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Original Article

Alport's Syndrome: A Study of Systemic Manifestations

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Abstract

Aim: Alport's Syndrome is a rare hereditary, progressive renal disease leading to end stage renal disease associated with hearing defects and ocular anomalies. We studied the clinical profile of patients with Alport's syndrome from unrelated families and highlighted the classical symptoms, signs and laboratory findings, which can alter the prognosis of the disease.

Methods: A case record based observational retrospective study was done on 18 patients with Alport syndrome from unrelated families admitted to Kasturba Hospital from Jan. 2000 to May 2011. Clinical and laboratory features were recorded.

Results: 7 patients had a positive family history. The mean of diagnoses was 19 years. 13 patients had positive ocular manifestations and all patients had progressive high frequency sensorineural hearing loss. 5 had history of hypertension. Echocardiogram revealed left ventricular hypertrophy in 6 patients. Proteinuria was present in all with a mean 24 hour proteinuria of 2 grams. Renal failure was seen in 6 patients and 8 patients ultrasound abdomen revealed bilateral grade 2-3 parenchymal changes at the time of diagnosis. Mean stage of chronic kidney disease was stage 3.

Conclusion: In this cohort of Alport's syndrome males presented predominantly. Microscopic hematuria, proteinuria, hypertension, ocular signs and deafness were major presenting signs and symptoms. This descriptive study enumerates the classical symptoms, signs and laboratory features of the rare disorder Alport's syndrome in a large cohort.

Keywords: Alport's syndrome, Hematuria, Hypertension, Lenticonus, Retinitis pigmentosa, Sensorineural hearing loss

Introduction:

Alport's syndrome is a rare, hereditary disease. It is a severe, progressive, non-immune form of nephritis[1] and it is characterised by progressive kidney dysfunction, sensorineural hearing loss and ocular manifestations.[2,3] The prevalence of this disease is 1 in 50,000 and its incidence rate is higher among males than females.[4] The prognosis is worse in males as compared to females and most males die due to progressive renal damage during the third decade of their life.[5] Defect in the collage type IV chains of the basement membrane causes the disease. Most of the cases are X-linked (80%-85%) resulting from mutations in the gene coding for the alpha-5 chain of collagen type IV (gene COLA45) whereas autosomal recessive (10%-15%) cases result from mutations of genes coding for alpha-3 or alpha-4 chain of collagen type IV (genes COL4A3 or COL4A4) and autosomal dominant (5%) from mutation of alpha-3 or alpha-4 chain of collagen type IV (genes COL4A3 or COL4A4).[6]

Materials and Methods:

The ethical committee of the institution at which the study was carried out at approved the study. A retrospective review of case records of patients diagnosed to have Alport's syndrome who came at Kasturba hospital, Manipal in between the time period of January 2000 to December 2010 was done to look at the clinical profile of family history. The diagnosis of Alport's syndrome was made according to criteria proposed by Gubler and colleagues[7] – which include hematuria with or without proteinuria, hypertension and chronic kidney disease with the following characteristics: established kidney disease which progresses to kidney failure in at least one relative, visual impairment and sensorineural hearing loss in the patients or their kinsmen. All underwent ophthalmologic and otologic evaluations including audiometry and relevant laboratory investigations such as urine analysis for proteins, urine microscopy, blood urea, serum creatinine and ultrasound of the abdomen. Chronic kidney disease staging was done as per standard criteria.

Results:

There were 18 patients with Alport's syndrome of which 14 were males and 4 were females. The male to female ratio was 3.5:1. The mean age of the patient at the time of diagnosis was 19 years. Seven patients (38.8%) had positive family history of kidney disease.

Presenting complaints [Table 1]

Seven patients (38.8%) presented with deafness, seven patients (38.8%) with abnormal vision and four patients (22.2%) with gross hematuria. Two patients (11.1%) presented with facial puffiness, two patients abdominal pain and pedal oedema. Five patients (27.7%) gave a positive history of progressive dyspnoea and fatigue were present in four (22.2%).

Ophthalmologic findings [Table 2]

Thirteen (72.2%) patients had ocular signs. Four patients (22.2%) had anterior lenticonus, three (16.6%) patients had posterior lenticonus, two patients (11.1%) presented with both anterior and posterior lenticonus, two (11.1%) patients presented with Retinitis pigmentosa and two patients (11.1%) with idiopathic vision defect.

Otologic Evaluation:

All cases presented with sensorineural hearing loss which was bilateral and progressive in nature.

Other investigations:

All cases had microscopic hematuria at presentation with four (22.2%) patients also giving a history of gross hematuria. Sixteen patients (88.8%) were anemic(1) with mean Hemoglobin of 6 gm/dl. Proteinuria was present in all the patients which was progressive with a mean value of 2000 mg per 24 hour urine sample **[Table 3]**.

Five patients (27.7%) presented with a history of hypertension. Echocardiogram of six (33.3%) patients revealed left ventricular hypertrophy. Ultrasonography revealed grade 2-3 parenchymal changes of kidneys in eight (44.4%), eight (44.4%) patients with grade 1 parenchymal changes and two (11.1%) showed normal kidneys at the time of diagnosis. Renal failure was seen in six (33.3%) and mean stage of chronic kidney disease was stage 3.

Discussion:

The study describe a cohort of 18 patients of Alport's syndrome with male predominance. Microscopic hematuria, proteinuria, hypertension, ocular signs and deafness were major presenting signs and symptoms. Ocular signs included anterior lenticonus, posterior lenticonus and Retinitis Pigmentosa.

Table 1: Presenting complaints

Presenting Complaint	No. Of patients	Percentage
Gross haematuria	4	22.2%
Facial puffiness	2	11.1%
Dyspnoea	5	27.7%
Deafness	7	38.8%
Abnormal vision	7	38.8%
Abdominal pain	2	11.1%
Fatigue	4	22.2%
Pedal edema	2	11.1%

Table 2: Ophthalmologic findings

Clinical findings	No. Of patients	Percentage
Retinitis Pigmentosa	2	11.1%
Anterior lenticonus	4	22.2%
Posterior lenticonus	3	16.6%
Anterior and posterior lenticonus	2	11.1%
Idiopathic vision defect	2	11.1%

Table 3: Amount of Proteinuria

Amount of proteinuria	No. Of patients	Percentage
1+	6	33.3%
2+	5	27.7%
3+	2	11.1%
4+	5	27.2%

Conclusion:

This descriptive study enumerates the classical symptoms, signs and laboratory features of the rare disorder Alport's syndrome in a large cohort. The need for checking for ocular and otologic signs of Alport's syndrome in all children with hematuria is emphasised. This study looks at the systemic manifestations and speaks of their significance and how they can be used and developed as a diagnostic tool, or to develop a high index of suspicion in ambiguous cases, as well as to be used as an early screening tool in people who have had a family history of Alport's Syndrome, so that treatment can be started as early as required to delay the onset and prevent the progression to an overt and serious stage of the disease for as long as possible. Lack of genetic analysis and the retrospective nature of the study are limitations.

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