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Case report

Hereditary renal and retinal dysplasia — the Senior-Loken syndrome

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The association of nephronophthisis (medullary cystic disease of the kidney) and tapeto-retinal degeneration was first described by Senior[1] and by Loken[2] in 1961. Tapeto-retinal degeneration covers several hereditary disorders characterised by degeneration of the choroid and retina leading to blindness. We present here the case of a boy known to have Leber's amaurosis, a severe form of retinal degeneration, and mental retardation, who presented with chronic renal failure. This is the first description of the condition in Ireland.

CASE HISTORY

An eleven-year-old boy was admitted to Ava Paediatric Medical Unit, Belfast City Hospital, with a three-day history of malaise, nausea, and vomiting. On the day of presentation he had a number of generalised twitching episodes.

Since the age of two years he had been recognised as being developmentally delayed. Poor vision was brought to the attention of ophthalmologists at age five years and a suspected diagnosis of Leber's amaurosis was confirmed by an electroretinogram at age eleven years. There had been no suspicion of renal disease at this time. Urinalyses performed when he was aged seven and aged nine years were normal. He was the third of six children of unrelated parents and there was no family history of renal or eye disease. He was attending a school for visually handicapped children and had profound visual and educational handicaps.

On examination he was having tetanic spasms. He was dull and lethargic. He was clinically anaemic but not dehydrated. Blood pressure was 160/110 mmHg. Visual acuity was poor, with a right-sided strabismus. Fundoscopy showed pigmentary disturbance in both macular areas with diffuse peripheral atrophy. The remaining physical examination was normal.

Investigations showed serum sodium 137 mmol/l, potassium 3.5 mmol/l, urea 62.0 mmol/l (normal range 2.5 – 6.6 mmol/l) and creatinine 836 μmol/l (20 – 80 μmol/l). Serum calcium was 1.4 mmol/l (2.2 – 2.7 mmol/l), phosphate 3.3 mmol/l (1.1 – 1.9 mmol/l) and alkaline phosphatase was $>$ 430 iu/l (56 – 190 iu/l), indicating early renal osteodystrophy. He had a normochromic

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normocytic anaemia, haemoglobin concentration 6.2 g/dl. Urinalysis showed the presence of blood and 1 g/l of protein, and culture was sterile. In a 24-hour collection of 2.4 litres, urine sodium concentration was 160 mmol/l, potassium 30 mmol/l and protein 1.43 g (normal $<$ 150 mg). Creatinine clearance was 6.6 ml/min/1.7 m^2 (normal 98 – 150 ml/min/1.7 m^2). Renal ultrasonic scan showed two kidneys of normal size with increased echogenicity and loss of definition of the cortico-medullary junction.

These findings were consistent with acute-on-chronic renal failure, with tetany secondary to the resultant hypocalcaemia. Management consisted of administration of calcium supplements, phosphate binding agents, a high fluid intake, 1-alpha hydroxycholecalciferol, nifedipine to control the hypertension and subsequently sodium bicarbonate and potassium supplements with a protein-restricted diet. With this regimen his symptoms were controlled and blood pressure, serum calcium and phosphate levels returned to normal. Serum urea fell to 26 mmol/l, but creatinine remained grossly elevated at 775 µmol/l. Urinary output continued to exceed 2 litres daily, with persistent loss of sodium and potassium. Since discharge he has been reasonably well but no further improvement in renal function has occurred. A live donor graft from a relative has been offered for him should his condition deteriorate.

DISCUSSION

The syndrome described by Senior and Loken is a rare disorder combining a renal disease resembling familial juvenile nephronophthisis (previously known as medullary cystic disease) with tapeto-retinal degeneration. The term tapeto-retinal degeneration covers a group of familial and hereditary disorders characterised by progressive degeneration of the choroid and retina but varying in nature and severity. It is inherited in an autosomal recessive manner and progresses at a variable rate. Tapeto-retinal degeneration and familial juvenile nephronophthisis have been associated with other abnormalities including peripheral dysostosis,[3] mental retardation[2] and cerebellar ataxia,[4] mental retardation being present in the case described. The heterogeneity of this condition is further evidenced by the variable age at onset of the retinal lesion. In some families this may be congenital whereas in others its onset is in childhood.[5]

The earliest presenting signs of the renal component are polyuria and polydipsia secondary to defective urinary concentrating ability. Thus in a child with nausea, vomiting and poor intake, rapid dehydration is a hazard and in this instance precipitated acute-on-chronic renal failure. The onset is insidious and most cases do not present until renal failure is advanced. Urinalysis is essentially normal with no haematuria or albuminuria until late in the illness. Invariably there is excessive urinary loss of sodium. Anaemia, hypocalcaemia and hyperphosphataemia are proportional to the degree of renal failure. Nephronophthisis will not recur after renal transplantation.

The ocular component of Senior-Loken syndrome may be either Leber's amaurosis, retinitis pigmentosa or retinitis punctata albescens.[6] The case described here had Leber's amaurosis, a severe form of tapeto-retinal degeneration leading to blindness in early infancy. In Leber's amaurosis nystagmus and visual impairment usually occur in early infancy, the severity being disproportionate to the ophthalmoscopic changes. Ophthalmoscopy shows diffuse fundal pigmentation with pallor of the optic disc and narrowing of the retinal arteries. These changes may not be apparent until the age of six despite

severe visual impairment. The electroretinogram is characteristically flat at an early stage of the disease.

Awareness of the possibility of familial juvenile nephronophthisis in patients with Leber's amaurosis is important because it usually leads to death in the first or second decade. It is now agreed that children with nephronophthisis should undergo detailed ophthalmic assessment, including an electroretinogram. Children with primary tapeto-retinal degeneration should have measurements of blood pressure, urinary concentrating ability and renal ultrasound scan. Early diagnosis, control of hypertension and restriction of protein intake may prolong the time before renal replacement therapy is necessary.

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