Case Report

Genetic Insights into Alport Syndrome: A Case Report Highlighting COL4A3 Mutation and Ocular Phenotype

Ruchi Shukla*, Aparajita Shukla, Rinkle Nahar, Swarastra Prakash Singh, Ashutosh Kumar Mishra

Department of Ophthalmology, All India Institute of Medical Sciences, Raebareli, Uttar Pradesh, India

Abstract

Alport syndrome is a hereditary disorder characterized by ocular abnormalities, sensorineural hearing loss, and progressive renal involvement. We report a case of a 19-year-old female who presented with complaints of infrequent flashes of light in the left eye. Ophthalmic evaluation revealed high myopia, anterior lenticonus confirmed by anterior segment optical coherence tomography (AS-OCT), and temporal macular thinning on macular OCT. Systemic workup demonstrated bilateral moderate sensorineural hearing loss and severe proteinuria, with normal renal function. Genetic testing identified a probable compound heterozygous pathogenic variant in the *COL4A3* gene, confirming autosomal recessive Alport syndrome. This case underscores the pivotal role of detailed ophthalmic examination as an early diagnostic clue and highlights genetic analysis as an essential tool for definitive diagnosis, prognostication, and guiding multidisciplinary management.

Keywords: Anterior lenticonus, Alport syndrome, COL4A3 mutation, Hearing loss

Introduction

Alport syndrome is an inherited disorder caused by mutations in the COL4A3, COL4A4, or COL4A5 genes located on chromosome 2, affecting type IV collagen in the basement membranes of the kidney, cochlea, and eye. The COL4A3, COL4A4, and COL4A5 genes are responsible for producing the α3, α4, and α5 chains of type IV collagen, respectively. The glomerulus, cochlea, corneal Descemet's and Bowman's membranes, lens capsule, inner limiting membrane, and retinal Bruch's membrane all incorporate collagen IV, a crucial structural protein of the basement membrane.[1] About 10 and 5% of instances of Alport syndrome are autosomal recessive (ARAS) and autosomal dominant (ADAS), respectively, with the other 85% of cases following an X-linked inheritance pattern (XLAS).[2] About 1 in 5,000 people have Alport syndrome, which causes high-frequency sensorineural hearing loss and eventual renal failure. Dot-and-fleck retinopathy, anterior lenticonus, and, in rare cases, posterior polymorphous corneal dystrophy are ocular characteristics that help with diagnosis and usually appear gradually.[3]

Dot-and-fleck retinopathy, which is the consequence of altered retinal pigmentation, is the most prevalent retinal finding in Alport syndrome. As in this instance, this characteristic is typically asymptomatic, has no effect on eyesight, and doesn't need any kind of intervention. Temporal macular thinning, which may be linked to decreased foveal reflex, pigmentary changes at the fovea, vitelliform-like lesions, or, in rare cases, the formation of a macular hole, are further potential changes. Lenticonus is a key diagnostic sign of Alport syndrome. These ocular features can serve as important diagnostic clues and may aid in the early detection of the disease. This report details a patient with Alport syndrome who presented with typical ocular symptoms and visual difficulties.

Address for correspondence: Ruchi Shukla,
Department of Ophthalmology, All India Institute of Medical Sciences, Raebareli, Uttar Pradesh, India
E-mail: ruchi.shukla05@gmail.com

How to cite this article: Shukla R, Shukla A, Nahar R, Singh SP, Mishra AK. Genetic Insights into Alport Syndrome: A Case Report Highlighting COL4A3 Mutation and Ocular Phenotype. UP Journal of Ophthalmology. 2026;14(2): 100-103.
Received: 24-06-2026, **Accepted:** 14-07-2026, **Published:** 01-08-2026

UP JOURNAL OF OPHTHALMOLOGY
An Official Journal of Uttar Pradesh State Ophthalmological Society, UPSOS (Northern Ophthalmological Society, NOS)
p-ISSN: 2250-1916 | DOI: 10.56692/upjo.2026140210

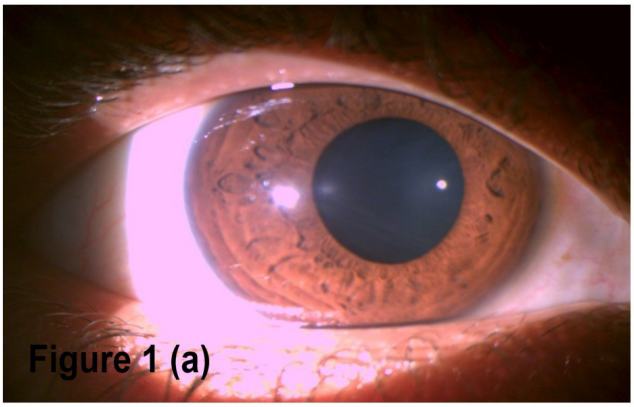

Figure 1a: Slit-lamp examination using direct focal illumination showing a protrusion of the anterior lens capsule in the right eye.

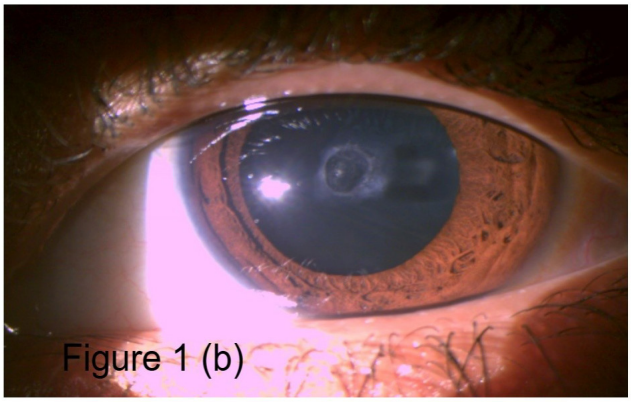

Figure 1b: Slit-lamp examination using direct focal illumination showing a conical protrusion of the anterior lens capsule, indicative of anterior lenticonus in the left eye

Case Report

A 19-year-old female presented to the outpatient department in 2025 complaining of infrequent light flashes in her left eye that had been occurring for three to four months. Diabetes, systemic hypertension, or trauma were not present in the patient's past. Informed consent was obtained from the patient.

On ophthalmic examination, the best-corrected visual acuity (BCVA) was 6/18 in the right eye and 6/12 in the left eye. The patient had a manifest refraction of -12.50 sphere in the right eye and -8.50 sphere in the left eye.

On slit-lamp examination, the cornea and anterior chamber of both eyes were found to be normal. Direct focal illumination revealed protrusion of the anterior lens capsule in the right eye, while a conical protrusion of the anterior lens capsule, consistent with anterior lenticonus and anterior capsular opacity, was seen in the left eye. (Figure 1(a, b)) Sclerotic scatter and retroillumination highlighted an irregular light reflex and distortion of the red reflex, confirming the lenticular abnormality. Intraocular pressure was 16 mm Hg in both eyes. Dilated fundus examination demonstrated myopic fundus changes bilaterally, consistent with high myopia, with no signs of retinal breaks or detachment.

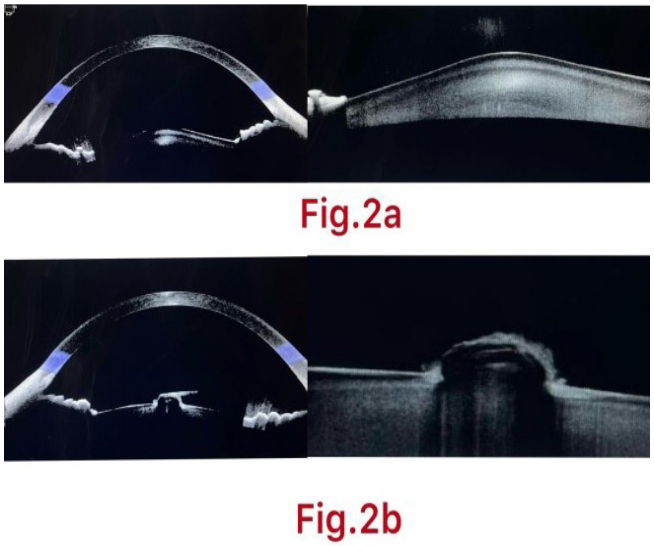

Figure 2: Anterior segment optical coherence tomography (AS-OCT) of both eyes (2a OD and 2b OS) confirms anterior lenticonus, a hallmark ocular finding in Alport syndrome

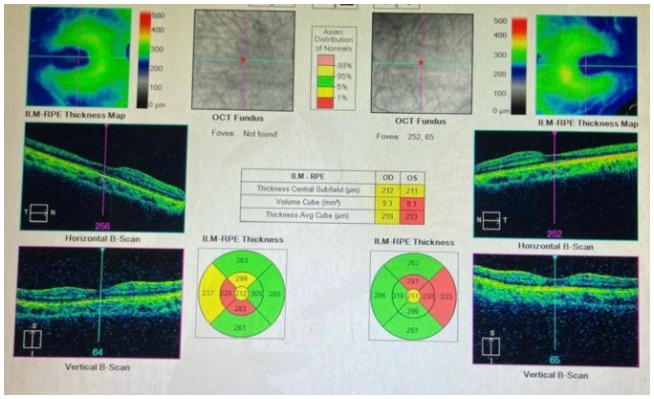

Figure 3: Macular optical coherence tomography (OCT) demonstrates temporal thinning in both eyes, consistent with Alport syndrome

AS-OCT of both eyes showed anterior lenticonus, a hallmark ocular finding in Alport syndrome (Figure 2). Macular OCT revealed temporal thinning in both eyes. (Figure 3). The patient underwent systemic examination. She had bilateral moderate sensorineural hearing loss on audiometry (Figure 4).

Proteinuria was found by urinalysis, although creatinine, urea, and electrolytes were all within acceptable ranges. There was no evidence of hematuria. Further quantitative analysis of urinary proteins demonstrated significant albuminuria, with urinary albumin (microalbumin) measured at 892 mg/L (reference range: <30 mg/L). Urinary creatinine was 30 mg/dL, resulting in an albumin-to-creatinine ratio (ACR) of 2973.3 mg/g, which is markedly elevated compared to the normal range (<30 mg/g). This value is consistent with clinical albuminuria (severe), indicating significant glomerular dysfunction.

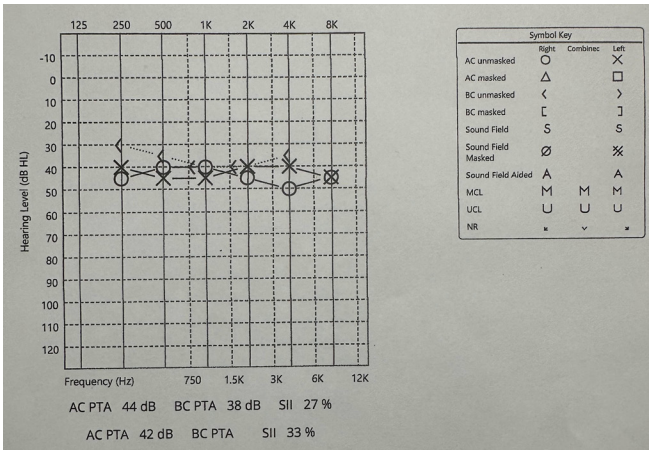

Figure 4: Bilateral moderate sensorineural hearing loss on audiometry

The ultrasound scan of the abdomen was normal. A potential diagnosis of Alport syndrome was contemplated in light of the clinical findings. Genetic analysis revealed a probable compound heterozygous pathogenic variant and a variant of uncertain significance (VUS) in the COL4A3 gene, involving exon 49 and exon 37, consistent with autosomal recessive Alport Syndrome (ARAS).

Given the ocular findings and the known systemic association, the patient was advised lens extraction and intraocular lens implantation to improve vision. The patient and her family were advised genetic counselling and nephrological evaluation and kidney biopsy for further assessment of renal involvement.

Discussion

Heterozygotes with a pathogenic variant often present with hematuria and may occasionally develop proteinuria, hypertension, or mild renal dysfunction. However, unlike X-linked Alport syndrome, these individuals rarely experience the characteristic hearing loss or ocular manifestations.[4] In contrast, our patient demonstrated pathognomic ocular changes and sensorineural hearing loss along with severe proteinuria, despite being heterozygous for ARAS and lacking hematuria or elevated blood pressure.

The ocular manifestations of Alport syndrome are essential diagnostic markers, especially for patients with an incomplete systemic presentation. In our case, genetic testing along with ocular phenotype was instrumental in establishing the diagnosis by confirming the presence of a pathogenic variant, which guided appropriate clinical management. Anterior lenticonus, observed in this case, is a classic finding resulting from defective basement membrane integrity, leading to progressive lenticular deformation. Macular thinning, particularly in the temporal region, has been reported in Alport syndrome and may contribute to visual disturbances. In this case, macular OCT scans confirmed temporal thinning. While less sensitive, OCT provides a more objective assessment compared to peripheral retinopathy.[5] Macular holes, whether lamellar or giant, are rare and are attributed to collagen IV abnormalities affecting the internal limiting membrane (ILM) or Bruch's membrane.[6]

In X-linked disease, anterior lenticonus is seen in about half of affected men but is uncommon in women, whereas in the autosomal recessive form it is frequently present in both sexes. Posterior lenticonus may occur but is rare.[2] In our case, the presence of anterior lenticonus in a female suggested the possibility of autosomal recessive inheritance.

Anterior lenticonus is absent at birth but manifests later in life, with progression as age advances. This lens abnormality leads to increasing myopia and gradual visual decline. In cases where vision is significantly affected, surgical management may be necessary to restore visual function.[2] High myopia, as observed in this patient, is another ocular finding that may be associated with the syndrome.[7] In light of the characteristic ocular manifestations and their established systemic correlation with Alport syndrome, the patient was counseled regarding the need for surgical intervention. Lens extraction with intraocular lens implantation was recommended as the appropriate management strategy to address the anterior lenticonus and associated refractive error, with the goal of improving visual acuity and overall quality of life.

Various studies have shown that X-linked and autosomal recessive Alport syndrome carry the highest risk for progression to kidney failure, as well as nearly all individuals with autosomal recessive inheritance, eventually developing end-stage renal disease. Current guidelines emphasize that individuals with a heterozygous pathogenic COL4A3 or COL4A4 variant should receive renin–angiotensin–aldosterone system (RAAS) blockade as soon as microalbuminuria, hypertension, or renal impairment is detected, as this intervention significantly delays disease progression. Additionally, cascade genetic testing of first-degree relatives is recommended for early identification and management.[4]

In our case, the patient demonstrated marked albuminuria, indicating a high risk for future renal deterioration despite the absence of hematuria or hypertension. Recognizing this early, we promptly referred the patient to a nephrologist for initiation of RAAS blockade, aiming to reduce intraglomerular pressure and slow the decline in kidney function. This highlights the critical role of early detection, supported by genetic confirmation and ocular findings, in enabling timely nephroprotective therapy and improving long-term outcomes.

Although renal disease remains the primary concern in Alport syndrome, ophthalmic evaluation plays a vital role in early diagnosis and disease monitoring. AS-OCT is particularly useful in detecting anterior lenticonus, while macular OCT helps assess retinal changes. Given the progressive nature of the disease, regular ophthalmic follow-up is essential to monitor visual function and detect complications such as retinal detachment.

The coexistence of anterior lenticonus and macular thinning in a highly myopic patient should prompt suspicion

of Alport syndrome, even when renal manifestations are not apparent. This case illustrates the diagnostic relevance of ocular findings in systemic disease and emphasizes the value of genetic testing not only in confirming the diagnosis and guiding prognosis but also in shaping further management and family counseling. Early identification enables timely initiation of RAAS blockade, which can delay or even prevent renal failure, while a multidisciplinary approach optimizes long-term outcomes.

Informed Consent

Obtained.

Conflict of Interest

No conflict of interest

Financial Disclosure

The study received no financial support.

References

1. Kabosova A, Azar DT, Bannikov GA, Campbell KP, Durbeej M, Ghohestani RF, et al. Compositional differences between infant and adult human corneal basement membranes. Invest Ophthalmol Vis Sci. 2007 Nov;48(11):4989-99. doi: 10.1167/iovs.07-0654.
2. Savige J, Sheth S, Leys A, Nicholson A, Mack HG, Colville D. Ocular features in Alport syndrome: pathogenesis and clinical significance. Clin J Am Soc Nephrol. 2015 Apr 7;10(4):703-9. doi: 10.2215/CJN.10581014.
3. Ramakrishnan R, Shenoy A, Meyer D. Ocular Manifestations and Potential Treatments of Alport Syndrome: A Systematic Review. *J Ophthalmol*. 2022;2022:9250367. Published 2022 Sep 8. doi:10.1155/2022/9250367
4. Savige J, Lipska-Zietkiewicz BS, Watson E, et al. Guidelines for Genetic Testing and Management of Alport Syndrome. *Clin J Am Soc Nephrol*. 2022;17(1):143-154. doi:10.2215/CJN.04230321
5. Ahmed F, Kamae KK, Jones DJ, Deangelis MM, Hageman GS, Gregory MC, et al. Temporal macular thinning associated with X-linked Alport syndrome. JAMA Ophthalmol. 2013 Jun;131(6):777–82. doi: 10.1001/jamaophthalmol.2013.1452.
6. Rahman W, Banerjee S. Giant macular hole in Alport syndrome. Can J Ophthalmol. 2007 Apr;42(2):314–5. PMID: 17392861.
7. Sonarkhan S, Ramappa M, Chaurasia S, Mulay K. Bilateral anterior lenticonus in a case of Alport syndrome: a clinical and histopathological correlation after successful clear lens extraction. BMJ Case Rep. 2014 Jun 26;2014:bcr2013202036. doi: 10.1136/bcr-2013-202036.