m²/day supported by diuretics and use of crystallization inhibitors, is the most important strategy. Appropriate initial assessment of all stone formers at first presentation will minimize the chance of accelerated morbidity in this dangerous condition.

REFERENCES

1. Marangella M. Transplantation strategies in type I primary hyperoxaluria: the issue of pyridoxine responsiveness. *Nephrol Dial Transplant* 1999; 14:301-303.
2. Leumann E, Hoppe B. The primary hyperoxalurias. *J Am Soc Nephrol* 2001; 12:1986-1993.
3. Hoppe B, Graft D, Offner G, *et al.* Oxalate elimination via hemodialysis or peritoneal dialysis in children with chronic renal failure. *Pediatric Nephrol* 1996; 10:488-492.
4. Broyer M, Burnner FP, Brynger H, *et al.* Kidney transplantation in primary oxalosis: data from the EDTA Registry. *Nephrol Dial Transplant* 1990; 5:332-336.
5. Cochat P, Basmaison O. Current approaches to the management of primary hyperoxaluria. *Arch Dis Child* 1993; 82:470-473.
6. Scheinman JI, Najarian JS, Mauer SM. Successful strategies for renal transplantation in primary oxalosis: *Kidney Int* 1991; 25:804-811.
7. Jamieson NV. The result of combined liver/kidney transplantation for primary hyperoxaluria 1984-1997. The European PH1 Transplant registry report. *European pH1 Transplantation Study Group. J Nephrol* 1998; (Suppl I) :36-41.