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Preliminary Report : EVIDENCE OF AUTOSOMAL RECESSIVE FORM OF ALPORT SYNDROME IN IRAN

D.D. Farhud [1] , MD, PhD, MG; T.Rezaie Jami, BS; M.R. Khosh-sorour [2], MD; M. Islami [3], MD; B.Broumand [4], MD, F A C P

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Abstract

Alport syndrome is a progressive hereditary nephritis leading to renal failure. Nearly all of the documents declare that Alport syndrome is inherited as X-linked dominant trait and reports of autosomal inheritance form is very rare. This paper presents an Iranian large Alport family with autosomal recessive inheritance. In our patients Alport disease was confirmed with electron microscopic studies of renal biopsies.

Introduction

Alport syndrome in an inherited progressive renal disease, characterized by hematuria and eventually renal failure, often accompanied by sensorineural hearing loss and ocular lesions such as lenticonus and retinal flecks(1). It is usually inherited as a X-chromosome linked

1- Dept. of Human Genetics and Anthropology, School of Public Health, Tehran Univ. Med. Sci P.O.Box 14155-6446.

2- Dept. of Ophthalomolgy, Farabi Eye hospital, Tehran Univ. Med. Sci, Tehran- Iran.

3- Dept. of ENT, Amir Aalam hopsital, Tehran Univ. Med. Sci, Tehran-Iran.

4- Dept. of Nephrology, Iran Univ. Med. Sci., Tehran- Iran.

dominant trait, but autosomal forms have been described(5,9).
Electron microscopy usually shows irregular thickness and splitting of Glomerular Basement Membrane(GBM).

Materials and Methods

An investigation was started to identify families with Alport syndrome to determine the hereditary pattern of the disease in Iran.

Nearly all of the documents declare that Alport syndrome is inherited as X-linked dominant trait and reports of autosomal inheritance form is very rare.

The existence of an autosomal recessive form is less clear. However a female offspring of a first-cousin marriage who was found to have nephritis, deafness and characteristic electron microscopic features was described(7). The parents were unaffected but two maternal uncles had chronic nephritis and neurosensory deafness. Other investigators have found 4 families in which autosomal recessive inheritance seemed likely because of parental consanguinity and unaffected parents(3).

This paper presents an Alport syndrome kindred with autosomal recessive inheritance. Our patients had the characteristic electron microscopic changes on their renal biopsy specimens(6) as described in 1969, and they had at least one of the three following criteria:

1) Positive family history of hematuria with or without renal failure
2) Chracteristic ocular signs
3) Progressive sensorineural deafness

Results and Discussion

The pedigree of two families are shown in fig 1.

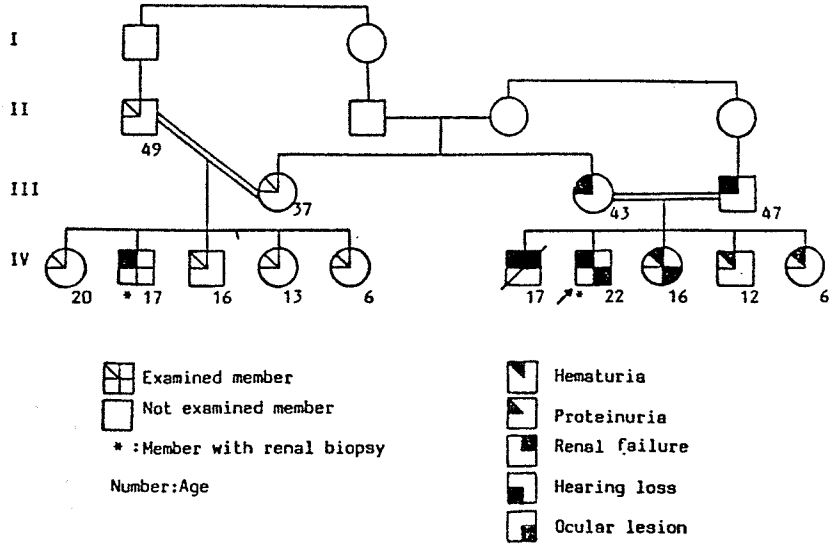

Fig. 1.- Pedigree of a kindred with Alport syndrome.

In this kindred the family history is positive for renal disease with hematuria. In IV-2 and IV-7 ultrastractural analysis of renal biopsy revealed in some capillary basement membranes are thin, and others are thickened. In all capillaries the lamina densa is poorly formed and shows splitting and splintering. In IV-2, electron dense particles are seen in some basement membranes(Fig 2).

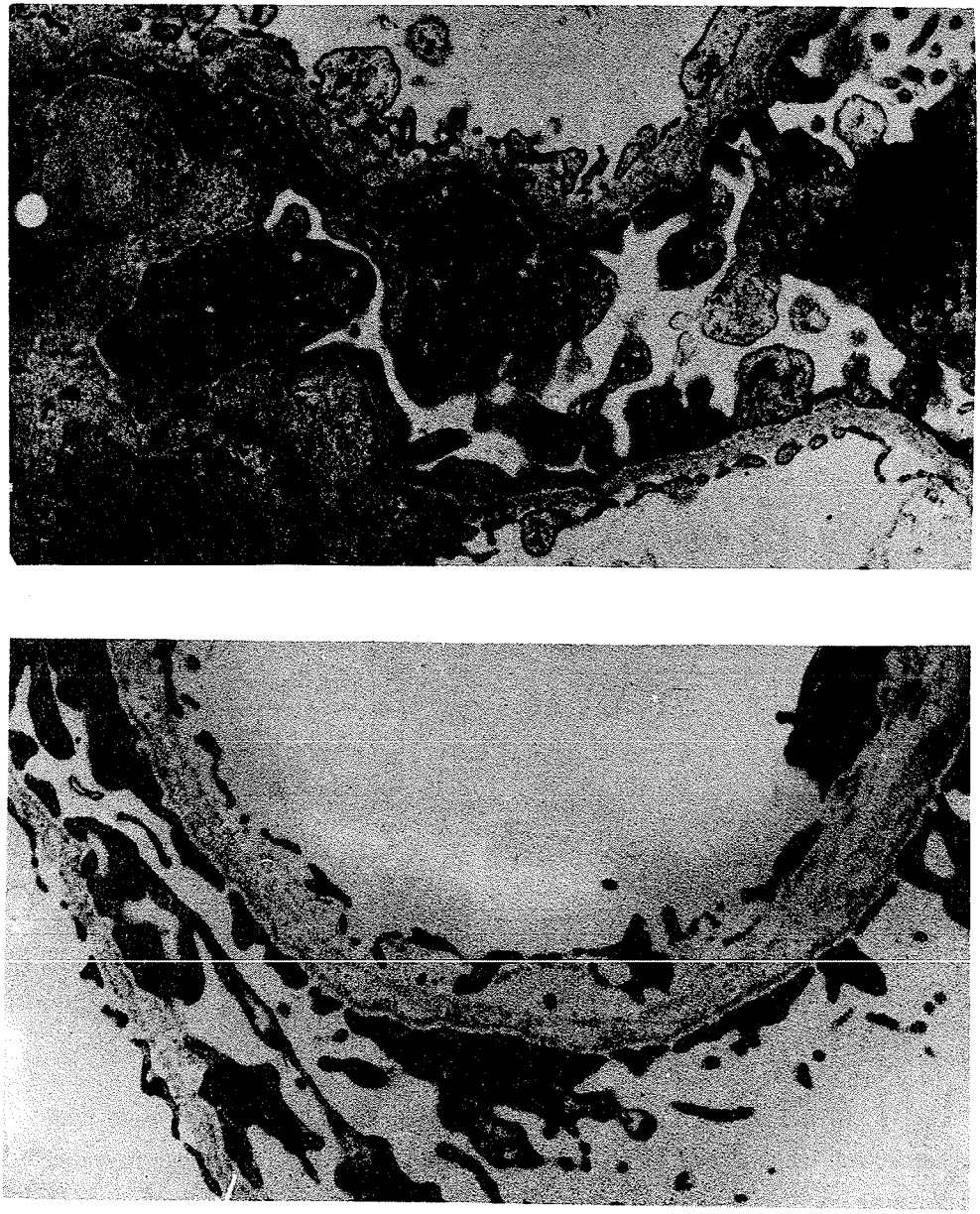

Fig 2- Electron micrographs show alterations of glomerular basement membrane in IV-2 (above) and IV-7 (below).

Singificant clinical findings are reported below:

IV-7(proband), 22 years old, showed hematuria and proteinuria at age 14. BUN, serum creatinine and audiologic testing have been normal till now. Ophthalmologic examination showed bilateral corneal arcus. The prevalence of this finding in general population in the age range of 20-30 is about 17% (2) but the prevalence in Alport syndrome is reported to be somewhat more(8,4). Otherwise the eyes were normal.

III-3 and III-4(The proband's parents), is known to have hematuria and trace proteinuria for the last 8 years. They have first cousin marriage.

IV-6(The proband's brother), died with renal failure at age 17, while he was undergoing his first hemodialysis treatment.

IV-8(The proband's sister). 16 years old, showed hematuria at age 15, ocular examination showed normal fundi and vision but slit lamp examination revealed bilateral punctate lens opacities. Similar lesion have already been reported in Alport syndrome(6,7) although no lens opacity is characteristic of Alport syndrome(9).

IV-9 and IV-10(The proband siblings), 9 and 10 years old show hematuria.

III-2(The proband's maternal aunt), 37 years old, and III-1 her husband had related marriage and they didn't show hematuria.

IV-2(son of III-1), 17 years old, showed hematuria and proteinuria at age 16, BUN, serum creatinine and ocular examination are normal at present.

IV-1, IV-3, IV-4 and IV-5 (children of III-1), appeared to be healthy at the time of this report.

The pedigree analysis of this family and first-degree relatives of parents with their asymptomatic or microsymptomatic features revealed an autosomal recessive inheritance of Alport syndrome in a large family.

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