Senior-Loken syndrome. Case reports of two siblings and association with sensorineural deafness

Michael P Clarke, Timothy J Sullivan, Christopher Francis, Reuben Bauman, Theo Fenton, William G Pearce

Abstract

Two siblings with Senior-Loken syndrome are described. The need for a full evaluation of renal function and hearing in children with a retinal dystrophy is emphasised.

Early onset rod cone dystrophies have been described in association with a number of renal lesions. The most common is that associated with nephronophthisis (medullary cystic disease). We report two siblings with the triad of nephronophthisis, retinal dystrophy, and sensorineural hearing loss.

Case reports

Two siblings (the older female, the younger male) were the products of a first cousin marriage between parents of Indian subcontinent origin.

CASE 1

The girl presented at 2 years of age with nystagmus. Vision was reduced in both eyes and the nystagmus was rapid, fine, horizontal, and pendular. There was a low myopic refractive error and the fundus was within normal limits. A diagnosis of autosomal recessive achromatopsia was made.

By the age of 9 years she complained of poor vision particularly in dim light. Her visual acuity was counting fingers at 7 feet (2 m) in the right eye and at 10 feet (3 m) in the left eye. Near vision was N36 in each eye. Colour vision was normal. Rapid, fine, horizontal pendular nystagmus was still present. Examination of the fundi showed narrowing of the retinal arterioles and pink optic discs with no pigmentation.

An electroretinogram (ERG) was performed at this time which showed no response. The diagnosis was revised to Leber's congenital amaurosis.

Audiological testing at this time demonstrated mild to moderate sensorineural hearing loss.

The following year she presented with fatigue, pallor, and nocturia. There was glycosuria and generalised aminoaciduria characteristic of a renal tubular defect. Her haemoglobin was 62 g/l and her creatinine clearance 2.5 ml/min/1.73 m.

Renal ultrasound showed slightly shrunken kidneys and numerous cysts in the cortico-medullary region. A renal biopsy showed severe chronic tubulointerstitial nephritis and global glomerulosclerosis affecting more than 90% of the glomeruli. Immunofluorescence was negative for immunoglobulin and complement.

On electron microscopy there was thickening of tubular basement membrane which was split

into multiple layers. The glomerular basement membrane was normal.

The diagnosis of end stage renal failure secondary to nephronophthisis was made and peritoneal dialysis was started. Ophthalmic examination at this time showed a visual acuity of perception of light only in the right eye and 20/200 in the left eye. The nystagmus was now coarse and slow but remained pendular. The anterior segments were normal with no evidence of keratoconus or lenticonus. The refractive error was -5.50 DS/ $+1.25$ DC $\times 090$ in both eyes. The optic discs were now pale and arterioles were attenuated. There was no evidence of retinal pigmentation or white spots in the fundus.

Her sensorineural hearing loss had become more profound, and she was fitted with bilateral hearing aids.

CASE 2

The brother of case 1 was seen at the age of 6 months when his sister first presented. He did not fixate or follow unless the target was large. There was rapid fine horizontal pendular nystagmus. There was a low hyperopic refractive error and the fundus was within normal limits.

Over the next few years global developmental delay became apparent and a seizure disorder developed. A computed tomographic (CT) head scan was normal.

An abdominal ultrasound at age 7.5 years showed his kidneys to be of normal size and to contain corticomedullary cysts. Renal biopsy was similar to his sister's but showed less advanced disease. He was found to have moderate sensorineural hearing loss. At 7.5 years his ophthalmic examination showed him to be able to follow a light and to have positive optokinetic nystagmus (OKN) in each eye. Nystagmus was fine, horizontal, and jerky. The anterior segments were normal with no keratoconus or lenticonus, and the refractive error was -1.00 DS/ $+2.00$ DC $\times 090$ in the right eye and $+1.00$ DS in the left eye. The fundi showed pale discs with attenuated vessels and no white spots or pigmentation.

Discussion

Senior in 1961¹ described a family where six of 13 children had nephronophthisis and tapetoretinal degeneration indistinguishable from Leber's amaurosis.

Loken in the same year² described two siblings of non-consanguineous parents. One had mental retardation and seizures and was blind with normal appearing fundi. The second sibling was

Hospital for Sick
Children, Toronto,
Canada
Department of
Ophthalmology
M P Clarke
T J Sullivan
C Francis

Department of Pathology
R Bauman

Department of Renal
Medicine
T Fenton

Department of
Ophthalmology,
University of Alberta,
Edmonton, Canada
W G Pearce

Correspondence to:
M. Clarke, FCOphth,
Royal Victoria Infirmary,
Newcastle upon Tyne,
NE1 4LP.

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also blind with normal appearing fundi but was of normal intelligence. Both siblings had severe renal failure and at biopsy their kidneys showed renal tubular atrophy and dilatation. Pathological examination of the eyes showed no identifiable photoreceptors and normal retinal pigment epithelium. Nephronophthisis is an autosomal recessive condition which presents with end stage renal failure in childhood.³ Histological examination of the kidneys showed fibrosis or dilated tubules with thickened tubular basement membrane.⁴ There are often secondary changes in the glomeruli and cysts are present at the corticomedullary junction.

Nephronophthisis may be associated with hepatic fibrosis⁵ and may be familial. There are a number of ocular syndromes associated with nephronophthisis. Senior-Loken syndrome refers to nephronophthisis and retinal dystrophy. This combination in conjunction with skeletal dysplasia with cone shaped epiphyses is referred to as Saldino-Mainzer syndrome.⁶ Nephronophthisis, retinal dystrophy, severe deafness, diabetes mellitus, and obesity constitute Alstrom syndrome.⁷ Retinal dystrophy, skeletal deformities, and respiratory insufficiency are seen in Jeune's dystrophy.⁸ In Bardet-Biedl syndrome nephronophthisis may be present.⁹ Neither of the cases presented here had polydactyly or skeletal abnormalities other than mild renal osteodystrophy. Neither child was obese or diabetic.

The retinal lesion in Senior-Loken syndrome is variable and may be severe infantile onset retinal dystrophy^{10,11} or a more typical retinitis pigmentosa.¹² Sector retinitis pigmentosa¹³ and predominant cone receptor involvement have also been reported. In addition to the features of

Senior-Loken syndrome the two cases presented here also showed moderate sensorineural hearing loss bilaterally. This has not been reported previously in association with nephronophthisis and retinal dystrophy and may represent a genetically linked condition.

These cases highlight the need for all children with a retinal dystrophy to have assessments of both their renal function and hearing.

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