ALPORT'S SYNDROME

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SUMMARY

Alport's syndrome (hereditary nephropathy) is a progressive nephropathy characterized by focal and segmental thickness of the basement membrane with cleft formation in the lamina densa of the basement membrane, sensorineural deafness, lenticular opacities, corneal and retinal abnormalities. The course of the disease is rapid in males and father to son transmission does not occur. The commonest mode of transmission is X linked though autosomal mode of inheritance is well described. Patients with Alport's syndrome don't get Goodpasture syndrome unless they are transplanted because they lack Goodpasture antigen .We studied 10 cases of Alport's syndrome at the department of medicine Hayat Abad Medical Complex Peshawar 1997-2001. Out of 10 cases 9 were males (90%) and only 1 (10%) case was a female. Most of the cases were young, 5-15 years 8 cases (80%). 9 cases (90%) had non-nephrotic range proteinuria and 5 cases (50%) had normal creatinine at the time of diagnosis. Corneal, retinal abnormalities and sensorineural deafness was fairly common (100%). All cases had microscopic haematuria and only 1 (10%) case had macroscopic haematuria. We conclude that Alport's syndrome should be considered in the differential diagnosis of haematuria when there is deafness or a family history of renal disease.

INTRODUCTION

Alport's syndrome is a rare disease accounting for less than 2% cases of end stage chronic renal failure[1]. It has got variable inheritance both autosomal and X linked[2]. The disease is characterized by progressive nephropathy, sensorineural deafness and characteristic lenticular and retinal changes[3]. Father to children transfer does not occur and the disease affects females less severely. In 15% cases there is no family history. Perhaps the disease is acquired as a result of mutation in the gene encoding for certain basement membrane antigens[4]. Alport's syndrome should be considered in the differential diagnosis when there is a family history of renal disease with associated deafness. Little is

known about the epidemiology of the disease locally. We conducted a retrospective study of 10 cases of Alport's syndrome who were diagnosed at the department of medicine Hayat Abad Medical Complex 1997-2001 to study the age and sex distribution, morphology of the disease, the degree of proteinuria and renal failure.

MATERIAL AND METHODS

All cases that were suspected to have Alport's syndrome had a comprehensive history, physical examination and base line investigation done. An informed written consent was taken from the patient or the relative. All cases had a thorough ophthalmological examination done by an ophthalmologist. An E.N.T. specialist saw all patients and had an audiogram done. Exclusion criteria were a single kidney, hydronephrosis, urogenital malformation or bleeding diathesis, which cannot be corrected. A kidney biopsy was performed via a monopty needle (Bard U.K.) under local anesthesia and ultrasound guidance.

RESULTS

Out of 10 cases 9 were males and only one case was female as shown in Table 1. Their age distribution is shown in Table 2. The degree of proteinuria at the time of presentation is shown in Table 3. The extent of renal impairment is shown in Table 4. The frequency of ophthalmological and sensorineural abnormality is shown in Table 5.

SEX DISTRIBUTION n=10

Male	9 (90%)
Female	1 (10%)

TABLE – 1

AGE DISTRIBUTION n=10

5-10 years	3 (30%)
11-15 years	5 (50%)
16-20 years	2 (20%)

TABLE – 2

THE DEGREE OF PROTEINURIA n=10

<3 Grams	9 (90%)
>3 Grams	1 (10%)

TABLE – 3

SERUM CREATININE n=10

0.4-1 mg	5 (50%)
1.1-5 mg	2 (20%)
5.1-10 mg	2 (20%)
10.1-15 mg	1(10%)

TABLE – 4

n = 10

Corneal abnormalities	10[100%]
Lenticular opacities	10[100%]
Retinal abnormalities	0 [0%]
Sensorineural loss	10[100%]

TABLE – 5

All cases had microscopic haematuria and only one had macroscopic haematuria, which had no association with infection.

DISCUSSION

Alport's syndrome is classically inherited as X linked trait[2]. Autosomal mode of inheritance has been described where women are as severely affected as men[2]. In about 15% cases there is no family history and is perhaps due to spontaneous mutation in the gene[2,3]. Alport's syndrome commonly affects men and females are commonly carriers manifested by haematuria. We had 90% cases of males in our series.

Alport's syndrome commonly manifests as haematuria and proteinuria in early childhood. Blood pressure and serum creatinine is usually normal initially. Progression to end stage renal failure is variable but is commonly seen by 2nd or 3rd decade of life[4]. The diagnosis can be made much early by screening family members which is difficult in our setup because we had only the index case and one or two relatives at the time. While the rest of the family members were advised to come for screening but did not turn up. Most of our patients (80%) were 5-15 years old, which is similar to the international figures. 50% cases, had normal urea and creatinine at the time of diagnosis. Only 2 cases (20%) were hypertensive who had advanced renal failure.

A variety of extra renal manifestations are seen in Alport's syndrome[5]. The most common manifestations are sensorineural hearing loss, which may progress to complete deafness. Eye changes e.g. anterior lenticonus, cataracts and whitish perimacular lesions in the retina is frequently seen. All of our cases had sensorineural hearing loss, lenticonus and lenticular opacities but there were no retinal lesions. Hematological abnormalities e.g. giant platelets were not there in our series as it is there in autosomally acquired disease[6].

The hallmark of Alport's syndrome is splitting of glomerular basement membrane on electron microscopy[7]. Light microscopic abnormalities are non-specific and include focal increase in the glomerular cellularity, which progresses to glomerlosclerosis[8]. We have not got electron microscope through out our country so it was not done. There is no treatment available for the disease. However a similar form of X linked hereditary nephropathy in dog, the splitting of basement membrane and the progression to end stage renal failure can be delayed by restricting protein and phosphorus[9]. Renal transplantation is the treatment of choice. The disease does not recur in the graft. Patients with Alport's syndrome do not develop Goodpasture syndrome because they lack Goodpasture antigen[10,11,12]. About 5% cases that are transplanted develop Goodpasture syndrome after renal transplantation[13,14,15].

CONCLUSION

Alport's syndrome is a rare cause of chronic renal failure but should be considered in the differential diagnosis of haematuria and proteinuria in children. In males it progresses rapidly to end stage renal failure while in females it has got benign course. The classical histology is possible with electron microscopy and we need to have at least one in the country. More research is needed to study its true incidence and prevalence, course of the disease, inheritance and genetic abnormalities.

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