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A case of Alport's syndrome: Genetic and rare disease

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Abstract
Alport syndrome (AS) is a heterogeneous basement membrane disease characterised by haematuria with progressive hereditary nephritis, high-frequency sensorineural hearing loss (SNHL) and pathognomonic ocular lesions. It is one of the spectra of diseases representing hereditary nephritis, which inevitably leads to end-stage renal disease (ESRD). Here we report a case of Alport's syndrome with all the characteristic features. It is important to recognize Alport's syndrome early in the course of the disease. This is facilitated by an integrated approach to diagnosis Early diagnosis can improve longevity and improve prognosis of Alport's syndrome patients.

Keywords: Alport's syndrome, SNHL, haematuria

Introduction
Alport's syndrome is an inherited progressive renal disease that is accompanied by sensorineural hearing loss and ocular abnormalities that affects 1 in 50,000 live births [1, 2]. It is a primary basement membrane disorder arising from mutations in genes encoding several members of the type IV collagen protein family. The disease is genetically heterogeneous, existing in X-linked, autosomal recessive, and autosomal dominant forms [3, 4]. Eighty percent of the disease is X-linked, 15% autosomal recessive, and 5% autosomal dominant. The most common, X-linked form arises from mutations in COL4A5, the gene encoding the alpha-5 chain of type IV collagen [5, 6, 7].

Case Presentation
A 35-year-old male presented with bilateral progressive diminution of vision from last 6 months, progressive hearing loss from last 8 months, and loss of appetite from last 1 year, and shortness of breath from last two month. Patient had progressive renal illness since 9 years of his age managed conservatively for that. He had intermittent episodes of haematuric since last 3 years. There was no other similar illness in the family.
On physical examination; detailed summarized in table no. 1

Table 1

Physical examination	Observation
Pulse rate	110/minute (tachycardia)
Blood pressure	160/110 (hypertensive)
Respiration	Bilateral coarse crackles in lower lung
Slit lamp examination	Anterior lenticonus in right eye

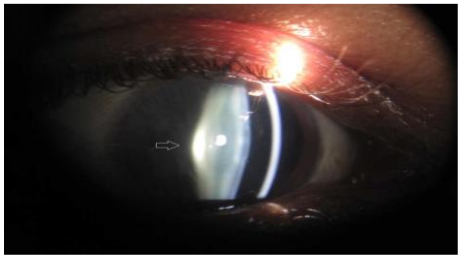

Fig 1: Slit-lamp examination of the right eye showing Anterior lenticonus (grey arrow).

His laboratorial investigation; summarized in table no. 2

Table 2

Investigation	Observed value
Hemoglobin	5.2 gm/dl
WBC	9000/mm^3
Electrolytes	Normal range
Blood urea	210 mg/dl
Urine output	950ml/day
Serum Creatnine	11.20 mg/dl
Urine examination	proteinuria
Audiometry	Bilateral severe sensorineural hearing loss for higher frequencies

On renal biopsy, podocyte hypertrophy was seen on light microscopy. No specific immune deposits were detected by immunofluoroscense. On ultrastructural examination, irregular alteration of thick and split glomerular basement membrane segments were observed. On the basis of typical triad of positive family history, sensorineural deafness and medical renal disease diagnosis of Alport's syndrome made. Patient

Treated with diuretics, antihypertensive, blood transfusion, maintenance hemodialysis and hearing aid.

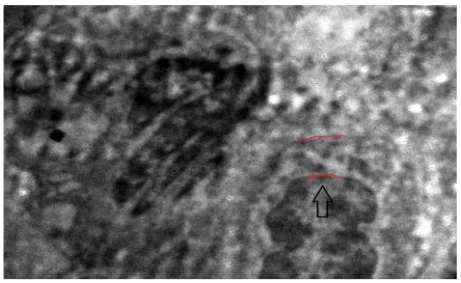

Fig 2: thick and split glomerular basement membrane segments

Discussion

AS was first identified in a British family by Dr Cecil A Alport in 1927 [1, 2]. However, it was William Howship Dickinson who made significant contributions for diagnostic characterisation of the disease and proposed that at least three of the following four criteria to establish the diagnosis of AS including family history of haematuria, evidence of GBM thickening and splitting in kidneys, progressive, high-tone SNHL and anterior lenticonus with retinal flecks; a disease complex attributed to basement membrane structural defect [3, 4].

This is usually preceded by asymptomatic microhematuria. Early in the course the plasma creatinine and blood pressure are normal, but eventually hypertension, azotemia, and proteinuria develop. End-stage renal disease is usually seen in males between the ages of 16 and 35, but some families have more indolent disease and develop renal failure in their 40s or 50s [5, 6]. Extrarenal manifestations most commonly include eye and ear changes. Sensorineural hearing loss can take place and initially involve the high tones but can eventually affect the ability to hear conversational speech. Eye changes include anterior lenticonus, white or yellow flecking of the perimacular region of the retina, and corneal lesions such as posterior polymorphous dystrophy and recurrent corneal erosions. No definite treatment exists for Alport syndrome [7, 8]. Supportive treatment for Alport syndrome includes ACE inhibitors, which have been used to treat hypertension as well as reduce proteinuria. Cyclosporine has also been used to halt disease progression in those patients with severe proteinuria. In those patients with end-stage renal disease, both dialysis and transplantation are options, however anti-glomerular basement membrane disease can develop in 3-4% of transplanted patients. Gene therapy for Alport syndrome is being studied. Animal studies are underway to evaluate the delivery of human alpha-5 (IV) chain of GBM in a canine model of X-linked Alport's syndrome [9, 10].

Conclusion

It was concluded; it important to recognize Alport's syndrome early in the course of the disease. This is facilitated by an integrated approach to diagnosis. Early diagnosis can improve longevity and improve prognosis of Alport's syndrome patients.

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