Iranian J. Publ. Health, 1999, Vol. 28, Nos. 1 - 4

AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD) IN A LARGE IRANIAN FAMILY

D.D. Farhud[1], MD, PhD, MG; H. Sadighi[1], MD, T. Rezaie-Jami [1], MSPH; B. Broumand [2], MD; H. Bahari[1], MD

Key words: *ADPKD, PKD, kidney disease, renal failure, Iran*

Abstract

Study of a family with autosomal dominant polycystic kidney diseases (ADPKD) in five generations, including 96 healthy and 47 affected individuals, has been carried out in Tehran.

Investigation on individuals, including final diagnoses by clinical findings, sonography, radiography and laboratory results, have lead to the completion of genealogical chart of the family. The affected individuals have reached a stage of the disease with confirmed occurance of renal damages.

Uncertain diagnoses, unconfirmed statements of the family members about probable presence of the diseases in some other members, and also the death of some members by other reasons were not possible to be registered in the chart.

Up to now the chart has been the largest and the most complete in Iran, compared with the ones reported in the available literature.

Introduction

Cystic diseases of the kindney are the cause of over 10% of all end stage renal disease (ESRD). One of the most common monogenic disorders in human is autosomal dominanat polycystic kidney disease (ADPKD), affecting 1/1000 live births with three types reported, on the basis of the involoved chromosomes.

Linkage studies have shown that the majority (85%) of cases are due to mutations in PKD1 on chromosome 161, and mutations in PKD2 on chromosome 4q account for most of the remaining cases (7). The disease may become symptomatic in neonate (oligohydramnion syndrome: Potter syndrome), childhood or early adult

1- Dept. of Human Genetics & Anthropology, School of Public Health and Institute of Public Health Research, Tehran University of Mediacal Sciences, P.O.Box 14155-6446, Tehran, Iran.

2- Dept. of Nephrology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.

life, but it usually is discovered in the third, fourth or fifth decade of life (4,6).

However, in some cases it is never discovered or reported (5). Various forms of plycystic kidney disease accounts for up to 10% of patients requiring renal replacement therapy (1).

Progressive formation and enlargement of cysts in the kidney and other organs such as the liver, spleen, pancreas and lungs are characteristics. The cysts might be detectable by or before the age of 20. Cortex and medulla of both kidneys usually have large numbers of spherical cycts within membranes. Formation of the cysts is thought to result from failure of union of the collecting and convoluted tubules of some nephrons. The diameters vary from a millimeter to few centimeters. New cysts do not form, but the present ones enlarge and cause pressure and destruction of adjacent tissues. The kidney's parenchyma may be normal, nephrosclerotic or show interstitial nephritis (2,4).

The disease usually starts with flank pain, at times, due to haemorrhage in a cyst, causing haematuria, leading to anaemia. 10% of patients pass urinary calculi, 75% present with hypertention. Proteinuria usually exists, urinary infections happen sometimes along the course. Acute renal problems may be caused by the closure of the ureters, due to infection, caluculi, clot or cysts. 50% of patients become uraemic. Also proteinemia, hematuria, pyelonephritis, gastrointestinal symptoms, hypertonia in 50-70% of cases, brain aneurism in 30% and hepatic cysts in 30% of patients have been observed. Liver may function normally and the cysts might show no sign and epigastric discomfort may not be present (4,6).

Materials and methods

Most members of the family under study were referred to several private physicians' offices, some referred to the Nephrology Division of the Shariati University Hospital. The rest of the patients were found by searching, follow up and questioning the other family members. Among them few deceased cases, without extensive medical files were found. About half of the cases lived in Tehran and the other half in other cities; so the coworkers had to travel to those cities to examin the patients to obtain laboratory results and other information. Few cases lived in other countries.

The findings were confirmed by repeated nephrologic examinations,

laboratory findings, ultrasonography, radiology, and short term hospitalization (for different medical reasons) for some of the patients.

Due to some difficulties, such as the unknown addresses, deceased ones and incooperative individuals, specifications were not used in the pedigree or the discussions.

Results and discussion

Adult Polycystic Kidney Disease with clinical signs of dehydration, hypertention, large and palpable kidneys in 47 the most affected individulas (20 males and 27 females), was diagnosed in a large Iranian Moslem family, in 5 generation with 143 members, living in Iran and few in other countries (Fig 1, Table 1). The disease was in most cases realized in the third decade of life, and as dehydration causes great discomfort, it became apparent during hot seasons.

In the available patients, renal calculi were observed in 21% of the individuals. Renal colic existed in most of the affected persons. Hematuria was persent, at times, in some of them. Cysts in other parts of the body, specially in liver, were not detected. Known CNS bleeding, including ruptured cerebral aneurysm, were observed in 11% of the cases and heart failure in 6.5%. The existing literature have shown nearly similar observations (4).

The affected cases in the pedigree were observed to be less than the expected 50%. This is due to the fact that some had deceased, prior to be diagnosed and the relatives have reported them as healthy members.

Acknowlegdement

The authors are thankful to those who have assisted in gathering the data, including the personnel in the hospitals and private section, but most specially, to the patients and their families, for their cooperations in providing information, physical and laboratory examinations.

Figrue 1- Pedigree of an Irainian ADPKD kindred

Table 1. The numbers of affected and non affected individuals, male and female, in the family

Members	Male	female	Total
Affected	20	27	47
Non affected	48	48	96
Total	68	75	143

References

1- Brazda E, Ofner D, Riedmann B, Spechtenhauser B, Margreiter R (1996): The effect of nephrectomy on the outcome of renal transplantiation in patients with polycystic kidney disease. *Ann-Transplant.* 1(2): 15-8.

2- Emery AEH, Rimoin DL (1995): *Principles and Practice of Medical Genetics.* Churchill Livingstone, NY.

3- Farhud DD, Rezaie - Jami T, Bahari H, Brounmand B (1998): Presentation of a large Iranian family affected with autosomal dominant polycystic kidney disease. 21st Annual Meeting of Human Genetics Society of Australasia, Fermentle, W. Australia, 21-24 July 1997.

4- Harrison's Principles of Internal Medicine, 13th ed, McGraw-Hill, N.Y. 1994.

5- Higashihara E, Nutahara K, Kojima M, Tamakoshi A, et al (1998): Prevalence and renal diagnosis of diagnosed autosomal dominant polycystic kidney disease in Japan. *Nephron.* 80(4): 421-7.

6- McKusick VA (1996): *Mendelian Inheritance in Man.* The Johns Hopkins Univ. Press. Ninth Edition.

7- Pei Y, He N., Wang K, Kasenda M et al (1998): A spectrum of mutations in the polycystic kidney disease -2 (PKD2) gene from eight Canadian kindreds. *J. Am Soc. Nephrol.* 9(10): 1853-60.