HEREDITARY NEPHRITIS - A CASE SERIES

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Abstract:
Alport syndrome is a primary basement membrane disorder whose most common and earliest manifestation is gross or microscopic hematuria. Hematuria is usually persistent in males and may be intermittent in females. Bilateral sensorineural hearing loss is a characteristic feature observed frequently, but not universally. Anterior lenticonus is the ocular manifestation seen associated with 15 - 20 percent of patients. Two pairs of siblings with Alport syndrome that presented to our OPD at the same time period are hereby presented. Two of them presented with features of renal failure while two others presented with altered sensorium. All the four cases had sensory neural hearing loss and anterior lenticonus. We present this case series as they all presented as sporadic cases without any significant family history.

Keyword: Alport syndrome, hereditary nephritis

INTRODUCTION
ALPORT SYNDROME is a rare inherited progressive form of glomerular disease with deafness and ocular abnormalities. It is the second commonest genetic cause of renal failure. Thin basement membrane disease is thought to be underlying disease in 25% of patients with microscopic proteinuria. It was first identified in a British family by Dr. Cecil A. Alport in 1927.

CASE HISTORY
Two brothers of 18 & 23 years were admitted with complaints of decreased urine output, swelling of both legs of one month duration. There was no family history of any renal disease. On examination they were pale with features of volume overload. The elder brother had cataract in his right eye. The blood urea and creatinine was raised in both with an initial creatinine value of 29 in the elder brother and 11 in the younger. Both had hyperkalemia. There was 2+ albuminuria and hematuria in urine routine examination. Sonogram demonstrated contracted kidneys in both the siblings with increased cortical echoes and the corticomedullary differentiation was lost. Both of them had normocytic normochromic anaemia. All other investigations were normal including negative HIV, HBsAg, anti HCV and ANA.
Audiogram revealed bilateral moderate sensory neural hearing loss in both of them. Slit lamp examination showed bilateral anterior lenticonus in both with a cataract in right eye of the elder brother. They were treated with haemodialysis and fluid restriction. Renal biopsy was deferred because of contracted kidneys in both of them. In the other two siblings aged 16 and 19 years, the 19 year old was admitted with altered sensorium in intensive care unit. On examination he was found to be drowsy, there was no neck stiffness and the plantars were flexor. Random blood glucose was done which came out to be normal. The urea and creatinine of the elder brother was 200 and 18 respectively. On further detailed history he had an episode of hematuria one month back and he was having hearing loss since childhood. His younger brother who was 16 years of age was also hard of hearing, though he denies any history of hematuria or oliguria. The younger one’s urea and creatinine were normal. Urine examination of both of them showed 3+ hematuria. Ultrasound showed contracted kidney in both with altered corticomedullary differentiation. Both of them had progressive hearing loss since childhood which on audiogram revealed as moderate sensory neural hearing loss. Slit lamp examination showed anterior lenticonus in both of them.
DISCUSSION
Alport syndrome is a hereditary, hematuric, non immune glomerulonephritis that is characterised ultra structurally by progressive irregular thickening, thinning and lamellation of glomerular basement membrane and genetic mutation in COL4A3, COL4A4 or COL4A5 gene. It is associated with sensory neural hearing loss and ocular findings. It has a prevalence of 1 in 50000 live births and accounts for 0.3 – 2.3 % of all end stage renal disease. Chronic hematuria is a cardinal sign of this disease. The primary defect lies in the Type IV collagen that forms the basement membrane. It composed of 3 alpha chains that form triple-helical structures through specific interactions of C-terminal non-collagenous domains. Six distinct IV collagen chains are encoded by six different genes distributed on three chromosomes. COL4A1 and COL4A2 at 13q34 COL4A3 and COL4A4 at 2q35-37 COL4A5 and COL4A6 on chromosome X There are three modes of inheritance viz X-linked inheritance (80% cases, Mutations in the COL4A5 gene on the X chromosome)3, AR (15% mutation in COL4A3 or COL4A4 genes), AD (5% due to mutation in COL4A3 or COL4A4 genes)4. Mutations impair their deposition into this collagen network, leading to secondary changes in GBM composition that predispose to the development of glomerulosclerosis. These chains are located in Bowman’s capsule & basement membranes of the glomerulus, distal convoluted tubule, base ment membranes of the cochlea & eye5. The ocular findings include anterior lenticonus seen in 30% of X linked cases which is pathognomonic of Alport syndrome6. They also have sensory neural hearing loss due to impaired adhesion of organ of Corti7. Leiomyomas are also seen in some patients with X linked inheritance. A diagnosis is made with clinical features, renal biopsy/skin biopsy and genetic testing. Renal transplantation is the only definitive treatment, although anti GBM disease may occur in a minority.

Angiotensin converting enzyme inhibitor and angiotensin receptor blockers can be given to delay the development of end stage renal disease8. Cyclosporine has questionable role in management9. In our case there was no family history of any renal disease. This probably reflects a denovo mutation in the genes in these two pairs of siblings making these cases rare and interesting.

REFERENCES


