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AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE: MAPPING TO CHROMOSOMAL REGION OF 6p21 – CEN IN A TURKISH CHILD*

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SUMMARY: Beşbaş N, Özen S, Saatçi Ü, Çağlar M, Mucher G, Zerres K. (Units of Nephrology and Rheumatology, and Pathology, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey and Institüt für Hemangenetik der Universitat, Bonn, Germany). Autosomal recessive polycystic kidney disease: mapping to chromosomal region of 6p21-cen in a Turkish child. Turk J Pediatr 1998; 40: 245-247.

Autosomal recessive polycystic kidney disease (ARPCD) is a congenital kidney disease with severe prognosis. We present a male infant who was diagnosed prenatally by ultrasonography. He died at two months of age in a septic stage. The genetic defect for ARPCD has been mapped to chromosomal region of 6p21-cen. This represents the first study from this region of the world. The linkage studies up to this date fail to show genetic heterogeneity. *Key words: autosomal recessive polycystic kidney disease, genetics.*

Autosomal recessive polycystic kidney disease (ARPCD) is a rare heritable disease affecting the kidneys and liver with a usually grave prognosis. Fusiform dilatations of the collecting tubules are noted and the classical hepatic involvement is in the form of congenital hepatic fibrosis[1,2]. There is great variation in the severity of the involvement of these organs, creating a heterogeneity in the clinical spectrum of the disease[3]. On the other hand, in spite of the wide variability in clinical presentation, only a single ARPCD locus has been reported[4,5].

We herein present a newborn with ARPCD with a fatal outcome.

Case Report

This male infant was diagnosed prenatally by ultrasonography to have polycystic kidney disease, thorax hypoplasia and oligohydramnios. Postnatal ultrasonography confirmed the diagnosis of ARPCD. The kidneys were markedly

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enlarged with increased echogenicity and medullary regions were more echogenic than the cortex. The mother and father had normal kidneys and no consanguinity. At birth he was hospitalized for respiratory distress. He had mild impairment of renal function at birth with a BUN level of 54 and serum creatinine of 1.4 mg/dl. At discharge he was put on antihypertensive therapy for his hypertension. He was readmitted two months later with a general deterioration in his condition. On admission he was ill-looking with marked edema and ascites. He had marked anemia and hematuria and proteinuria on urine examination. Results of renal function tests were as follows: BUN 45 mg/dl, serum creatinine 1.5 mg/dl, uric acid 5 mg/dl, serum albumin 2.9 g/dl, and normal liver function tests. E.coli was grown on urine culture. He was put on intravenous antibiotics and was transfused fresh blood. Nevertheless, he died on the 14th hour of hospitalization. Postmortem examination of the kidneys confirmed the diagnosis of ARPCD.

Linkage analysis was performed (in Dr. Klaus Zerres's laboratory) for the parents and the index case with appropriate markers (Fig. 1). The genetic defect previously defined for ARPCD, mapping to chromosomal region of 6p21-cen, was identified. Prenatal diagnosis has been planned for the next child of the family.

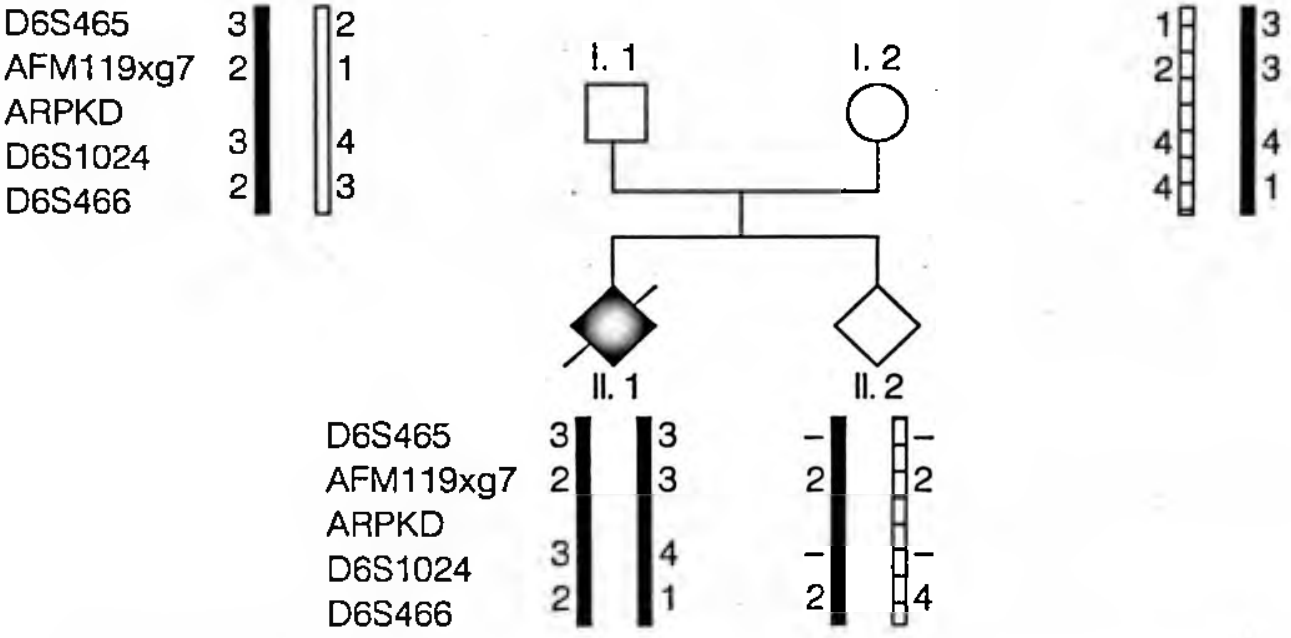

Fig. 1: Linkage analysis of the family members for the susceptible region on chromosome 6.

Discussion

Autosomal recessive polycystic kidney disease is a childhood disease with a varying clinical spectrum and age of presentation[1-3]. This child had pulmonary complications and a rapid fatal course probably complicated by ysepsis but without prominent liver involvement. Although ARPCD is usually accepted to have a grave prognosis, the southwest pediatric nephrology group has shown that chance of survival is not that poor and that aggressive medical management

is indicated[2]. In the largest series of ARPCD in children, Zerres et al.[3] reported that only 11 percent of their patients died and that urinary tract infections and hypertension were major aspects needing medical care.

Zerres et al.[4] first mapped the ARPCD locus to 6p21-cen with no evidence of genetic heterogeneity in the studied different clinical phenotypes. Guay-Woodford et al.[5] confirmed the existence of a single ARPCD locus in their patients with a varying spectrum of clinical presentation. The genetic defect has been mapped to the same locus in this Turkish patient, supporting the absence of genetic heterogeneity. On the other hand, the fact that there is only one ARPCD gene for a large spectrum of clinical features suggests that there are other complementing genetic factors in the disease manifestation.

This represents the first study on this subject from Turkey. Including our own case, all families tested thus far from different parts of the world show the same locus to be susceptible. The mutation-carrying chromosomes thus seem to descend from different ancestors. Prenatal diagnosis is quite feasible when the family members are available.

Addendum

Linkage analysis with chromosome 6p markers was performed during the second pregnancy. This study demonstrated that the fetus was heterozygous and not homozygous for the ARPCD gene. The mother has just delivered a healthy baby with normal ultrasonography findings.

REFERENCES

1. Bernstein J, Slovis TL. Polycystic diseases of the kidney. In: Edelmann CM Jr (ed). Pediatric Kidney Disease (2nd ed). Boston: Little Brown and Co; 1992: 1139-1157.
2. Cole BR, Conley SB, Stapleton FB. Polycystic kidney disease in the first year of life. J Pediatr 1987; 111: 693-699.
3. Zerres K, Rudnik-Schoneborn S, Deget F, et al. Autosomal recessive polycystic kidney disease in 115 children: clinical presentation, course and influence of gender. Acta Paediatr 1996; 85: 437-445.
4. Zerres K, Mucher G, Bachner L, et al. Mapping of the gene for autosomal recessive polycystic kidney disease to chromosome 6p21-cen Nat Genet 1994; 7: 429-432.
5. Guay-Woodford LM, Muecherr G, Hopkins SD, et al. The severe perinatal form of autosomal recessive polycystic kidney disease maps to chromosome 6p21.1-p12; implications for genetic counseling. Am J Hum Genet 1995; 56: 1101-1107.