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BRIEF REPORT

Reversal of oxalosis cardiomyopathy after combined liver and kidney transplantation

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Abstract Few data have been published on the course of oxalosis cardiomyopathy after combined liver and kidney transplantation in hyperoxaluria patients with myocardial involvement. We report the case of a primary hyperoxaluria type 1 patient with renal failure who developed end-stage cardiomyopathy. Left venticulography showed severe diffuse hypokinesia and left ventricular ejection fraction was calculated at 12%. Endomyocardial biopsy demonstrated platelike calcium oxalate crystals within the myocardium and the connective tissue, and mild perivascular fibrosis. The patient was first considered for combined liver-heart-kidney transplantation, but as his cardiac function improved slightly with an intensive dialysis program, combined liver and kidney transplantation was performed. Normal cardiac function was demonstrated at 1-year follow-up, and comparative endomyocardial biopsy showed regression of the myocardial oxalate deposits. This case adds stronger clinical, hemodynamic, and histopathological evidence that severe oxalosis cardiomyopathy may be reversed after combined liver and kidney transplantation.

Keywords Hyperoxaluria · Oxalosis · Cardiomyopathy · Liver transplantation · Kidney transplantation · Case report

Introduction

Combined liver and kidney transplantation (CLKT) has emerged as the treatment of choice for patients with type 1 hyperoxaluria and end-stage kidney failure, in whom liver replacement treats the hepatic enzymatic deficiency, while kidney transplantation replaces the main target of the disease [4]. However, only a few data have been reported on the course of myocardial oxalosis after CLKT. In systemic oxalosis myocardial calcium oxalate deposits may induce conduction system abnormalities, tachy- and bradyarrythmia, and cardiomyopathy [5].

We report the case of a primary hyperoxaluria type 1 patient with renal failure who developed end-stage oxalosis cardiomyopathy. One year after CLKT he had normal cardiac function, and comparative endomyocardial biopsy showed regression of the myocardial oxalate deposits.

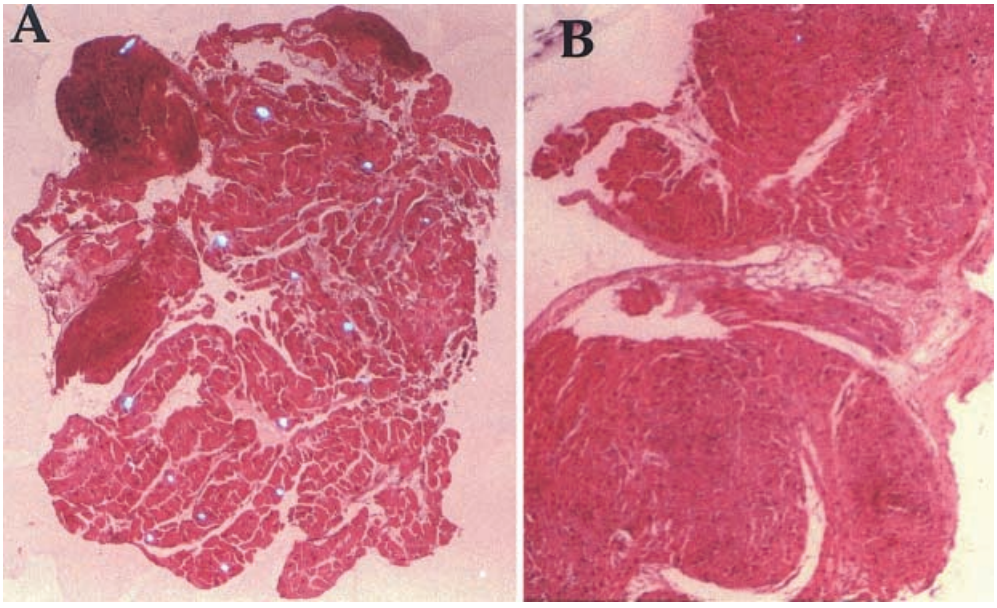

Fig. 1 Endomyocardial biopsy specimen obtained before (**A**) and 1 year after (**B**) liver and kidney transplantation. Hematoxylin-eosin viewed under polarized light, ×40. **A** Numerous platelike oxalate crystals (*light blue spots*). **B** A significant decrease in the oxalate deposits

Case report

A 20-year-old man with primary type 1 hyperoxaluria was evaluated for transplantation. The patient required regular hemodialysis at the age of 19 years; at this time cardiac echographic findings were normal. Seven months later the patient developed New York Heart Association (NYHA) stage III–IV cardiomyopathy. Electrocardiography showed an intra- auricular conduction alteration and incomplete right bundle branch block. At cardiac catheterization his cardiac index was 2.9 l/min^{-1} m^{-2}. Postcapillary pulmonary arterial hypertension was demonstrated (pulmonary arterial pressure 75/47 mmHg, pulmonary wedge pressure 37 mmHg). Left venticulography showed severe diffuse hypokinesia and left ventricular ejection fraction (LVEF) was calculated at 12%. Endomyocardial biopsy demonstrated platelike calcium oxalate crystals within the myocardium and the connective tissue, and mild fibrosis (Fig. 1A). The patient was first considered for combined heart-liver-kidney transplantation. However, with medical treatment including converting enzyme inhibitor and pyridoxine, and with intensive hemodiafiltration (6 h, 6 times per week), LVEF improved to 30%, as determined by echography. The patient was then scheduled for CLKT.

In June 1998 the patient underwent CLKT. The liver replacement used our standard technique of piggyback liver transplantation with temporary surgical portocaval shunt, as described by Belghiti et al. [1]. The procedure was uneventful, without cardiac complication. At postoperative day 7 hepatic artery thrombosis was diagnosed, and the patient underwent successful surgical hepatic artery repermeabilization. The immunosuppressive regimen consisted in a standard triple therapy combining azathioprine, tacrolimus, and methylprednisolone. Azathioprine and methylprednisolone administration was interrupted at postoperative month 3, according to our standard immunosuppressive protocol for liver recipients. No acute rejection episode of the liver or kidney grafts was been noted in the follow-up. Functionally the patient recovered within a few weeks to NYHA stage I.

Postoperative cardiac echography studies showed progressive normalization of heart function, and electrocardiographic findings normalized. At postoperative month 12, protocol biopsies of the liver and kidney grafts were performed, and informed consent was obtained for cardiac catheterization and endomyocardial biopsy during the same procedure. Cardiac catheterization and ventriculography showed normalization of the hemodynamic data and of LVEF (65%). Endomyocardial biopsy showed regression of the calcium oxalate crystals within the myocardium (Fig. 1B). At 3-year follow-up the patient was still asymptomatic, with normal liver, heart, and kidney function.

Discussion

Primary hyperoxaluria type 1 is an autosomal recessive disorder characterized by a deficiency of liver-specific peroxisomal alanine-glyoxylate aminotransferase. This disease induces an increase in oxalate urinary excretion, causing urolithiasis and nephrocalcinosis. As progressive renal insufficiency occurs, insoluble oxalate deposits accumulate throughout the body, mainly in the musculoskeletal, cardiovascular, and peripheral nervous systems, causing systemic oxalosis. Cardiac involvement is a major source of mortality in hyperoxaluria patients on dialysis and may manifest as conduction system abnormalities, tachy- and bradyarrythmias, and cardiomyopathy. Cardiac histopathological analyses describe calcium oxalate deposition within the conduction system, the small intramyocardial vessels, and the myocardium [3,7]. Secondary inflammatory response to oxalate deposits may also induce thickening and degeneration of collagen fibers, fatty infiltration, mononuclear cell infiltration, and frank fibrosis [5].

When the patient described here was evaluated for transplantation, his cardiac function was deemed not to allow combined liver and kidney transplantation. Encouraged by some experience with combined liver and heart transplantation [2] and by the young age of

the patient, combined heart-liver-kidney transplantation was first considered. As cardiac function seemed to improve with intensive hemodiafiltration, experience reported in the literature on oxalosis cardiomyopathy was reviewed. Most of the hyperoxaluria type 1 patients who underwent CLKT did not show evidence of myocardial oxalosis [4]. Only a few reports describe some regression of myocardial oxalosis, but the follow-up periods were short. Two patients were reported to present preoperative heart conduction abnormalities that normalized after CLKT [6,8]. Two other reports presented isolated cases of hyperoxaluria type 1 patients with severe dilated cardiomyopathy that partially reversed after CLKT; Rodby et al. [7] presented the case of a hyperoxaluria type 1 patient with cardiomyopathy who underwent CLKT; cardiac function improved after CLKT as evaluated by cardiac to thoracic ratio and scintigraphy that demonstrated improvement in LVEF from 24% preoperatively to 34% at 3 months' follow-up. Fyfe et al. [3] published the case of a 33-year-old patient with hyperoxaluria type 1 and severe dilated cardiomyopathy that reversed after CLKT, with LVEF calculated by scintigraphy at 25% preoperatively to 48% at 2 months' follow-up; moreover, comparative endomyocardial biopsies demonstrated marked regression of the calcium oxalate deposits after CLKT. Therefore, as these cases suggested that oxalosis cardiomyopathy may significantly reverse after CLKT, and as LVEF improved slightly with intensive hemodialysis, cardiac replacement was deemed unnecessary in our patient. However, although the absence of portal hypertension greatly facilitates the procedure, liver transplantation may be hazardous in these patients with altered LVEF, especially at liver graft reperfusion [7].

In conclusion, this case adds stronger clinical, hemodynamic, and histopathological evidence that severe cardiomyopathy secondary to type 1 hyperoxaluria may reverse after CLKT and should not be considered a contraindication to the procedure, although severe LVEF alteration significantly increases the operative risks.

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