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Case Report

Paediatrics Section

Senior Loken Syndrome

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ABSTRACT

Senior Loken Syndrome (SLS) is a rare genetic disorder having juvenile nephronophthisis and retinal degeneration progressing to blindness and end stage renal disease. The present case report is about two sisters who presented with decreased visual acuity and end stage renal disease. Both had decreased vision, pallor, deranged renal function test and chronic malnutrition. Investigations revealed anaemia, uraemia, raised creatinine, low Glomerular Filteration Rate (GFR). Ophthalmology examination revealed nystagmus, retinal examination depicted pale optic disc and pigmentary changes in the retina. Renal ultrasound showed grade III renal parenchymal changes and bilateral cortico-medullary cysts. These cases are presented to highlight the importance of timely recognition of renal derangement in patients with retinal disease to delay end stage renal disease.

Keywords: End stage renal disease, Nephronophthisis, Retinal degeneration

CASE REPORT

A nine-year-old girl child presented with decreased vision since 2 years of age which further decreased with age and polyuria since last 6 months. She was born through non-consanguineous marriage and had a history of previous blood transfusions for anaemia. She presented in the emergency with severe pallor and acidotic breathing. General physical examination revealed that child was malnourished with a weight of 18 kg (< 3 SD), height of 112 cm (< 3 SD). She also had nystagmus in the eyes and visual acuity examination revealed perception of light only. Laboratory findings were suggestive of end stage renal disease (Hb 4g/dl, S. urea 98mg/dl, Creatinine 7mg/dl, Serum sodium = 145meq/l, Serum potassium = 6.5 meq/l). Arterial Blood Gas (ABG) showed metabolic acidosis with compensated respiratory alkalosis. Her, Glomerular Filteration Rate (GFR) was 8.8ml/min/1.73m^2. Ophthalmology examination revealed nystagmus, retinal examination depicted pale optic disc and pigmentary changes in the retina. Renal ultrasound showed grade III renal parenchymal changes and bilateral cortico-medullary cysts.

When enquired about the family history, we discovered that her seven-year-old younger sister also had decreased vision. Her clinical examination revealed that she had pallor, nystagmus in the eyes and had received blood transfusion 6 months back. Her investigations revealed anaemia (Hb 7g/dl), deranged renal function tests and serum electrolytes (S. urea 56 mg/dl, Creatinine 3.9mg/dl, Serum sodium = 139meq/l, Serum potassium = 4.1 meq/l). Her GFR was 14.7 ml/min/1.73m^2. Retinal examination depicted pigmentary changes in the retina. Renal ultrasound showed renal parenchymal changes. Anthropometery was suggestive of chronic malnutrition with weight of 14 Kg (< 3 SD), height 104 cm (< 3 SD).

The elder sister was admitted in Paediatric ICU and anaemia was managed with Packed Red Blood Cells (PRBC) transfusions, hyperkalemia was managed as per unit protocols and haemodialysis was planned but the patients left against medical advice because of family constraints and were lost to follow-up. Unfortunately we could not get genetic testing due to financial constraints.

DISCUSSION

Senior Loken Syndrome (SLS) was first reported by Loken et al., in 1961 in a brother and sister duo, with the main features of nephronophthisis and Leber congenital amaurosis [1] and in the same year Senior et al., also reported oculorenal syndrome in the families and the renal changes were same as those in Fanconi familial juvenile nephronophthisis [2]. Other names for the syndrome are Renal retinal syndrome, Juvenile nephronophthisis with Leber amaurosis, Renal dysplasia and Retinal aplasia.

SLS is a rare autosomal recessive disorder with an incidence of 1/100000. More incidences is seen in families with consanguineous marriages with almost 150 cases reported worldwide [3].

SLS presents with renal nephronophthisis and retinal degeneration. Renal abnormality starts with polyuria and progresses later to end stage renal disease. Renal nephronophthisis, a heterogeneous ciliary dysfunction, or as named renal ciliopathy, is a disease causing cystic kidneys or renal cystic dysplasia and the most common genetic cause of chronic renal failure in the first two decades of life. There are three clinical variants infantile, juvenile and adolescent types, depending on the age of onset of the manifestations and on the causative genes, with the median age of onset being 1 year (infantile), 13 years (Juvenile) and 19 years. In Nephronophthisis (NPHP), there is genetic involvement and mutation in NPHP genes lead to “ciliopathies” i.e., Mutation of primary cilia which are sensory organelles that connect mechanosensory, visual, osmotic and other stimuli for cell cycle control leading to multisystem involvement and broad spectrum of extra-renal manifestations [4,5]. At least 14 different NPHP genes have been identified which are associated with Nephronophthisis (NPHP) nephrocystin genes including (NPHP1, NPHP2, NPHP3, NPHP4, NPHP5, NPHP6, NPHP7, NPHP8 and NPHP9, NPHP10, NPHP11, NPHP12, NPHP13 and NPHPL1) [6-8].

The disease begins with polyuria, polydipsia with later appearance of anaemia and toxic accumulation of the products of protein breakdown in the blood (uraemia) which progresses to end stage renal disease. Radiological examination i.e., ultrasonography shows increased echogenicity with renal cysts in the corticomedullary junction. Histology of the disease shows interstitial fibrosis, tubular atrophy with corticomedullary cyst development and tubular basement membrane disruption [9].

The retinal diseases associated with SLS are retinitis pigmentosa, sector retinitis, Leber Congenital amaurosis and tapeto-retinal degeneration. Night blindness can be the manifestation and visual fields are severely constricted and vision can be limited to light perception [10].

Author and year	Institution	Age	Clinical features		Unusual features	Genetic study
			Eye involvement	Renal involvement		
HK Aggarwal et al., [11] 2013	Pt.B.D.Sharma Institute of Health Sciences Rohtak	19-years-old male	Retinitis pigmentosa	Renal failure, bilateral kidneys revealed increased echogenicity with a loss of corticomedullary differentiation.	Short metacarpals and madarosis (loss of eyebrows)	Not done
NP Singh et al., [12] 1998	Maulana Azad Medical College and Associated Lok Nayak Hospital New Delhi	35-year-old male	Retinitis pigmentosa Elder sister Retinitis pigmentosa	Multiple corticomedullary cysts and medullary cysts in both kidneys Elder sister Renal failure	Short status, kyphoscoliosis, small hands (short metacarpals) and cutis laxa (similar findings in sister)	Not done
S Giridhar et al., [13] 2006	Institute of Child Health and Hospital Chennai	Twins 11year females	Retinitis pigmentosa	Shrunken kidneys, grade III renal parenchymal disease, b/l cortico-medullary cysts	Dysmorphic features (high forehead, depressed nasal bridge, micrognathia, brachydactyly, clinodactyly, sandle gap)	Not done
R Janardhanan et al., [14] 1997	Medical college and hospital Trivandrum	13 year female Brother 15 year	Retinitis pigmentosa **Brother:** Retinitis pigmentosa	B/l contracted kidneys (2.3 5.3 cm) Hyperechoic; CMD lost ; 3*5.1 cm; Hyperechoic CMD lost Brother: B/l renal parenchymal disease	None	Not done
R Hemachandra [15] 2014	Mahatma Gandhi Medical College and Research Institute, Puducherry	**Case I:** 12 year female **Case II:** 16 year male	**Case I:** Retinal dystrophy. **Case II:** Retinitis pigmentosa	**Case I**: Bilateral small kidneys with increased echogenecity and few small cysts in both the kidneys. **Case II:** Bilaterally echogeinc kidneys with loss of corticomedullary differentiation.	None	Not done
Present case 2016	G.G.S. Medical College and Hospital Faridkot	Elder sister 9 year Younger sister 7 year	**Elder sister:** Pigmentary changes in the retina. **Younger Sister:** Pigmentary changes in the retina.	**Elder sister:** Grade III renal parenchymal changes and bilateral cortico-medullary cysts. **Younger sister:** Renal parnchymal disease.	None	Not done

[Table/Fig-1]: Table showing the comparative features of the cases reported in literature (from India) [11-15].

Our patient presents with clinical progression of renal disease and ultrasonography consistent with NPHP and retinal disease is also suggestive of SLS. We could find only few case reports which have been published from India [11-15] [Table/Fig-1].

CONCLUSION

Association of retinal disease with renal disease in SLS guides us to consider patients presenting with retinal disease for renal evaluation and if NPHP is suspected, patients need regular monitoring of kidney and liver function, renal ultrasound, eye examinations to prevent/ delay end stage renal disease and improve quality of life.

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