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A RARE PRESENTATION OF ALPORT SYNDROME IN A FEMALE WITH BOTH ANTERIOR AND POSTERIOR LENTICONUS - CASE REPORT

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Abstract : We report a rare case of Alport syndrome in a female with both anterior and posterior lenticonus. A 40 year-old female presented to our ophthalmology department for regular work up from\ the nephrology department as the patient had chronic kidney disease stage 5 planned for renal transplant. At initial presentation, the patient had right eye anterior lenticonus and posterior lenticonus associated with renal failure. The patient was diagnosed with Alport syndrome based on a positive family history of the disease and clinical findings. The occurrence of severe form of alport syndrome in a female is a rare finding. Also the presence of posterior lenticonus which is a rare presentation in alport syndrome made this an interesting case for presentation.
Keyword : Alport Syndrome, X-linked Disease, Anterior Lenticonus, Posterior Lenticonus.

Introduction:

Alport syndrome is a rare clinical entity characterized by the familial occurrence of hemorrhagic nephritis and sensorineural deafness (Alport 1927). Alport syndrome has a prevalence of 1/5000, with 85% of affected individuals having the X-linked form, where the affected males develop renal failure and usually have high-tone sensorineural deafness by the age of 20. The typical ocular signs are dotand- fleck retinopathy, which occurs in 85% of the affected adult males, anterior lenticonus, which occurs in about 25%, and rare posterior polymorphous corneal dystrophy. Anterior lenticonus is considered a characteristic sign of Alport syndrome. Posterior lenticonus has been described as a rare manifestation in Alport syndrome and a review of the literature revealed a relative paucity of reports. Other ocular manifestations include recurrent corneal ulcers, cataract, peripheral coalescing retinopathy and macular hole. We present here a case of Alport syndrome in a female with anterior lenticonus and posterior lenticonus. Males have one X and one Y chromosome and females have two X chromosomes. X-linked Alport Syndrome is caused by mutations in the COL4A5 gene, which resides on the X chromosome. Xlinked disorders cause more severe symptoms in affected males than in affected females because males have only one X chromosome. Males with XLAS are severely affected and always develop kidney failure sometime in their lives, because they do not have a normal copy of the gene to buffer the effect of the mutant gene. Females, who have two X chromosomes, have two copies of the COL4A5 gene. In girls with XLAS, one copy of the gene carries a mutation, but the other copy is normal. The normal copy of the gene counters the effect of the mutation, so that girls with XLAS usually have milder symptoms than boys. However, girls with X-linked Alport syndrome can also develop kidney failure and should not be considered as only carriers of XLAS. A male with XLAS will pass the affected X chromosome gene to all of his daughters and they will have XLAS. A male cannot pass an X-linked gene to his sons because the Y chromosome (not the X chromosome) is always passed to male offspring. A female with XLAS has a 50% chance with each pregnancy of having an affected child. Approximately 10 – 15% of XLAS mutations occur randomly (spontaneously), where neither parent carries a mutation.

Case report:

A 40-year-old female (figure 1) suffering from systemic hypertension, chronic kidney disease stage 5 with suspected chronic interstitial nephritis was admitted in the nephrology ward for management. Patient underwent hemodialysis. Her pre transplant work up was started. Husband was prospective kidney donor. Patient was sent for ophthalmology and ENT opinion as a part of routine work up. A renal biopsy showed irregular thickening of basement membrane of glomeruli with focal sclerosis. Her only brother had died of chronic renal disease at the age of eighteen. There was no other similar illness in the family. At the time of presentation her main complaint was vomiting, dyspnea and fatiguability. Systemic evaluation showed hypertension (BP-160/100 mm hg) and anemia. Her biochemical workup revealed increased blood urea (286 mg/dl) and serum creatinine (10.2 mg/dl). There was borderline hyponatremia and hypokalemia. Urine examination showed proteinuria 2+ and microscopic haematuria. Her hemoglobin levels was 4 g/dl. Her viral markers were negative. Bilateral small kidneys (8.5 X 3.8 cm right; 7.5 X 3.6 cm left) with grade 2 parenchymal changes were noted on ultrasonography. Audiometry detected a bilateral

Moderate sensorineural hearing loss more towards left ear. Patient underwent left eye cataract surgery 5 years back. Ocular examination revealed defective distant vision right eye. Her visual acuity in the right eye was 6/60 improving to 6/18 with -2.5 sph/-2.0 cyl 15 degrees axis and left eye had 6/18 improving to 6/9 with -1.0sph/-0.50 cyl 160 degree axis. Slit-lamp examination revealed anterior lenticonus (figure 2), posterior lenticonus (figure 3) and posterior subcapsular cataract in the right eye and pseudophakia in the left eye. Otherwise anterior segment was normal. oil droplet reflex (figure 4) seen with retroillumination in the right eye . Intraocular pressure in both eyes were within normal limits. Fundus examination was apparently normal except for arteriolar attenuation changes (figure 5).

Figure 1 (female alport syndrome)

Figure 2 (anterior lenticonus)

Figure 3 (posterior lenticonus)

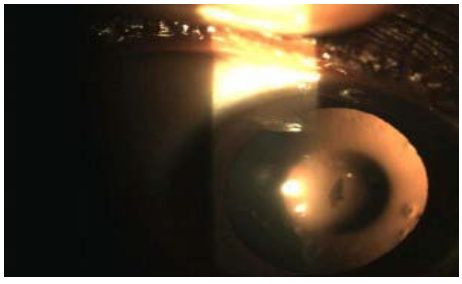

Figure 4 (oil droplet reflex)

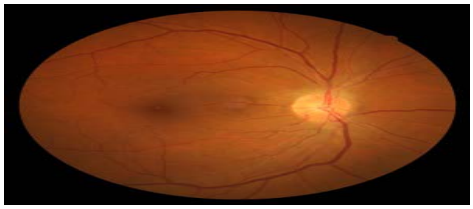

Figure 5 (picture of fundus)

Discussion:

In 1927, Cecil A. Alport described three generations of a family with combinations of progressive hereditary nephritis and deafness. Hereditary nephritis or the Alport syndrome is an inherited disease characterized clinically by progressive kidney disease accompanied with sensorineural hearing loss and ocular abnormalities. With an incidence of 1 in 50,000 live births, the Alport syndrome accounts for 0.3 to 2.3% of endstage kidney disease. The mode of inheritance is X-linked in 80%, autosomal recessive in 15%, and autosomal dominant in 5%.It is caused by mutations in the COL4A5 collagen gene, giving rise to defective type IV collagen, which is a major structural component of the basement membranes in the renal glomeruli, cochlea, and lens. Sensorineural deafness occurs in approximately 80% of the cases and ocular findings have been reported in roughly 40%. Gregory et al., describe the following diagnostic criteria for the Alport syndrome:

1. Family history of nephritis with unexplained hematuria;
2. Persistent hematuria without evidence of other renal problems;
3. Bilateral sensorineural hearing loss up to 2000 - 8000 Hz;
4. Mutation in the COL4A5gene;
5. Immunohistochemical evidence of complete lack of the Alport epitope in the glomerular basement membrane (GBM);
6. GBM thinning or splitting;
7. Ocular lesions like anterior lenticonus, posterior subcapsular cataract, posterior polymorphous corneal dystrophy, and retinal flecks;
8. Progression to end-stage renal disease (ESRD) in at least two family members;
9. Macrothrombocytopenia; and 0. Diffuse leuomyomatosis of the esophagus or female genitalia. Out of the 10, at least four findings must fulfill the criteria, for diagnosis of the Alport syndrome. The Alport syndrome is confirmed with renal biopsy in the immunohistochemical methods. Antibodies are used to detect the presence or absence of alpha 3, alpha 4, and alpha 5 in chains of the type 4 collagen. There is no definite treatment for the Alport syndrome. Angiotensin-Converting- Enzyme (ACE) inhibitors have been used to treat hypertension and reduce proteinuria. In patients with ESRD, both dialysis and transplantation are done. Gene therapy for the Alport syndrome is being studied. Animal studies are underway, to evaluate delivery of the human alpha-5 (IV) chain of GBM in a canine model of the X-linked Alport syndrome.

Conclusion:

In conclusion, Alport syndrome affects multiple systems, including the eye. The ocular manifestations are important to recognize in order to determine the proper medical and surgical therapy. Posterior lenticonus, which was once considered as an isolated manifestation is being reported more frequently in association with Alport syndrome, suggesting that posterior lenticonus is part of the disease. Also the existence of a severe form of alport syndrome in

a female is a rare presentation.

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