DOI: 10.7860/JCDR/2025/76787.21296

Case Series

Ophthalmology Section

A Case Series of Alport Syndrome with Posterior Lenticonus

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ABSTRACT

Alport syndrome is a genetic disorder primarily affecting the kidneys, eyes, and ears, characterised by a classical triad of haematuria, anterior lenticonus, and sensorineural deafness. This case series examines the ocular manifestations, particularly posterior lenticonus, in three patients with Alport syndrome evaluated at a tertiary care centre. By integrating current findings from recent studies, this series highlights the significance of ophthalmic assessment in diagnosing and managing Alport syndrome.

Keywords: Collagen IV, Genetic disorders, Haematuria, Sensorineural deafness

INTRODUCTION

Alport syndrome is a genetic disorder marked by progressive renal failure, sensorineural hearing loss, and ocular abnormalities due to mutations in the COL4A5 (X-linked) or COL4A3 and COL4A4 (autosomal recessive) genes. These mutations lead to the absence of the collagen IV α3α4α5 network in the basement membranes of the kidneys, cornea, lens capsule, and retina, causing varied clinical manifestations [1]. Common ocular findings include corneal opacities, anterior lenticonus, posterior lenticonus, fleck retinopathy, and temporal retinal thinning [2]. While these changes often do not impair vision, more severe complications, such as posterior polymorphous corneal dystrophy, giant macular hole, and maculopathy, can result in visual loss [3]. This case series presents three cases of posterior lenticonus in patients with Alport syndrome, highlighting diagnostic challenges and management strategies.

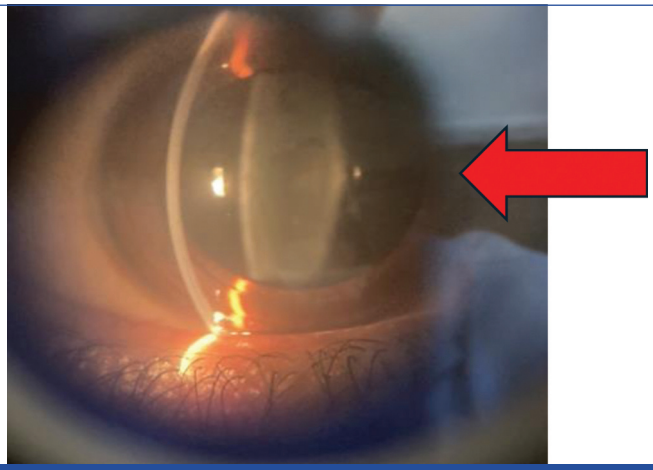
CASE SERIES

Case 1

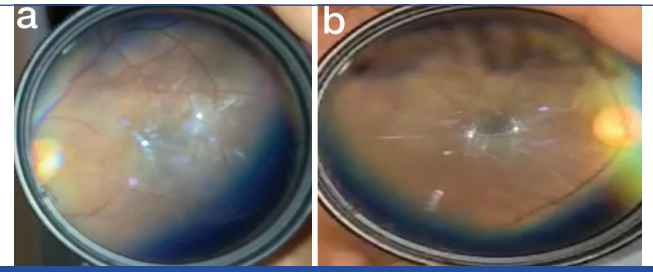
A 17-year-old male presented to the Nephrology outpatient department with complaints of intermittent haematuria and left loin pain persisting for a year. Ultrasonography revealed left-sided hydronephrosis. The patient also reported visual disturbances and was referred to department of ophthalmology.

On ophthalmic examination, his uncorrected visual acuity was 6/9 p in both eyes, improving to 6/6 p with correction. Slit-lamp examination showed a cone-shaped projection on the posterior pole of the lens in both eyes, suggestive of posterior lenticonus [Table/Fig-1]. Fundus examination with an indirect ophthalmoscope revealed white or yellow granulations in the mid-periphery of the retina and around the macula, consistent with dot-and-fleck retinopathy. A dull macular reflex, or "lozenge sign," was also noted, which has been described as indicative of Alport syndrome [Table/Fig-2a,b] [2]. The patient was suspected to have Alport syndrome and was referred to ENT, where audiometric testing [Table/Fig-3] confirmed sensorineural hearing loss. The patient was referred back to nephrology for further management and scheduled for regular follow-ups.

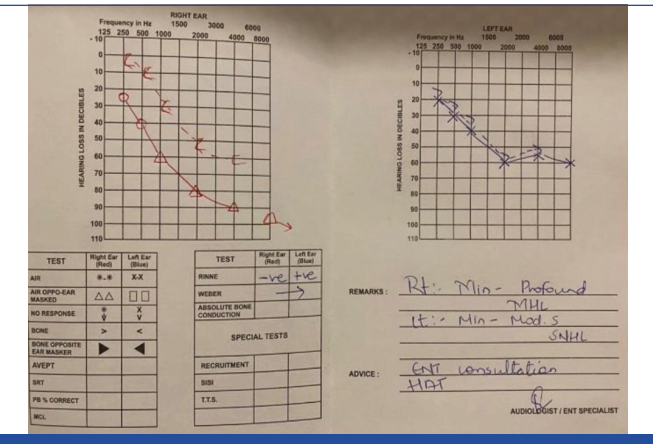
The patient was informed about the funduscopy changes and was advised to have a three-monthly follow-up in the Ophthalmology department.



[Table/Fig-1]: Slit lamp examination of right eye illustrating posterior lenticonus.



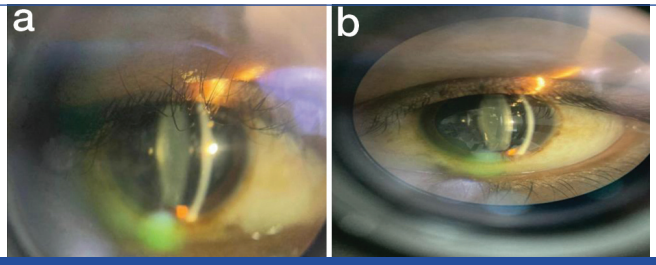
[Table/Fig-2]: Fundus examination of left and right eye illustrating fleck-shaped retinopathy and lozenge sign.



[Table/Fig-3]: Audiometry result confirming sensorineural hearing loss.

Case 2

A 22-year-old male reported to the Ophthalmic department with the chief complaint of progressive, painless blurring of vision in both eyes for six months. His uncorrected visual acuity was 6/36 p in the right eye and 6/60 p in the left eye, which improved to 6/18 p in both eyes with correction. Slit-lamp examination revealed posterior lenticonus bilaterally [Table/Fig-4a,b]. Fundus examination was within normal limits. No significant hearing impairment was detected at the time of presentation, and all audiometry findings were normal.



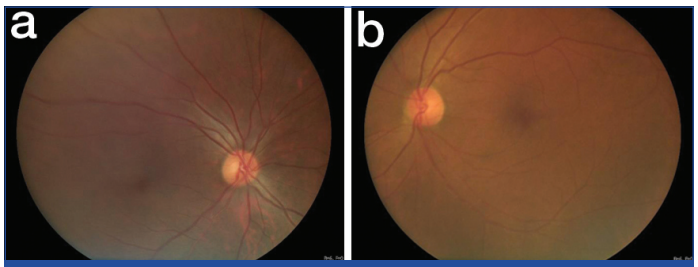
[Table/Fig-4]: Slit examination of the right eye and left eye demonstrating posterior lenticonus in both right and left eye. a) Right eye; b) Left eye.

The patient also reported a history of recurrent haematuria with 2-3 episodes per month. Urinalysis confirmed microscopic haematuria, a commonly observed early symptom of Alport syndrome [2]. The patient was diagnosed with Alport syndrome and advised to follow up with nephrology for renal monitoring. He was also advised to undergo cataract extraction with posterior chamber intraocular lens implantation for ocular correction. The patient was counselled regarding the funduscopy findings and advised to return for ophthalmic evaluation on a 'symptom-onset' basis-particularly if experiencing any reduction in visual acuity or complaints such as defective or diminished vision for near or distance. However, the patient did not report back, and hence, no follow-up evaluation was recorded.

Case 3

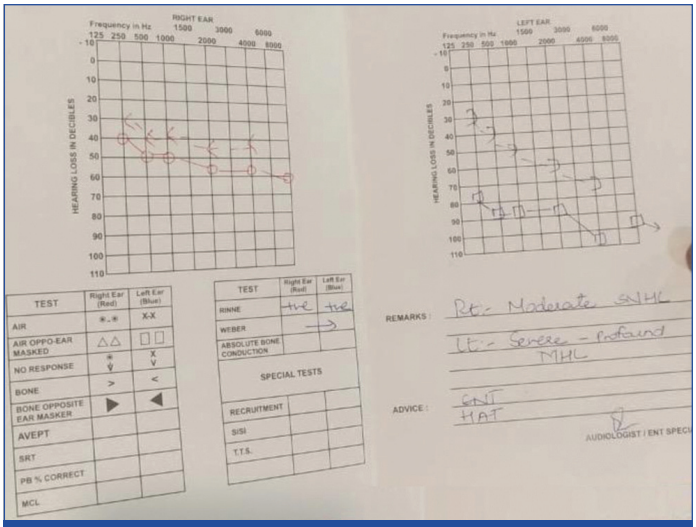
An 18-year-old male, previously diagnosed with Alport syndrome, was referred to the Ophthalmology department for evaluation of possible ocular abnormalities. The patient reported no visual complaints and had not used corrective lenses. His best-corrected visual acuity was 6/6 in both eyes.

Slit-lamp examination revealed posterior lenticonus in both eyes, while the rest of the examination was normal [Table/Fig-5a,b]. Fundus examination was unremarkable. Audiometric testing conducted in the ENT department confirmed bilateral sensorineural hearing loss [Table/Fig-6]. The patient had no active renal symptoms.



[Table/Fig-5]: Slit lamp examination (Fundus) of right eye and left eye. a) Right eye; b) Left eye.

The diagnosis of Alport syndrome was confirmed based on an electron microscopy examination conducted in the Nephrology department, which revealed mesangial widening with two to three cells per mesangial region in the glomerulus. The foot processes were diffusely flat and showed microvilli formation. The capillary loops displayed alternating thick and thin regions, with the thick regions demonstrating splitting and vacuole formation of the lamina densa. However, the typical basket weave appearance was not observed. The patient was advised to have a six-monthly follow-up and to return sooner if there was any reduction in visual acuity. Additionally,



[Table/Fig-6]: Audiometry examination confirming sensorineural hearing loss.

he was advised to undergo genetic screening for Alport syndrome. At the time of presentation, the visual acuity was 6/6 in both eyes. Therefore, the patient has been advised to return for follow-up every six months, and no active intervention was required.

DISCUSSION

This case series highlights the ocular features in Alport syndrome, with posterior lenticonus as a notable finding in all three cases. While anterior lenticonus is more commonly reported in Alport syndrome, posterior lenticonus is an equally significant finding. The presence of lenticonus, whether anterior or posterior, is considered a hallmark of Alport syndrome and can strongly indicate the condition when combined with renal and auditory symptoms [4,5]. Fleck retinopathy, as observed in Case 1, is another feature typical of Alport syndrome and may aid in diagnosing X-linked Alport syndrome. Temporal retinal thinning, particularly in males with X-linked inheritance, is also noted as a sensitive marker for Alport syndrome [1].

Fundus photography, slit-lamp examination, and OCT are essential for identifying lenticonus and retinopathy, especially in the absence of genetic testing, which may be costly or unavailable. Dot-and-fleck retinopathy, like that seen in Case 1, is a common manifestation in X-linked Alport syndrome and serves as a diagnostic marker, often appearing even when clinical retinopathy is not apparent [6].

Studies indicate that ocular signs, particularly lenticonus and central fleck retinopathy, can predict early renal failure. The presence of posterior lenticonus and retinal thinning in Alport syndrome supports the use of comprehensive ophthalmic examinations as a non-invasive, accessible diagnostic tool, especially when genetic testing is not feasible [7]. Sensorineural hearing loss, confirmed in two of the cases, aligns with previous findings that hearing impairment often occurs in male patients with X-linked inheritance. In female patients, the condition tends to progress more slowly and may initially present with milder symptoms [7].

Given the multisystemic nature of Alport syndrome, a collaborative approach involving nephrology, audiology, and ophthalmology is essential for effective management. Early treatment, such as ACE inhibitors for patients at high risk of renal progression, has shown promise in delaying end-stage renal disease [6]. Additionally, early ophthalmic intervention, such as lens extraction, can improve visual outcomes in cases where lenticonus impairs vision [7].

CONCLUSION(S)

In conclusion, this case series underscores the importance of comprehensive ocular evaluation in patients with Alport syndrome, even in the absence of overt visual complaints. Posterior lenticonus, although less commonly reported than anterior lenticonus, was a

significant finding in all the cases presented. Recognising this and other ocular manifestations, such as fleck retinopathy and temporal retinal thinning, can aid in the early diagnosis of Alport syndrome, especially when genetic testing is not readily accessible. Early identification of these ocular features can also help predict disease severity and the potential for renal progression, supporting timely interventions that may improve patient outcomes. A multidisciplinary approach involving nephrology, audiology, and ophthalmology is essential for the optimal management of this complex, multisystem disorder.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Nov 14, 2024
- Manual Googling: Mar 29, 2025
- iThenticate Software: Apr 02, 2025 (16%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Nov 12, 2024**
Date of Peer Review: **Jan 31, 2025**
Date of Acceptance: **Apr 02, 2025**
Date of Publishing: **Aug 01, 2025**