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Case Report

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CASE REPORT ON ALPORT SYNDROME

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ABSTRACT

Alport syndrome is a genetic disorder of glomerulus caused due to mutation in type IV collagen, a key component of the glomerular basement membrane. It is clinically manifested with symptoms which include haematuria, proteinuria, deafness, anterior lenticonus and retinal discolouration. Diagnosis is mainly done by renal biopsy and medical history. No specific therapy is recommended for alport syndrome. Symptomatic treatment includes: Angiotensin Converting Enzymes inhibitor/ Angiotensin receptor blocker, 3-Hydroxy-3-methyl-glutaryl-coenzyme A reductase inhibitors, non-dihydropyridine calcium channel blocker. In this report, we present a 12 year old boy with complaints of fever, pain in abdomen and loss of appetite. He is a known case of alport syndrome, hypertension, end stage renal disease and underwent renal transplantation. On laboratory examination his creatinine, urine micro-albumin to creatinine ratio, C - reactive protein was elevated. In hospital he was treated with Intravenous fluids, antibiotics, immunosuppressants and antihypertensive.

KEYWORDS: Alport syndrome, End stage renal disease, Renal Transplantation, Hypertension, Proteinuria, Angiotensin converting enzyme inhibitors.

INTRODUCTION

Alport syndrome is a severe non immune form of nephritis. It is a rare hereditary disease characterised by progressive loss of kidney function, sensory, neural hearing impairment and ocular symptoms. It affects about 1 in 50,000 live births.[1,2] Males are more affected than females.[3] Abnormalities in type IV collagen is said to be the main cause of alport syndrome.[4] Type IV collagen is a protein, a key component of glomerular membrane that plays a crucial role in functioning of kidneys and glomeruli. Mutation of genes such as COL4A3, COL4A4 and COL4A5 make abnormal type IV collagen.[6,7] This results in preventing the kidneys from filtering blood and leaking of blood and protein to the urine. This can eventually leads to progressive loss of kidney function and ultimately causes renal failure.[8] Type IV collagen is also present in inner ear structures especially, organ of corti and also helps in retaining the shape of lens and colour of retina. Thus, disruption of Type IV collagen can lead to hearing loss, misshaped lenses and abnormal colouration of retina.[9] Anterior lenticonus is a major eye finding in people affected with alport syndrome which causes lens to become cone shaped.[10] Symptoms usually begin in early childhood: primary symptoms include haematuria and proteinuria followed by edema, bone weakening and osteodystrophy, If left untreated, can lead to end stage renal disease.[5] Subdivisions of alport Syndrome are autosomal dominant alport syndrome, autosomal recessive alport syndrome, COL4A3-Related nephropathy, COL4A4- Related nephropathy, COL4A5- Related nephropathy and X-linked alport syndrome (XLAS). X linked alport syndrome is the most common among other types. Diagnosis is mainly done by clinical criteria which includes: positive family history, persistent haematuria, renal biopsy, characteristic ophthalmic signs, high tone sensorineural deafness.[11]

There is no specific therapy for alport Syndrome.[12] Management of alport syndrome focus on delaying progression and end stage renal disease.[14] ACE inhbitors (Angiotensin Converting Enzymes inhibitors) /ARBs (Angiotensin receptor blocker) are started at the onset of proteinuria.[12] This will help in normalizing albumin in urine and slows the disease progression. Mechanism involved in the RAAS (Renin Angiotensin Aldosterone System) inhibitors is the reduction of intraglomerular pressure. HMG CoA (3-Hydroxy-3-methyl- glutaryl-coenzyme A) reductase inhibitors role involves the dual RAAS blockade to target urinary proteins blunted glomerulosclerosis and calcium channel blockers preserves the glomerular filtration rate and prevent progression to ESRD (End Stage Renal Disease).[15]

CASE REPORT

A 12 year old male patient was presented with complaints of fever since 3 days, decreased appetite and pain in abdomen in a tertiary care hospital. His systemic history was remarkable for alport syndrome and progressive end stage renal disease, for which he has underwent surgical procedure of renal transplantation, where his grandfather was the donor. He is a known case of hypertension and is on regular medications namely T. Amlodipine 5 mg twice daily, T.Atenolol 25mg twice daily. Renal biopsy was done 3 years ago, which revealed diffused mesangial proliferation and electron microscopy showed glomerular basement membrane thickening and lamellation.

The present laboratory examination findings were: elevated serum creatinine, elevated CRP, elevated urine microalbumin to creatinine ratio which is depicted in table no.1. Patient was treated with IV fluids, Inj. Piperacillin-Tazobactam 3.2 gm q 6th hrly, T. Paracetamol 650mg twice daily, T. Tacrolimus 1 mg once daily, T. Prednisolone 10 mg once daily, T. Mycophenolate Mofetil 750-0-500mg. On discharge the child was stable, no further fever spikes and was having good oral intake. Discharge medications given were Inj. Ceftazidine 1 gm twice daily for 8 days, T. Tacrolimus 1 mg twice daily, T. Amlodipine 5 mg once daily, Livogen once daily, T. Prednisolone 10 mg 1-0-0 alternative days, T. Mycophenolate Mofetil 750-0-500 mg.

Table no. 1: Laboratory investigations.

Sl.No.	Laboratory parameters	Patient values			Normal limit
		1st day	2nd day	3rd day	
1.	Serum creatinine	1.6	1.6	1.3	0.7-1.3mg/dl
2.	CRP	70		64.4	0-6mg/dl
3.	Urine micrroalbumin	55.3			1.3-20mcg/mg
4.	Microalbumin/creatinine	68.47			1.3-30

DISCUSSION

Alport syndrome is a hereditary disease affecting the glomerular membrane. Past medical history, renal biopsy reports and clinical symptoms are the foremost criteria for the diagnosis of this disease. Currently there is no definite pharmacological management for the disease. Surgical procedures and symptomatic treatment paves the way to prevent the disease progression. In this case report, the patient underwent renal transplantation and was on immunosuppressive therapy of T.Tacrolimus and T.Mycophenolate mofetil. He is a known case of hypertension where he was on T.Atenolol and T.Amlodipine. B-blockers is not preferred as a choice of drug for hypertensive patients with chronic kidney disease. Atenolol is a hydrophilic beta-blocker and are eliminated through urine. Therefore dosage adjustment is needed for atenolol in patient with chronic kidney disease.[16] ACE inhibitors/ARB drugs are the drugs given for symptomatic proteinuria. A few studies suggest that ACE inhibitors are contraindicated in patient with renal insufficiency. However some researchers recommend that the patients with renal insufficiency can be started on low doses of ACE inhibitors with careful monitoring of creatinine and potassium levels.[17] Proteinuria appears to be an important risk factor for renal function deterioration. ACE inhibitors have been shown to reduce proteinuria more effectively than other antihypertensives. Their antiproteinuric effect seems to be independent of the underlying renal disease, and is mediated by a specific, not yet fully known mechanism. During ACE inhibitor treatment, Urinary protein loss related phenomena, such as hypoalbuminemia will also improve. Furthermore, ACE inhibition has been shown to prevent the renal function deterioration that is frequently observed in patients with renal disease. Recently it has been shown that in proteinuric patients with renal disease the initial proteinuria lowering response to ACE inhibition predicts long-term renal function outcome during the treatment. As the more proteinuria is lowered initially, the better renal function will be preserved over the following years. Because of these favourable effects ACE inhibitors have become a widely used class of agents in nephrology. They are not only prescribed for lowering blood pressure in the hypertensive renal patient, but also as symptomatic treatment of patients with proteinuria, and to prevent renal function loss in patients.[18]

CONCLUSION

From the research studies mentioned above, suggestions have been put forward for the treatment of proteinuria by ACE inhibitors/ARBs with close monitoring of potassium and creatinine levels. As health care professionals, pharmaco-therapeutic management given must be correlated with the relevant laboratory interpretations.

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