Exclusion of Primary Hyperoxaluria Type I (PHI) in End-Stage Renal Failure by Enzymatic Analysis of a Percutaneous Hepatic Biopsy

S.H.		Morgan ^a
C.J.		Danpure ^b
M.R.		Bending ^a
A.J.		Eisinger ^a

^aSouth West Thames Regional Renal Unit, St. Helier Hospital, Carshalton, and ^bM.R.C. Clinical Research Centre, Harrow, UK

Dr. S.H. Morgan, South West Thames Regional Renal Unit, St. Helier Hospital, Wrythe Lane, GB-Carshalton, Surrey SM5 1AA (UK)

Sir,

We would agree with Murty et al. [1] that renal transplantation may not be contra-indicated in patients with end-stage renal failure (ESRF) due to primary hyperoxaluria. The timing of this manoeuvre, however, is critical to avoid the consequences of oxalate deposition within the newly transplanted kidney [2, 3]. The histological extent of oxalosis in the nephrectomy specimens described, although indicating a possible diagnosis of primary hyperoxaluria, will not define the type and may not, in clinical practice, be very helpful, since the majority of patients presenting with ESRF have small kidneys, and biopsy therefore not possible. The indications for pre-transplant nephrectomy are, in addition, few.

The metabolic defect in PHI, the commonest variant of primary hyperoxaluria, has been ascribed to a deficiency in the activity [4] or subcellular distribution [5] of alanine: glyoxylate aminotransferase (AGT), which is a peroxisomal enzyme [6] almost entirely confined to liver [7]. The activity of this enzyme and its subcellular distribution can be determined on hepatic tissue obtained at percutaneous needle biopsy [5,8]. This has been shown to be invaluable in the diagnosis of PHI where this suspected diagnosis might not otherwise be excluded.

We recently reviewed a 44-year-old Caucasian man who presented to this unit in 1983 with chronic renal failure and a huge 'staghorn' calculus (fig. 1). By 1988 he required renal replacement therapy but attempts to establish vascular access for haemodialysis were unsuccessful and continuous ambulatory peritoneal dialysis was introduced. In the course of investigations to exclude a metabolic cause for his renal calculi, he was noted to have an elevated plasma oxalate concentration of 30 $\mu\text{mol/l}$ (normal range < 3 $\mu\text{mol/l}$). Although hyperoxalaemia of

Fig. 1. Plain abdominal X-ray showing a large right 'staghorn' calculus.

this degree is observed in ESRF of any cause [9], we felt that PHI should be excluded prior to his acceptance on our transplant programme. A percutaneous hepatic needle biopsy was therefore performed in February of last year. Although the AGT enzyme activity was lower than normal (2.9 $\mu\text{mol/h/mg protein}$; 65% of the mean normal level and just below the lower end of the

normal range), the amount of immunoreactive AGT protein and subcellular distribution were normal. These data were not in keeping with a diagnosis of PHI.

Lone renal transplantation can be considered in PHI, but should optimally be performed before the GFR has fallen below 20 ml/min/1.73 m² [9], and certainly before

Exclusion of PHI in ESRF by Enzymatic Analysis of a Percutaneous Hepatic Biopsy

337

the patient has spent any length of time on renal replacement therapy [2]. The metabolic defect in PHI may be definitively corrected by hepatic transplantation, with simultaneous replacement of the damaged kidney [3,10]. The place of hepatorenal transplantation, however, is controversial, given the overall survival for hepatic grafts, and it remains debatable whether this should be offered as definitive treatment once renal failure approaches, or held in reserve until one or more renal transplants have failed.

References

Murty, M.L.N.; Garg, I.; Date, A.; Jacob, M.G.; Kirubakaran, M.G.; Shastry, J.C.M.: Renal histology for the diagnosis of primary hyperoxaluria in patients with end-stage renal disease. *Nephron* 53: 81–82 (1989).

Watts, R.W.E.; Morgan, S.H.; Purkiss, P.; Mansell, M.A.; Baker, L.R.I.; Brown, C.B.: Timing of renal transplantation in the management of pyridoxine resistant type I primary hyperoxaluria. *Transplantation* 45: 1143–1145 (1988).

Morgan, S.H.; Watts, R.W.E.: Perspectives in the assessment and management of patients with primary hyperoxaluria type I. *Adv. Nephrology* 18: 95–100 (1989).

Danpure, C.J.; Jennings, P.R.: Peroxisomal alanine: Glyoxylate aminotransferase deficiency in primary hyperoxaluria type I. *FEBS Lett.* 207:20–24 (1986).

Danpure, C.J.; Cooper, P.J.; Wisc., P.J.; Jennings, P.R.: An enzyme trafficking defect in two patients with primary hyperoxaluria type 1: peroxisomal alanine: Glyoxylate aminotransferase re-routed to mitochondria. *J. Cell Biol.* 100:1345–1352 (1992).

Noguchi, T.; Takada, Y.: Peroxisomal localization of alanine: Glyoxylate aminotransferase in human liver. *Archs Biophys.* 796:645–647(1979).

Kamoda, N.; Minatogawa, Y.; Nakamura, M.; Nakanishi, J.; Okuno, E.; Kido, R.: The organ distribution of human alanine: 2-oxoglutarate aminotransferase and alanine: Glyoxylate aminotransferase. *Biochem. Med.* 25:25–34(1980).

Danpure, C.J.; Jennings, P.R.; Watts, R.W.E.: The enzymological diagnosis of primary hyperoxaluria type I by measurement of alanine: Glyoxylate aminotransferase activity in hepatic percutaneous needle biopsies. *Lancet* i: 289–291 (1987).

Morgan, S.H.; Purkiss, P.; Watts, R.W.E.; Mansell, M.A.: Oxalate dynamics in chronic renal failure. Comparison with normal subjects and patients with primary hyperoxaluria. *Nephron* 47: 253–257 (1987).

10 Watts, R.W.E.; Calne, R.Y.; Rolles, K.; Danpure, C.J.; Morgan, S.H.; Mansell, M.A.; Williams, R.; Purkiss, P.: Successful treatment of primary hyperoxaluria type I by combined hepatic and renal transplantation. *Lancet* ii: 475–485 (1987).