Urol Res (1990) 18:239–240

Urological Research

Association of polycystic kidney disease and an HLA haplotype within a family clan

L. X. Xu

Institute of Urology, Beijing Medical University, Beijing, People's Republic of China

Accepted: March 1, 1989

Summary. Nine members of a Chinese family underwent for HLA-A, -B. and -DR typing using microlymphocytotoxicity technique. The results of genotyping of the family showed that all four individuals who suffered from polycystic kidney disease shared the HLA-A9(Aw24), -Bw22, and -DR5 haplotype. It indicated that polycystic kidney disease was associated with an HLA haplotype in the family. We suggested that the HLA-A9(Aw24), -Bw22, -DR5 chromosome might carry the susceptibility gene of polycystic kidney disease in this family.

Key words: Polycystic kidney – Family HLA haplotype – Pedigree

Polycystic kidney is hereditary, but research has not revealed its genetic basis.

Herein, we report a pedigree in Beijing (The People's Republic of China), in which polycystic kidney disease was found associated with an HLA haplotype in four of the nine members (involving three generations) of the family.

Materials and methods

Patients details

A 10-year-old girl first came to our clinic on June 7, 1982. Her first episode of gross hematuria occurred at the age of 9. Physical examination revealed a blood pressure of 130/100 mmHg, and a palpable left kidney. Ultrasound Scan as well as IVU indicated the presence of polycystic changes in both kidneys with the largest cyst in the left kidney of 6 cm. The patient's parents, grandfather, aunt, cousin and two siblings were also examined in our clinic. Clinical examination including physical examination, B Scan Ultrasonography and HLA studies, verified polycystic disorder in the kidneys of her father and her younger sister (8 years old). Her grandmother had died of hypertension, uremia and polycystic disease.

Methods of investigation

Lymphocytes of each individual were isolated from peripheral blood by density gradient. Nylon wool separation method (scrubbed nylon fiber – 3 denier, 3.81 cm, type 200, made in USA Fenwal Laboratories), was accepted for separation B lymphocytes from T lymphocytes [3]. The microcytotoxicity text, now used for routine tissue typing [2, 4], was performed for HLA-A, -B, and -DR typing with 192 HLA-A, -B typing alloantisera (to detect 53 distinct HLA-A, -B locus antigens) and 29 HLA-DR (DR 1–7) typing alloantisera. This method of HLA typing is performed by applying standarized antisera of defined specificity to the lymphocytes to be tested together with complement and the then observing whether the test cells are killed (cytolysis). HLA DR cytotoxicity assay is established on isolated B lymphocytes.

Results

The results of genotyping of this family are detailed in Fig.1. In the case of the patient's grandmother, deduced haplotypes have been shown. Although this is a small pedigree of only 9 individuals, it is interesting to note that all four individuals who suffered from polycystic kidney disease shared the HLA-A9(Aw24), -Bw22 and -DR5 haplotype. The aunt, cousin and 3 other family members without clinical evidence of the disease did not express this haplotype.

Discussion

HLA can be defined as a series of cell surface molecules (gene products) coded for by a corresponding series of closely linked genes. The HLA haplotype is a segment of an autosome, the sixth chromosome [1]. Observations on this pedigree lead us to suggest that the HLA-A9(Aw24), -Bw22, -DR5 chromosome might carry the susceptibility gene of polycystic kidney disease in Tians's family.

It is noteworthy that the youngest sibling did not develop the disease, but inherited the HLA-A9(Aw24), part of the haplotype (HLA-A9(Aw24), -Bw22, -DR5) as

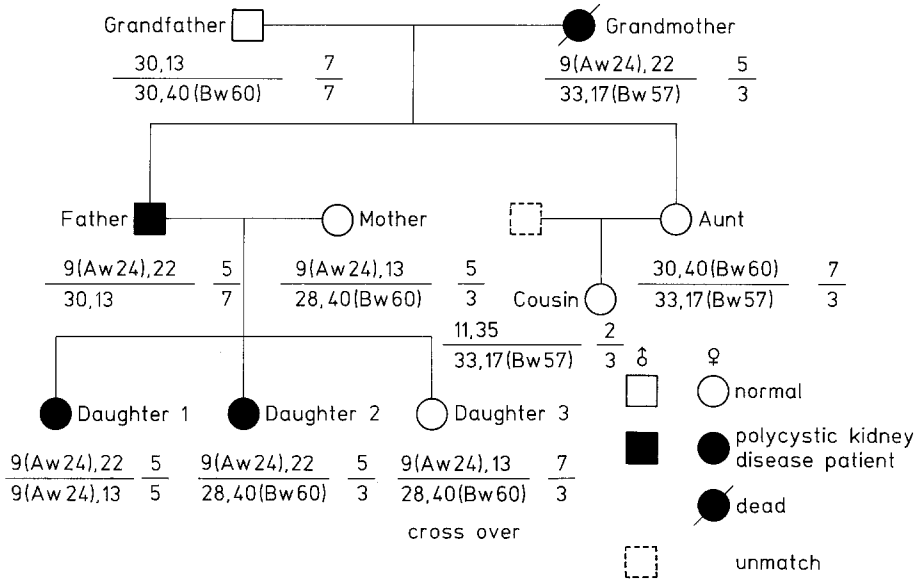

Fig. 1. Pedigree of family Tian with polycystic kidney disease

a result of crossing over in her paternal chromosome 6. Whether the child will develop polycystic kidney disease probably hinges on the presence or absence of the suspected disease – susceptibility gene to exist on the HLA-A9(Aw24) part of this haplotype.

Acknowledgement. The author wishes to acknowledge the courtesy of professor T. D. Lee of American Red Cross, Bethesda, USA and Thomas C. Fuller of Massachusetts General Hospital, Boston USA for providing most of HLA-A, -B, -DR typing sera.

References

1. Amos DB (1980) Genetics of the HLA system. In: McCullough JJ, Hansen J (eds) The biology and function of the major histocompatibility complex, chapt 1. American Association of Blood Banks, Washington, p 1
2. Dejelo CL, Mogor J, Zachary AA (1981) DR typing. In: Zachary AA, Braun WE (eds) The AACHT laboratory manual, chapt II. American Association for Clinical Histocompatibility Testing, New York, p3-1
3. Fotino M, Menon AK (1981) Nylon wool separation of T and B lymphocytes. In: Zachary AA, Braun WE (eds) The AACHT laboratory manual, chapt I. American Association for Clincal Histocompatibility Testing, New York, p8-1
4. Hopkins KA, Macqueen JM (1981) Basic microlymphocytotoxicity technique. In: Zachary AA, Braun WE (eds) The AACHT Laboratory Manual, chapt II. American Association for Clinical Histocompatibility Testing, New York, p1-1

Prof. Xu Ling-Xun
Institute of Urology
Beijing Medical University
1 Da Hong Luo Chang
Beijing 100034
People's Republic of China