Combined liver and kidney transplantation in two women with primary hyperoxaluria: Different roads led to different outcomes

Trasplante combinado de hígado y riñón en dos pacientes con hiperoxaluria primaria – quando diferentes caminos conducen a diferentes resultados

Dear Editor,

We report on two patients with end-stage renal disease (ESRD) due to primary hyperoxaluria type 1 (PH1) who underwent liver-kidney transplant (LKT), using different approaches and consequently with different outcomes.

The first patient is a 32-year-old woman with ESRD on intensive daily hemodialysis (HD) due to PH-1 (homozygous mutation g.12261G>T) with severe systemic oxalosis. Three years after the beginning of dialysis, she underwent a combined simultaneous LKT from a deceased 48-year-old donor. The postoperative period was uneventful and she had immediate diuresis and excellent hepatic function. In an attempt to decrease the serum oxalate pool, continuous venovenous hemodiafiltration was performed for the first 72 h, followed by intensive HD. Her plasma oxalate levels (pOx) progressively decreased while her urinary oxalate levels (uOx) increased at the same rate (Table 1). Three months post-transplant her serum creatinine (sCr) was 1.6 mg/dL pre HD and a renal graft biopsy was performed revealing oxalate deposits on the tubules and interstitium. Intermittent HD was continued for six months and after stopping dialysis she was kept under immunosuppression, bicarbonate therapy and high fluid intake. Although her pOx reached low levels (17 μmol/L, normal range = 3–11 μmol/dL), one year after LKT, graft dysfunction was present with sCr 4.5 mg/dL. Nevertheless, skin oxalosis, refractory anemia and ventricular dysfunction secondary to oxalate deposits had completely disappeared.

The second case is a 26-year-old female with ESRD due to genetic confirmed PH-1 (homozygous mutation p.I244T) non-responsive to pyridoxine on regular HD, also with systemic oxalosis, however to a lesser degree.

In this case sequential LKT was proposed and she underwent a liver transplant from a deceased donor, three years after the beginning of HD. She was kept on intermittent HD four times a week and her pOx levels were measured sequentially in order to evaluate the best timing for sequential kidney transplant (Table 2). Four months after the liver transplant, pOx was 18 μmol/L, so she was proposed for kidney transplant and received a renal graft from a 54 years old deceased donor. The post-operative period was uneventful and she was discharged with sCr of 1.5 mg/dL, without performing any dialysis session. One year post-transplant, she has stable sCr of 1.3 mg/dL, pOx levels of 15 μmol/L, uOx levels of 13 μmol/L with no signs of recurrent oxalosis.

Discussion

PH-1 is a rare metabolic disorder characterized by a dysfunction of the liver-specific enzyme alanine-glyoxalate aminotransferase resulting in excessive oxalate production. The deposition of calcium oxalate (CaOx) in the kidney leads to chronic kidney disease (CKD) and subsequent plasma CaOx saturation (plasma oxalate >30 μmol/L) with systemic oxalosis.[1]

The diagnosis of PH-1 is often delayed and about 30% of the patients first present with CKD.[2] Once ESRD is present, intensive dialysis might no be able to remove CaOx efficiently and the risk of systemic oxalosis increases worsening the

Table 1 – Evolution of 24-h urinary and plasma oxalate (uOx; pOx), serum creatinine (sCr) and dialysis treatment for patient 1.

	Pre Tx	72 h	10 d	1 M	3 M	6 M	1A
sCr (mg/dL)	6.03	2.56	0.71	0.84	1.6	2.1	4.5
uOx (mg/24)	25	8.4	47.7	48.4	160	255	39
pOx (μmol/L)	160				55	32	17
Dialysis	HD pre surg.	C-HDF	Intermittent HD 4/week			Stop HD	

C-HDF: continuous haemodiafiltration; Tx: transplant; HD: haemodialysis; d: day; h: hour; M: month.

Table 2 – Evolution of 24-h urinary and plasma oxalate (uOx; pOx), serum creatinine (sCr) and dialysis treatment for patient 2.

	Pre Tx	3 M Pos liver Tx	6 M Pos LK Tx
sCr (mg/dL)	8.12	7.17	1.7
uOx (mg/24)	–	–	13
pOx (μmol/L)	111	18	15
Dialysis	HD	HD	

Tx: transplant; LK Tx: liver kidney transplant; HD: haemodialysis; d: day; h: hour; M: month.

prognosis. Thus, some authors recommend planning pre-emptive transplantation at CKD stage 3-b.[3]

Since isolated kidney transplantation is frequently followed by recurrence of nephrocalcinosis due to the unremitting overproduction of oxalate, combined LK transplant has been accepted as the optimal approach to patients with PH-1 and ESRD.[1,4]

Combined LKT strategies are challenging, especially if systemic oxalosis is present. Sequential combined transplant (liver transplantation first) offers a metabolic advantage, since there is a correction of the enzyme defect, stopping oxalate production and allowing effective oxalate removal by HD before kidney transplant.[5,6] Simultaneous liver kidney transplantation has an immunologic advantage because the liver graft apparently has the potential to protect a simultaneously transplanted kidney from rejection, limits surgery risks and is more feasible regarding organ shortage.[7,8]

The first patient described presented severe systemic oxalosis with expected rebound of oxalate levels, which was why HD was continued for six months after transplant. Despite the progressively decreasing pOx levels, there was a concomitant increase of uOx levels that overcame the graft filtration capacity resulting in precocious recurrent oxalosis.

Regarding the second patient, a sequential LKT was preferred followed by serial measurements of pOx to set the right timing for kidney transplantation. There is no consensus of the optimal pOx levels for which the risk of recurrence is lower but since ESRD patients without PH-1 have higher oxalate levels than the normal range, when our patient presented pOx of 18 μmol/dL, we felt confident to proceed to kidney transplantation with great results.[9,10]

In conclusion, sequential transplant seems to be a better option in patients with PH-1 and ESRD with high oxalate load. The timing for kidney transplant after liver is not well defined but pOx sequential quantification and support therapy with intensive dialysis appears to be good approaches. Simultaneous transplant can be an option if the patient has low oxalate burden and less dialysis time. Either way, timely diagnosis with prevention of ESRD and pre-emptive liver transplant might be the best option.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this manuscript.

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