Clin Kidney J (2013) 6: 350–351
doi: 10.1093/ckj/sft050

CKJ

Correspondence and Personal Opinion

Transposition of the great arteries and autosomal-dominant polycystic kidney disease

Hassane Izzedine and Jacques Rottembourg

Department of Nephrology, Pitie-Salpetriere Hospital, Paris, France

Correspondence and offprint requests to: Hassan Izzedine; E-mail: hassan.izzedine@psl.aphp.fr

Keywords: ADPKD; ciliopathy; transposition of the great arteries

Transposition of the great arteries (TGAs) is a congenital cardiac malformation characterized by atrioventricular concordance and ventriculoarterial (VA) discordance. The exact aetiology remains unknown [1]. We report for the first time the existence of TGA in a newborn whose mother fulfilled the unified diagnosis criteria for autosomal-dominant polycystic kidney disease (ADPKD) [2] with a typical family history.

The patient was a 40-year-old woman with ADPKD diagnosed at the age of 35 years. Her paternal grandfather and uncle had been given a diagnosis of ADPKD. Her father was a 65-year-old man with ADPKD diagnosed at the age of 50 years during investigation of increased blood pressure (Figure 1). He had progressive kidney failure leading to iterative haemodialysis at the age of 55 years. Other possible manifestations of ADPKD were colonic diverticulosis, minor aortic insufficiency and severe vascular leucoencephalopathy. He died of metastatic colorectal cancer at the age of 65 years. Our patient, while normotensive with normal renal function [serum creatinine level of 0.58 mg/dL (51.04 µmol/L), MDRD creatinine clearance: 96 mL/min/1.73 m^2], developed arterial hypertension (150/90 mmHg) during the 20th week of pregnancy and was treated with labetalol and nicardipine. A male infant was born in good condition at 42 weeks' gestation with a birth weight of 2.955 kg. At 5 h, he was noted to be centrally cyanosed. Subsequent echocardiography diagnosed simple TGAs. At Day 9, he underwent an arterial switch operation and ventricular septal defect closure. His subsequent hospital course was uneventful and he was discharged home on the 19th postoperative day.

The association between TGAs in the newborn and ADPKD in his mother may not be fortuitous, suggesting a ciliopathy. The incidence of TGA is estimated at 1 in 3500–5000 live births, with a male-to-female ratio of 1.5–3.2:1. In 50% of cases VA discordance is an isolated finding, and in 10% of cases, TGA is associated with noncardiac malformations [1]. Several proteins encoded by these associated genes have been identified in primary cilia in renal tubular epithelia [3]. Abnormalities in cilia formation and function may play a role in the pathogenesis of ADPKD, the most common inherited renal disorder [4]. Mutations in the polycystin 2 gene cause, in addition to kidney and liver cysts, left-right laterality disorders in both mouse embryos and zebrafish (*Pkd2*-null) [1] and humans (*PKD2* deletion/duplication) (dextrocardia and situs inversus totalis) [5]. In humans, the cystic kidney diseases in which an association with left–right axis anomalies have been recognized are types 2, 3 and 6 nephronophthisis, which are due to mutations in the *INVS* (inversin), *NPHP3* (nephronophthisis 3) and *CEP290* (centrosomal protein 290 kDa) genes, respectively [5].

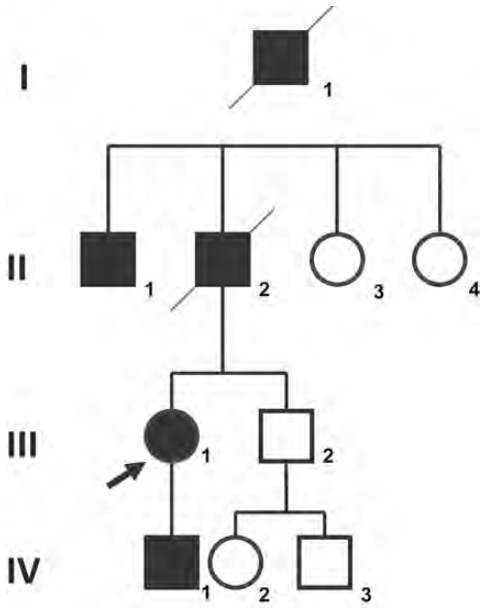

Fig. 1. Pedigree: Patient III-1 is the propositus.

We suggest screening of patients with a TGA to confirm the existence and assess the prevalence of this association.

Conflict of interest statement. None declared.

References

1. Martins P, Castela E. Transposition of the great arteries. *Orphanet J Rare Dis* 2008; 3: 27
2. Pei Y, Obaji J, Dupuis A *et al*. Unified criteria for ultrasonographic diagnosis of ADPKD. *J Am Soc Nephrol* 2009; 20: 205–212
3. Vogel P, Read R, Hansen GM *et al*. Situs inversus in *Dpcd/Poll*$^{-/-}$, *Nme7*$^{-/-}$, and *PKD1/1*$^{-/-}$ mice. *Vet Pathol* 2010; 47: 120–131
4. Grantham JJ. Clinical practice. Autosomal dominant polycystic kidney disease. *N Engl J Med* 2008; 359: 1477–1485
5. Bataille S, Demoulin N, Devuyst O, Audrézet MP, Dahan K, Godin M, Fontès M, Pirson Y, Burtey S. Association of PKD2 (polycystin 2) mutations with left-right laterality defects. *Am J Kidney Dis* 2011; 58: 456–460

Received for publication: 6.4.13; Accepted in revised form: 8.4.13