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Ocular manifestations of Alport syndrome

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Abstract

• AIM: To analyze the clinical manifestation of Alport syndrome, especially the ocular features.

• METHODS: The physical, ophthalmologic and audiologic examination results of thirty two patients with Alport syndrome were analyzed retrospectively.

• RESULTS: Thirty (93. 7%) patients had some family history. All patients had renal disease: eighteen (56. 3%) patients with chronic renal failure, four (12. 5%) patients with renal insufficiency, and the other ten (31. 3%) patients with hematuria. Twenty (62. 5%) patients had sensorineural deafness. Thirteen (40. 6%) patients had ocular deformity, five (15. 6%) patients had typical ocular changes: three patients with anterior lenticonus, and two patients with macular flecks.

• CONCLUSION: Ocular anomalies are not requisite for the diagnosis of Alport syndrome. But its typical ocular features should be recognized by the ophthalmologists which supports the diagnosis.

• KEYWORDS: Alport syndrome; anterior lenticonus; macular flecks

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INTRODUCTION

Alport syndrome, a hereditary nephritis accompanied by high tone sensorineural deafness and distinctive ocular signs, was first reported in the early 1900s by Dr. Cecil A. Alport in 1927[1]. Studies have demonstrated that it is caused by a genetic defect within one of the alpha chains of the type IV collagen, the major component of basement membranes (BM) in the kidney, inner ear, and eye, and the disease is genetically heterogeneous[2-6]. In this article, we analyzed patients with Alport syndrome retrospectively in order to assess their clinical manifestations, especially the ocular features.

MATERIALS AND METHODS

A total of 32 patients with Alport syndrome were analyzed retrospectively. They were 20 males and 12 females, aged from 13 to 55 years with a mean of 35. 3 years. The mean age of onset of the disease was 24. 9 years (range 1. 5-54. 0 years). The information collected included the gender and age of patient, age of onset of the disease, family history, mode of inheritance, brainstem electric response audiometry, renal function, renal biopsy, ophthalmic examination of cornea, lens and fundus.

The diagnosis of Alport syndrome could be made if at least three of the following criteria were present[5]: (1) Hematuria in other family members with or without chronic renal failure. (2) A kidney biopsy with the characteristic histological lesions (i. e. thickening and splitting of the glomerular basement membrane-GBM). (3) Ocular involvement, specifically, anterior lenticonus and macular flecked retinopathy. (4) Progressive auditory involvement (high-tone sensorineural deafness).

RESULTS

History of Genetic Inheritance Among the 32 patients, thirty cases (93. 7%) had family history, including X-linked dominant (XD) in 12 cases (8 males and 4 females); autosomal dominant (AD) in 3 cases (2 males and 1 female); autosomal recessive (AR) in 1 case (a female); dominant (D) in 4 cases (1 male and 3 females); and the other 10 cases can not be determined according the existing data.

Renal System All patients had renal disease: 18 (56. 3%) patients with chronic renal failure, 4 (12. 5%) patients with renal insufficiency, and the other 10 (31. 3%) patients with microscopic or macroscopic hematuria.

Among the 12 patients in whom renal biopsy was performed, 11 cases showed diffuse uneven thickness of GBM, and the lamellated GBM was seen in one patient.

Auditory System Twenty (62. 5%) patients had hearing loss: 14 cases with sensorineural deafness (8 males and 6 females); 5 cases with high-frequency decline (3 males and 2 females); 1 case (a male) with mixed deafness.

Visual System Ocular anomalies occurred in 13 (40. 6%) patients, which included anterior lenticonus, cataract, macular flecks and nystagmus. Among them, 5 cases (15. 6%) had the typical changes (3 with anterior lenticonus, and 2 with macular flecks). The typical ocular anomalies were coincided with longer course of disease (13. 2 years *vs* 9. 3 years in patients with other ocular anomalies), sensorineural

Table 1 The data of 13 Alport syndrome patients with ocular anomalies

No.	Age (yrs)	Sex	Age of onset of disease	Family history	Ocular examination				Physical examination		SND
					Anterior lenticonus	Cataract	Macular flecks	Nystagmus	Hematuria	Renal function	
1	31	M	8	XD	+	+	−	−	Mi	CRF	+
2	40	F	40	*	−	+	−	−	Mi	Nor	−
3	29	M	10	XD	+	−	−	−	Mi	CRF	+
4	27	M	22	XD	−	+	−	−	Mi + Ma	RI	−
5	21	M	17	*	−	−	−	+	Mi	RI	−
6	27	M	27	No	−	+	−	−	Mi	Nor	+
7	27	M	1.5	XD	−	+	−	−	Mi + Ma	CRF	+
8	20	M	15	XD	−	−	+	−	Mi	CRF	+
9	39	F	21	XD	+	+	−	−	Mi	CRF	+
10	37	F	36	XD	−	+	+	−	Mi	Nor	+
11	55	F	27	*	−	+	−	−	Mi	CRF	−
12	44	F	44	XD	−	+	−	−	Mi	RI	+
13	37	F	35	*	−	+	−	−	−	RI	−

M = Male; F = Female; XD = X-linked dominant inheritance; Mi = Microscopic hematuria; Ma = Macroscopic hematuria; CRF = Chronic renal failure; RI = Renal insufficiency; SND = Sensorineural deafness; Nor = Normal; * = Have some uncertain inheritance.

deafness and poor kidney function which could progress to renal failure (Table 1).

DISCUSSION

Alport syndrome is an inherited disorder of collagen that affects the kidney, the eye, and the cochlea. The disease exhibits variability in its clinical and pathological manifestations, and is genetically heterogeneous. Approximately 80% of patients with Alport syndrome is X-linked. In about 10%, the transmission is autosomal recessive and exceptionally autosomal dominant. In the remaining 10%, there is no family history[7]. Generally, Alport syndrome affects boys more than girls. In our study, X-linked dominant Alport syndrome is also the most common one.

The most significant organs affected in Alport syndrome are the renal system. Hematuria is the earliest clinical sign. This may be the primary presentation of the syndrome in children. As these patients get older, they begin to show additional signs of kidney disease, such as proteinuria and high blood pressure. These symptoms usually occur by the time the boys are teenagers. Boys with X-linked Alport syndrome develop kidney failure by the teenage years or early adulthood, but the onset of kidney failure can be delayed until 40 to 50 years of age in some patients. Most girls with X-linked Alport syndrome do not develop kidney failure. However, as women with Alport syndrome age, the risk of kidney failure increases[4]. In our study, all the patients had renal disease: 18 (56.3%) with chronic renal failure, 4 (12.5%) with renal insufficiency, and the other 10 (31.3%) with microscopic or macroscopic hematuria.

The appearance of the renal biopsy is the "gold standard" for the diagnosis of Alport syndrome. In our study, renal biopsy was performed in 12 patients; 11 cases showed diffuse uneven thickness of GBM, and the lamellated GBM was seen in one patient. Therefore, the medical anomalies are the primary basis for diagnosis of Alport syndrome, renal biopsy being the confirmatory investigation.

The auditory presentation of bilateral, symmetrical hearing loss in Alport syndrome is quite significant. Most of the patients have hearing loss by age of 10 years. Auditory manifestations appear to parallel the severity of renal involvement and may be coincident with the ocular signs. Females with Alport syndrome are less severely affected and the deficit is usually non-progressive. From our study, we found that most patients (62.5%) with Alport syndrome had sensorineural deafness, especially in male patients. Studies have found that such hearing loss is mainly caused by cochlear lesions, while the latter has a similar structure with the glomerular basement membrane [8].

Ocular anomalies have been reported in 9% to 82% of Alport syndrome patients[9,10]. They are rare in childhood and increase in frequency and severity with age. The types of ocular defects described mostly involve the lens, the retina and more rarely the cornea. The most common changes are anterior lenticonus and perimacular retinal flecks[11].

Anterior lenticonus is an abnormality in the shape of the lens of the eye and affects about 15% to 20% of patients with X-linked and autosomal recessive Alport syndrome. People with anterior lenticonus may have a slow progressive deterioration of vision requiring patients to change the prescription of their glasses frequently. This condition may also lead to cataract formation[12,13]. Some people with Alport syndrome have abnormal pigment of the retina called dot-and-fleck retinopathy, but this does not result in any abnormalities of vision[14]. Recurrent corneal erosion is another eye problem that can occur in people with Alport syndrome.

Ocular anomalies occurred in 13 patients (40.6%) in our group, but only 3 patients showed anterior lenticonus, and 2 patients showed perimacular retinal flecks. It had been reported that ocular characteristic changes always occurred in the late stage of Alport syndrome. Relatively long course of disease (13.2 years *vs*9.3 years) and lower positive rate of patients with characteristic changes in our group also

confirmed this viewpoint. In this study, we also found that the characteristic ocular changes occurred in patients with Alport syndrome, especially the anterior lenticonus, was mostly accompanied by sensorineural deafness and renal failure. The findings may suggest that occurrence of ocular characteristic changes, especially the anterior lenticonus, implies a worse prognosis of patients with Alport syndrome.

In summary, ocular anomalies are not requisite for the diagnosis of Alport syndrome. But ocular examination is a precious help for the diagnosis. Ocular anomalies, especially the typical ones can also determine the prognosis of nephropathy. When confronted with such patients, we should get their renal investigations and audiology examination for an early diagnosis of Alport syndrome and appropriate treatment.

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Alport 综合征眼部临床表现分析

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摘要

目的:总结 Alport 综合征的临床表现,尤其是眼部特征。

方法:回顾性分析 32 例被确诊为 Alport 综合征患者的内科、耳鼻喉科和眼科检查结果。

结果:患者 30 例(93.7%)有疾病家族史。所有患者均有不同程度的肾脏病变:18 例(56.3%)有肾功能衰竭,4 例(12.5%)肾功能不全,10 例(31.3%)血尿。患者 20 例(62.5%)有感音神经性耳聋。患者 13 例(40.6%)有眼部异常表现,其中 5 例(15.6%)为典型性改变:前圆锥晶体 3 例,黄斑周围斑点 2 例。

结论:眼部异常不是 Alport 综合征诊断的必需条件,但因其典型的眼科表现应当引起眼科医师的注意,以便早期诊断治疗。

关键词:Alport 综合征;前圆锥晶状体;黄斑斑点