CASE REPORT

Primary hyperoxaluric acidosis with endstage renal failure in an infant

Célia S. Macedo,1 Eneida M. Yoshida,2 Rosa Marlene Viero,3 Márcia C. Riyuzo,4 Herculano D. Bastos5

Abstract

Objective: to report a case of a child with endstage renal failure caused by primary hyperoxaluria.

Methods: the review of the literature showed the rarity of the disease. In France, the prevalence is about 1.05/million and the incidence rate is 0.12/million/year. A survey, performed in international specialized centers in 1999, documented 78 cases in infants; in 14% of them the initial onset symptom was uremia. The rarity and severity of the disease justify the description of this case.

Results: a girl presenting vomiting and failure to thrive within the first months of life developed end-stage renal failure at 6 months of age. She was being treated with dialysis. At 8 months of age, she was referred for investigation. She was undernourished and the laboratory examinations showed urea (69mg/dl), creatinine (2.2 mg/dl) and creatinine clearance (12.5 ml/min/1.73m2 SA). The routine urinalysis was normal, the renal ultrasound showed increased echogenicity in both kidneys; the dosage of urinary oxalate was 9.2mg/kg/day or 0.55mmol/1.73m2 SA; the urinary oxalate/creatinine ratio was 0.42. Renal biopsy showed calcium oxalate crystals throughout the renal parenchyma. The radiograph of long bones showed osteopathy and the ophthalmic examination showed flecked retinopathy. The child was treated with continuous ambulatory peritoneal dialysis and administration of pyridoxine was initiated.

Conclusions: primary hyperoxaluria should be considered as a differential diagnosis for endstage renal failure in infants, especially if there are no symptoms of other diseases.


Introduction

Primary hyperoxaluria is a rare disease characterized by the excessive production and accumulation of oxalate in the body; Lepoutre described a postmortem case of an infant with multiple kidney stones for the first time in 1925;1 most cases described later revealed high rates of consanguinity.2-4

Hyperoxaluria belongs to a rare group of autosomal recessive disorders. Two of these groups have been extensively studied: type I, characterized by high excretion of glycolate, and type II, with high urinary excretion of L-glycerate.5,2,3

The prevalence rate of primary hyperoxaluria type I in France is 1.05/million, with an incidence rate of 0.12/million/year.5 It is caused by peroxisomal alanine:glyoxylate aminotransferase (AGT) deficiency in the liver, resulting in accumulation of glyoxylate, which is converted into oxalate and glycolate. Primary hyperoxaluria type II is caused by cytosolic enzyme glyoxylate reductase D-glycerate dehydrogenase deficiency, causing an increase in oxalate and L-glycerate synthesis. The excess of oxalate in both
types of hyperoxaluria may precipitate in the urine, originating lithiasis and nephrocalcinosis.2,3,6

The involvement of renal function in hyperoxaluria type I is expected in children; chronic renal failure was reported in 50% of 16 children before the age of 10.7 Renal involvement in hyperoxaluria type II is usually less severe, although nephrocalcinosis and end-stage renal failure are also present.3

Clinical signs are heterogeneous and range from urolithiasis-related symptoms, at any age, to early onset of end-stage renal failure in children.2-3 Primary hyperoxaluria type I is believed to represent 1 to 2.7% of end-stage renal failure in children.8 Latta and Brodehl estimated that 1 in 5 to 15,000,000 between the ages of 0 and 15 years will have renal failure due to primary hyperoxaluria.8

Some authors consider a rare subgroup of patients with primary hyperoxaluria type I among infants (called infantile oxalosis), characterized by renal failure and advanced systemic oxalosis, usually without calcinosis. It has not been decided whether or not this group should be considered as part of primary hyperoxaluria type I.2-3 Infantile oxalosis is probably more related to high levels of serum oxalate and its consequences rather than being a subgroup of it, since two are the mechanisms that cause accumulation of oxalate in newborn infants: conversion of glyoxylate into oxalate instead of glycolate, and low glomerular filtration rate.

The objective of this study is to report a case of an infant with chronic, end-stage renal failure due to primary hyperoxaluria type I.

Case report

C.C.S., white, female, first child of nonconsanguineous parents, presented with previous history of frequent vomiting and low weight gain in the first months of life. The patient was admitted to hospital at six months, with fever, metabolic acidosis, seizures, oliguria, generalized edema, and acute respiratory disease, requiring mechanical ventilation for seven days. The initial results of biochemical exams were:

- Urea = 237 mg/dl
- Creatinine = 2.8 mg/dl
- Na = 133 mEq/L
- K = 4.6 mEq/L
- Ca = 9.3 mg/dl
- pH = 6.89
- Bicarbonate = 5.7 mmol/L
- Hemoglobin = 9.3 g%
- Hematocrit = 23.2%

The patient remained on continuous ambulatory peritoneal dialysis, and her lab exams yielded the following results:

- Urea = 69 mg/dl
- Creatinine = 2.20 mg/dl
- Phosphorus = 3.3 mg/dl
- Calcium = 8.8 mg/dl
- Sodium = 136 mEq/L
- Potassium = 4.5 mEq/L
- Creatinine clearance = 12.5 ml/min/1.73 m2 SC

The investigation yielded the following results: normal urinalysis; renal ultrasonography showing hyperechogenic kidneys of age-compatible size; abdominal x-ray with no abnormalities, level of 24-hour urine oxalate as follows: 9.2 mg/kg/day or 0.55 mmol/1.73 m2 SC and oxalate/creatinine ratio = 0.42. Renal biopsy was performed on the third day after hospital admission. The analysis of the collected material revealed a large amount of oxalate crystals in tubular cells, kidney interstitium and tubular lumen with foreign body granulomatous reaction around the crystals (Figure 1A). Glomeruli were secondarily affected by the obstructive process with glomerular collapse and dilation of the Bowman’s space (Figure 1B). Long bone radiographs revealed osteopenia and increased radiographic density transverse line in the growth plate region (Figure 2). Indirect fundoscopy showed hyperpigmented, punctiform lesions adjacent to hypopigmented areas of the retina that are compatible with the diagnosis of oxalate-induced retinopathy (Figure 3).

These results allowed implementing treatment with vitamin B6, 10mg/day. The patient was kept on continuous ambulatory peritoneal dialysis, received supplementation of iron, calcitriol, erythropoietin, sodium bicarbonate, and a high-calorie diet. The patient showed satisfactory improvement of her condition and was discharged from hospital after two months, being followed up at our Dialysis Unit.

Discussion

We described the case of an infant with primary hyperoxaluria type I who had end-stage renal failure in the sixth month of life, high urinary excretion of oxalate, and renal biopsy showing intense deposition of oxalate crystals in the lumen, tubular cells, and kidney interstitium, with secondary glomerular disorder, massive oxalate deposition in the retina, and bone lesion suggesting systemic oxalosis.

There is some controversy over the normal values for the urinary excretion of oxalate in infants. In 1991, Barratt studied 137 healthy children, including infants, and obtained the following values for the oxalate/creatinine ratio (mmol/mmol): geometric mean = 0.061, ranging from 0.015 to 0.26.9 In the present case, we had a molar ratio of 0.42, which denotes hyperoxaluria if we compare it to the values above. Although serum oxalate levels have not been measured, they would certainly be high, since oxalate content increases as glomerular filtration rate decreases. This way, extreme high level of serum oxalate is responsible
not only for oxalate deposition in the kidneys, but also for systemic oxalosis, which is characterized by bone disease, ocular involvement, neurological disorders, arteriopathy, and cardiopathy. This large deposition of oxalate should be considered when deciding on whether or not renal transplantation is necessary.

The basic characteristic of this disease is an enzyme defect that occurs in hepatocytes. Hyperoxaluria type I is caused by a defect in alanine:glyoxylate aminotransferase of liver cells with heterogeneous enzyme level. Two thirds of the patients have undetectable levels of alanine:glyoxylate aminotransferase catalytic activity while one third has a catalytic activity between 3 and 50% of the average normal activity. In one third of the patients with undetectable levels of alanine:glyoxylate aminotransferase, immunoreactive methods are used to detect this enzyme. These patients may have a defect in the cellular distribution of the enzyme, which is found in the mitochondrion rather than in hepatocyte peroxisomes, resulting in inadequate metabolic function.

The diagnosis of this defect in the enzyme is made by liver tissue biopsy and analysis of the alanine:glyoxylate aminotransferase catalytic activity, which was not carried out in this case because the patient had already developed renal failure. This procedure is important at the phase preceding the development of systemic oxalosis. In the existence of catalytic activity of alanine:glyoxylate aminotransferase (AGT), the use of pyridoxine may be properly recommended, since pyridoxine phosphate is the coenzyme for aminotransferase, including AGT. Pyridoxine (vitamin B6) has been used in cases of hyperoxaluria type I with variable responses in children aged one to two months. This treatment has been administered to siblings with infantile oxalosis with satisfactory results.

Five to 10% of the patients show partial or total response with the administration of pharmacological doses of pyridoxine. The remaining patients (90%) do not benefit from the treatment.

In the present case, pyridoxine was introduced at doses of 10 mg/day as therapeutic test, with the aim of reducing the excess of oxalate. The reduction rate of oxalate by continuous ambulatory peritoneal dialysis (CAPD) is knowingly lower than the synthesis in hyperoxaluria type I, and although there is improvement of renal failure, there is progression of systemic oxalosis. In the present case, new urine samples should be collected for control and/or oxalate serum levels should be measured so that pyridoxine therapy is either continued or interrupted.

As far as renal transplantation in hyperoxaluria type I is concerned, there is an ethical disagreement with regard to the use of living donors; however, this procedure has been used in children. Of ten children who were submitted to renal transplantation and received a kidney from a living donor, seven presented good renal function and six had no recurrence of hyperoxaluria.
In 1995, the North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) published a report of 22 children with hyperoxaluria type I who were submitted to transplantation. Seventeen of those children received the kidney from a living donor, related or not to 50% of the cases, and had adequate renal function after transplantation. Patients who underwent kidney transplantation from dead donors did not have any success.16 In 1999, NAPRTCS reported the evolution of 128 patients with hyperoxaluria, concluding that renal transplantation is a beneficial procedure, offering patients longer survival if compared with combined kidney-liver transplantation or with cases in which no transplantation was carried out.17 In our patient, renal transplantation is a therapeutic possibility with some restrictions due to the presence of intense systemic oxalosis. The ideal moment for renal or hepatic transplantation is before the development of advanced systemic oxalosis.19

Since alanine:glyoxylate aminotransferase is only found in significant amount in the liver and is located in the hepatic peroxisomes, liver transplantation has been used as the most efficient therapy in the last 10 years, along with conjugate kidney-liver transplants.3,20,21 A total of 98 conjugate transplants (kidney and liver) in 93 patients were reported in Europe, with a 65% survival rate of 10 years.22,23

The symptoms reported at the onset of primary hyperoxaluria type I are: failure to thrive (22%), urinary tract infection (21%) and uremia (14%).24 Our patient had failure to thrive in the first months of life; however, there was no diagnostic suspicion as this disease is not common and since many other factors may have contributed to this finding. The patient might have developed dehydration with hypovolemia and subsequent excessive oxalate deposition in renal tubules, causing irreversibility of the renal condition at the sixth month of life.

Our conclusion is that primary hyperoxaluria type I should be regarded as one of the differential diagnoses of renal failure in the first months of life, especially when no suggestive history of other diseases is present.

Acknowledgements

Thanks to professor Eliane Chaves Jorge, Department of Ophthalmology, School of Medicine, Botucatu (UNESP), for helping us with the photographs of retinal examination.

References


Correspondence:
Dra Célia S. Macedo
Departamento de Pediatria da Faculdade de Medicina de Botucatu - UNESP
Rubião Jr, s/n
18618-970 – Botucatu, SP, Brazil
Phone/Fax: +55 14 6802-6274 / 6802-6083
E-mail: pediatri@fmb.unesp.br