Bangladesh Journal of Medicine (BJM)
ISSN : 1023 - 1986
eISSN : 2408 - 8366

CASE REPORT

PROGRESSIVE NEPHRITIS, SENSORINEURAL HEARING LOSS, AND RETINAL ABNORMALITIES: A CASE OF X-LINKED ALPORT SYNDROME WITH GENETIC CONFIRMATION

MOHAMMAD SIRAJUL ISLAM[1], AHMED HOSSAIN[2], CHANDRA SHEKHAR BALA[3], MD. RANAUL ISLAM[4], PARTHA SAROTHI SARKER[5], MD. DHARUL ISLAM[2]

Abstract

Alport syndrome is a hereditary nephritis caused by mutations in the gene encoding type IV collagen, which presents with progressive kidney disease, sensorineural hearing loss, and eye abnormalities. We report a 20-year-old male who presented with acute kidney injury requiring hemodialysis, accompanied by progressive sensorineural hearing loss since age 8 and visual impairment requiring lens implantation. Family history revealed a deceased elder brother with renal failure. Clinical examination showed hypertension, bilateral pitting edema, bilateral sensorineural hearing loss, and ophthalmoscopic findings of pseudophakia, peripheral fleck retinopathy, and pale optic disc. Genetic analysis revealed a hemizygous COL4A5 c.1708G>C (p.Gly570Arg) mutation, classified as likely pathogenic according to ACMG guidelines.This case highlights the importance of comprehensive genetic testing in young patients with unexplained nephritis and its associated extra renal manifestations. Early diagnosis allows appropriate genetic counseling, family screening, and optimal therapeutic interventions including ACE inhibitors and renal replacement therapy.

Keywords: *Alport syndrome, COL4A5 mutation, hereditary nephritis, sensorineural hearing loss, genetic testing*

Date of submission: 11.11.2025 *Date of acceptance: 22.02.2025*

DOI: https://doi.org/10.3329/bjm.v37i1.87200

Citation: *Islam MS, Hossain A, Bala CS, Islam MR, Sarker PS, Islam MD. Progressive nephritis, sensorineural hearing loss, and retinal abnormalities: a case of X-linked Alport syndrome with genetic confirmation. Bangladesh J Medicine 2026; 37(1): 68-71.*

Introduction

Alport syndrome is a heterogeneous disease affecting the type IV collagen biosynthesis of basement membrane of the kidney, stria vascularis of the cochlea, descemet's membrane and bowman's layer of the cornea, lens capsule and inner limiting and bruch's membrane of the retina[1]. The most common renal manifestations are hematuria, proteinuria and chronic progressive renal dysfunction[2]. Some patients present with sensorineural hearing loss, corneal opacities, anterior lenticonus, cataract, fleck retinopathies and temporal retinal thinning[1].It is caused by mutations in COL4A3, COL4A4 and COL4A5, three of six human genes involved in basement membrane (type IV)

1. Assistant Professor, Dept. of Medicine, Tairunnessa Memorial Medical College & Hospital, Gazipur, Bangladesh
2. Professor (Rtd.), Dept. of Medicine, Sir Salimullah Medical College, Dhaka-1100, Bangladesh.
3. Assistant Professor, Dept. of Medicine, Sir Salimullah Medical College, Dhaka-1100, Bangladesh.
4. Medical Officer, Dept. of Medicine, Sir Salimullah Medical College, Dhaka-1100, Bangladesh.
5. Assistant Registrar, Dept. of Medicine, Sir Salimullah Medical College, Dhaka-1100, Bangladesh.

Address of Correspondence: Dr. Mohammad Sirajul Islam, Assistant Professor, Dept. of Medicine, Tairunnessa Memorial Medical College & Hospital, Gazipur, Bangladesh.

collagen biosynthesis[3]. Mutations in any of these genes prevent the proper production or assembly of the specialized type IV collagen network which is an important structural component of basement membranes in the kidney, cochlea and eye[4].We report a case of Alport syndrome confirmed through genetic analysis.

Case Report:

A 20-year-old, male, hypertensive, non-diabetic, presented with puffiness of face, generalized body ache, passage of scanty high color urine for 3 months, and lower abdominal pain. He was diagnosed as a case of acute kidney injury (AKI) initially and was put on hemodialysis in a tertial care hospital. On query he gave history of intraocular lens implantation in his left eye due to dimness of vision 2 years back. He also complaints of gradually progressive hearing loss since his 8 years of age. There is no history of breathlessness, cough, sore throat, joint pain, any skin lesion, wheels, any food or drug allergy, jaundice or hepatitis B virus infection in the recent past. On physical examination he was mildly anemic, bipedal pitting oedema present, scar mark of CV line present on the right side of the neck and scar mark of A-V fistula present over the left forearm, blood pressure was 145/90 mmHg with antihypertensive, pulse rate was 84 beats/min. Bed side urine examination found to have high colored and protein (+). The patient's elder brother died due to renal failure at the age of 35 years (Figure 1). The visual and auditory functions and renal functions of the patient's parents and elder sister were normal.

On abdominal examination, kidneys are not ballotable, no ascites and renal angles are not tender. There is wide and fixed splitting of second heart sound, visual acuity 6/24 on right side and 6/36 on left side. Rinne's test shows AC>BC and Weber's lateralized to the left ear. Ophthalmoscopic examination (Figure-2) reveals pseudophakia in left eye and peri foveal and peripheral flecks retinopathy in both eyes. Genetic study showed the COL4A5 c.1708G>C hemizygous mutation was detected in the peripheral blood DNA of the patient which was classified as likely pathogenic[5] (Table-1). The patient was treated with appropriate antihypertensive with renal replacement therapy.

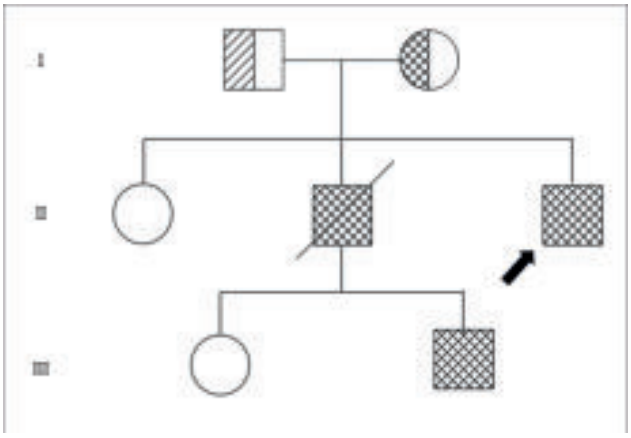

Figure-1: *Pedigree of the family. The arrow identifies the proband. The crossed symbol indicates the deceased individual.*

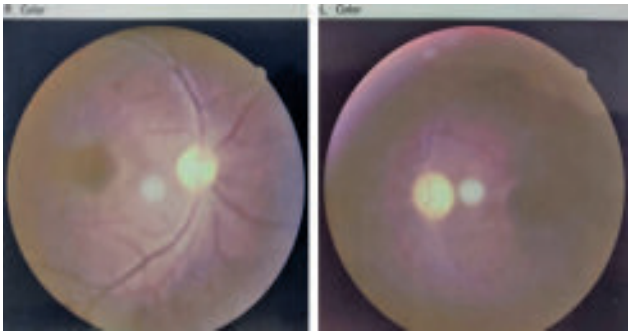

Figure-2: *Anterior segment showed Cataract (right eye) and Pseudophakia (left eye), Fundus examination revealed arteriolar attenuation, peri foveal and peripheral flecks retinopathy (both eye) and Pale optic disc (left eye).*

Table-I

Exome Sequencing Result

Gene	Chr.	Transcript Id	Variant coordinate (GRCh38) dbSNP ID	Variant type Zygosity	Variant Information	Classification as per ACMG[5] guideline
COL4A5	X	NM_000495 Exon 24	108597497 (Novel)	Missense* Hemizygous	c.1708G>C p.Gly570Arg	Likely pathogenic

Discussion

This case shows important features of X-linked Alport syndrome in a young Bangladeshi male. The patient had the three main signs of this disease: kidney problems, hearing loss, and eye problems. Genetic testing confirmed he had a harmful mutation in the COL4A5 gene. The patient developed kidney failure at age 20, which is typical for severe X-linked Alport syndrome. Most males with this condition need dialysis or kidney transplant in their twenties or thirties.w The specific gene change (c.1708G>C) affects an important part of type IV collagen protein. This protein helps form strong basement membranes in kidneys, ears, and eyes. When this protein is damaged, it causes the symptoms we see in Alport syndrome.x

The patient's severe symptoms match the type of genetic defect he has. Gene changes that affect glycine amino acids usually cause worse disease and earlier kidney failure.y This explains why our patient needed dialysis by age 20, which is earlier than many other cases. His hearing loss started at age 8, and he needed surgery for cataracts at age 18. These problems outside the kidney are common in X-linked Alport syndrome. That happen because the same defective protein affects the inner ear and eye. Hearing loss usually starts with high-pitched sounds first. The eye changes we saw (fleck retinopathy) are the most common eye finding in Alport syndrome.[1]p ,[11]

The patient's family history is very important. His older brother died from kidney failure at age 35. This strongly suggests the brother also had Alport syndrome. This supports the X-linked inheritance pattern we see in this family. It also shows why we need to check other family members and provide genetic counseling. Female relatives should be tested because they might carry the gene mutation. They may not have symptoms now but could develop problems later or pass the mutation to their children. Early diagnosis of Alport syndrome helps in many ways. It allows doctors to use protective medications for the kidneys when possible. It helps identify family members who need monitoring. It helps families understand the inheritance pattern for future pregnancies. It also helps plan for kidney transplant since young Alport patients usually do well with transplants.[12] Although our patient already had end-stage kidney disease, the diagnosis helped with family counseling and screening recommendations.

Several other kidney diseases can look similar to Alport syndrome in young males. These include thin basement membrane disease, IgA kidney disease that runs in families, and other genetic kidney diseases. However, the combination of early kidney failure, hearing loss, and eye problems strongly suggests Alport syndrome. Genetic testing confirmed this diagnosis. Our case adds new information about Alport syndrome in South Asian populations. The COL4A5 gene change we found has not been reported before. This represents a new disease-causing mutation that expands our knowledge of this gene.

This case report has some limitations. We did not have detailed hearing tests that could have better described the hearing loss. We did not have kidney biopsy results that could have provided more diagnostic information. We have limited long-term follow-up information. We also do not have complete family screening results. Despite these limitations, this case provides valuable information about X-linked Alport syndrome in a young South Asian male. It emphasizes the importance of thinking about hereditary kidney disease in young patients with unexplained kidney problems, especially when they also have hearing or eye problems.

Conclusion:

Genetic testing is required in patients with suspected Alport syndrome not only to confirm the diagnosis of X-linked disease but also the location and type of mutation. This help in predict the clinical course and prognosis of the individual. It is important to recognize Alport's syndrome early in the course of the disease to improve longevity and prognosis of Alport's syndrome patients.

Conflict of Interest:

The authors stated that there is no conflict of interest in this study.

Funding:

This research received no external funding.

Consent for publication:

Informed written consent was taken from the parents of the patient to publish details relevant to the disease and management.

Acknowledgments:

The authors were grateful to the staffs of the Department of Medicine in Sir Salimullah Medical College Mitford Hospital, Bangladesh

Competing interests:

None.

Authors' contributions:

All authors were involved in the management of the patient and all authors contributed to the conception, writing, and editing of the case report.

References

1. 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;10(4):703-9.
2. Pan S, Yu R, Liang S. Case report: A case report of Alport syndrome caused by a novel mutation of *COL4A5*. Front Genet. 2023; 14: 1-6.
3. Kashtan CE. Alport Syndrome: Achieving Early Diagnosis and Treatment. Am J Kidney Dis. 2021; 77(2): 272-9.
4. Nozu K, Nakanishi K, Abe Y, Udagawa T, Okada S, Okamoto T et al. A review of clinical characteristics and genetic backgrounds in Alport syndrome. Clin Exp Nephrol. 2019; 23(2): 158-168.
5. Richards S, Aziz N, Bale S, Bick D, Das S, Gastier-Foster J et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015; 17(5): 405-24.
6. Wang Y, Sivakumar V, Mohammad M, Colville D, Storey H, Flinter F et al. Clinical and genetic features in autosomal recessive and X-linked Alport syndrome. Pediatr Nephrol. 2014; 29(3): 391-6.
7. Kamiyoshi N, Nozu K, Fu XJ, Morisada N, Nozu Y, Ye MJ et al. Genetic, Clinical, and Pathologic Backgrounds of Patients with Autosomal Dominant Alport Syndrome. Clin J Am Soc Nephrol. 2016; 11(8): 1441-9.
8. Takemon Y, Wright V, Davenport B, Gatti DM, Sheehan SM, Letson K et al. Uncovering Modifier Genes of X-Linked Alport Syndrome Using a Novel Multiparent Mouse Model. J Am Soc Nephrol. 2021; 32(8): 1961-73.
9. Bekheirnia MR, Reed B, Gregory MC, McFann K, Shamshirsaz AA, Masoumi A et al. Genotype-phenotype correlation in X-linked Alport syndrome. J Am Soc Nephrol. 2010; 21(5): 876-83.
10. Watson S, Padala SA, Hashmi MF, et al. Alport Syndrome. [Updated 2023 Aug 14]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470419/
11. Jayaprasad B, Sathish K R, Chandrasekhar N, Upadhyaya N S, Mehta S. *Alport's syndrome* : A case report. Indian J Ophthalmol [serial online] 1994 [cited 2023 Dec 11]; 42: 211-2. Available from: https://journals.lww.com/ijo/pages/default. aspx/text.asp?1994/42/4/211/25561
12. 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; 10(4): 703-9.
13. Ghosh S, Singh M, Sahoo R, Rao S. Alport syndrome: a rare cause of uraemia. BMJ Case Rep. 2014; 1-4.