

# A Japanese Child with Senior-Loken Syndrome

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**Background:** Senior-Loken syndrome is a rare disease that combines familial juvenile nephronophthisis with retinitis pigmentosa. We describe the clinical features of a Japanese patient with Senior-Loken syndrome emphasizing the importance of the ophthalmic findings in determining a correct diagnosis.

**Case:** A 6-year-old Japanese girl had anemia, mental retardation, and poor vision.

**Observations:** Fundus examination and electroretinography revealed that the patient had retinitis pigmentosa. A subsequent percutaneous renal biopsy disclosed chronic tubulointerstitial nephritis.

**Conclusion:** The ophthalmic findings in our patient led to the diagnosis of Senior-Loken syndrome. A careful ophthalmic examination was helpful in correctly diagnosing the syndrome. **Jpn J Ophthalmol 2001;45:636–639** ©2001 Japanese Ophthalmological Society

**Key Words:** Familial juvenile nephronophthisis, retinitis pigmentosa, Senior-Loken syndrome.

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## Introduction

Senior-Loken syndrome is a rare disease that combines familial juvenile nephronophthisis with retinitis pigmentosa. In 1961, Senior et al<sup>1</sup> and Loken et al<sup>2</sup> described an association of tapetoretinal degeneration with familial juvenile nephronophthisis. Since then, this association of diseases has been given a number of names, including Senior-Loken syndrome,<sup>3</sup> tapetoretinal degeneration, familial juvenile nephronophthisis,<sup>4</sup> and familial renal-retinal dystrophy.<sup>5</sup> In addition, other skeletal and/or central neuronal abnormalities have been reported in association with the tapetoretinal degeneration and nephronophthisis in Western medical literature.<sup>6–9</sup>

Although Japanese patients with Senior-Loken syndrome have been reported,<sup>10,11</sup> no detailed ocular features of this rare syndrome have ever been reported in the Japanese patient population. Recently, we exam-

ined a Japanese girl with Senior-Loken syndrome. We report the ophthalmic findings in our patient.

## Case Report

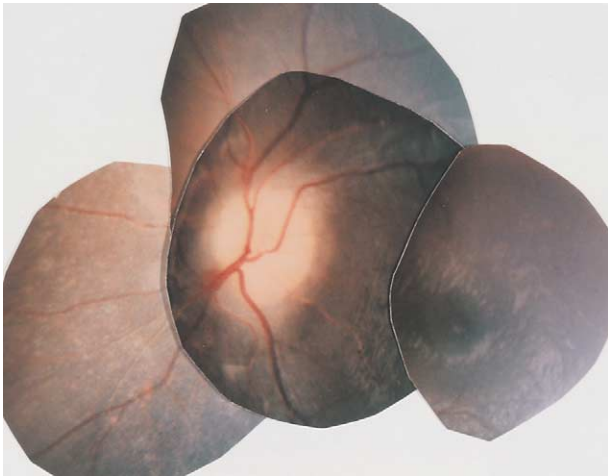
A 6-year-old Japanese girl had anemia, mental retardation, and poor vision. She was born after an uncomplicated pregnancy. Her parents were unrelated and were in good health. There was no known family history of ocular problems or renal disease. Mental retardation was observed at 1 year of age and the patient had been closely cared for by pediatricians since then. At age 2 years, she was found to have exotropia; no further ophthalmic examination was done. At age 6 years, she was admitted to our hospital for persistent anemia. Laboratory data indicated that she had renal insufficiency associated with metabolic acidosis, but ultrasonographic examination revealed normal-sized kidneys.

On ocular examination, coarse pendular nystagmus was noted. Her visual acuity could not be assessed because of severe mental retardation. The lens showed no cataractous changes in either eye. Fundus examination revealed hamartomatous pallor in both optic discs and diffuse cloudiness in retinal color (Figure 1). Some patchy areas of depigmenta-

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Received: December 11, 2000

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**Figure 1.** Fundus of 6-year-old patient with Senior-Loken syndrome. Hamartomatous pallor of optic discs and some patchy areas of depigmented retinal pigment epithelium can be seen. Retinal arterioles showed diffuse narrowing.

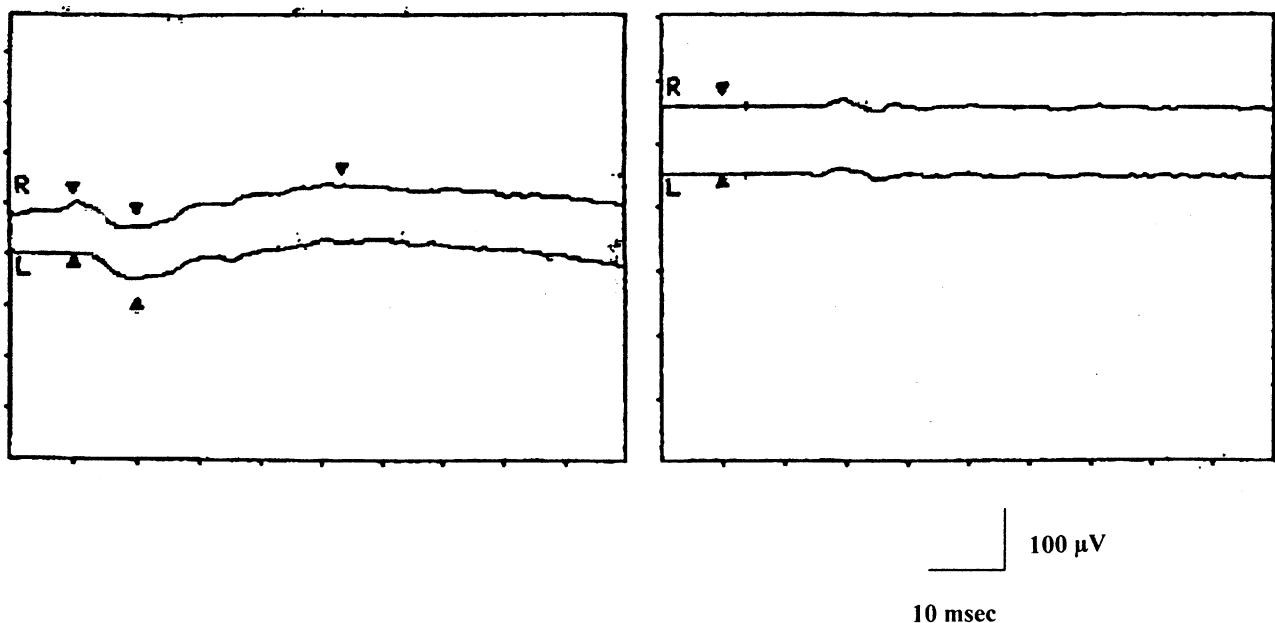
tion were seen in the retinal pigment epithelium. The retinal arterioles showed diffuse attenuation.

Electroretinography revealed that there was a severe decrease of the dark-adapted a- and b-wave amplitudes elicited by a bright-flash (20 J) (Figure 2). These findings were compatible with retinitis pigmentosa.

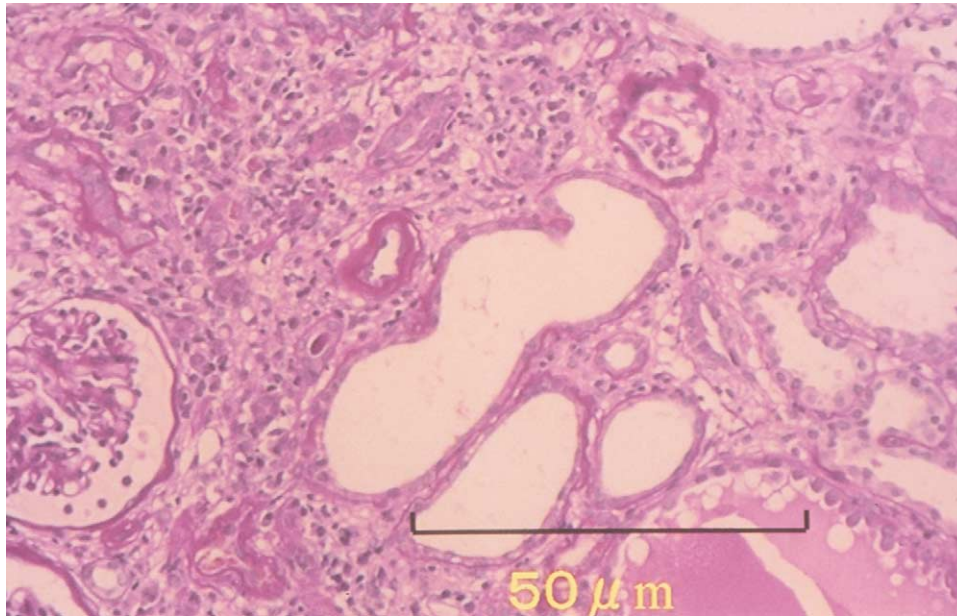
Considering these ophthalmic findings in association with renal failure, we suspected that this patient had Senior-Loken syndrome. A percutaneous renal biopsy was performed, and histopathologic examination revealed chronic tubulointerstitial nephritis consistent with a diagnosis of juvenile nephronophthisis (Figure 3). These findings confirmed the diagnosis of Senior-Loken syndrome. Since then, the patient has been treated with peritoneal dialysis.

### Discussion

Since Senior et al<sup>1</sup> and Loken et al<sup>2</sup> first described the clinical features of juvenile nephropathy with tapetoretinal dystrophy, other clinical observations have been reported in association with Senior-Loken syndrome in Western countries.<sup>3-9</sup> After Shinoda et al<sup>10</sup> first reported a Japanese patient with Senior-Loken syndrome, other Japanese cases have been reported.<sup>11</sup> To our knowledge, however, no report has ever described the ophthalmic findings, including the electroretinographic findings, in Japanese patients with this rare syndrome. The ophthalmic (Figures 1 and 2) and histopathologic (Figure 3) findings were compatible with a diagnosis of Senior-Loken syndrome. The ocular findings combined with the laboratory data of renal insufficiency led us to suspect this syndrome and prompted us to perform renal biopsy.



**Figure 2.** Electroretinograms elicited by bright flash (20 J) from dark-adapted eyes showing that both a- and b-waves are severely decreased. ▲ and ▼: range of a- or b-wave.



**Figure 3.** Percutaneous renal biopsy shows tubulointerstitial nephritis. Large region of interstitium shows tubular atrophy and fibrosis with infiltration of mononuclear leukocytes while most of glomeruli show varying degrees of periglomerular fibrosis with relatively normal tufts.

Therefore, it should be emphasized that a careful ophthalmic examination is quite helpful in the diagnosis.

The ocular findings in our patient were typical of juvenile retinitis pigmentosa in both fundus appearance and electroretinographic responses. These results suggest that the tapetoretinal degeneration associated with Senior-Loken syndrome has similar phenotypic expressions in Western and Japanese patients.

Recent molecular genetic studies have shown that a gene for familial juvenile nephronophthisis (NPH1), a pure renal form of familial juvenile nephronophthisis, can be mapped to chromosome 2.<sup>12,13</sup> However, the exact localization of the gene for Senior-Loken syndrome has not been found. Two hypotheses can be considered. First, different genes responsible for each entity (retinitis pigmentosa and juvenile nephronophthisis) are defective. And second, a single gene that plays an important role in the differentiation and development of both renal tubules and retina is abnormal. Further molecular genetic studies are needed to clarify these possibilities.

This study was supported in part by a grant from the Research Committee on Chorioretinal Degeneration and Optic Atrophy, the Ministry of Health, Labor, and Welfare of the Japanese Government (Dr. Nakazawa), Tokyo. This case was presented at the Annual Meeting of

Congenital Ocular Disorders conjoined with the 54th Annual Meeting of Japan Clinical Ophthalmology, Tokyo on November 3, 2000.

## References

1. Senior B, Friedmann AI, Braudo JL. Juvenile familial nephropathy with tapetoretinal degeneration. *Am J Ophthalmol* 1961;52:625-33.
2. Loken AC, Hanssen O, Halvorsen S, Jolster NJ. Hereditary renal dysplasia and blindness. *Acta Paediatr Scand* 1961;50:177-84.
3. Fillastre JP, Guenel J, Riberi P, Marx P, Whitworth J, Kuhn J. Senior-Loken syndrome (nephronophthisis and tapetoretinal degeneration). A study of 8 cases from 5 families. *Clin Nephrol* 1976;5:14-9.
4. Van Balen A, Collenburg J. Tapetoretinal degeneration and familial juvenile nephronophthisis (FJN). *J Pediatr Ophthalmol* 1976;13:32-6.
5. Senior B. Familial renal-retinal dystrophy. *Am J Dis Child* 1973;125:442.
6. Mainzer F, Saldino R, Ozonoff M, Minagi H. Familial nephropathy associated with retinitis pigmentosa, cerebellar ataxia and skeletal abnormalities. *Am J Med* 1970;49:556.
7. Saldino RM, Mainzer F. Cone-shaped epiphyses (CSE) in siblings with hereditary renal disease and retinitis pigmentosa. *Radiology* 1971;98:39.
8. Ellis DS, Heckenlively JR, Martin CL, et al. Leber's congenital amaurosis associated with familial juvenile nephronophthisis and cone-shaped epiphyses of the hands (the Saldino-Mainzer syndrome). *Am J Ophthalmol* 1984;97:233-9.
9. Lauweryns B, Leys A, Van Haesendonck E, Missotten L. Senior-Loken syndrome with marbled fundus and unusual

- skeletal abnormalities. A case report. *Graefes Arch Clin Exp Ophthalmol* 1993;231:242-6.
10. Shinoda M, Mototani T, Aizawa F. Die familiäre juvenile Nephronophthise. *Acta Paediatr Jpn* 1968;72:157-162.
  11. Hirabayashi S, Shigenatsu H, Iai M, Takashima S. A neurodegenerative disorder with early myoclonic encephalopathy, retinal pigmentary degeneration and nephronophthisis. *Brain Dev* 2000;22:24-30.
  12. Antignac C, Arduy CH, Beckmann JS, et al. A gene for familial juvenile nephronophthisis (recessive medullary cystic kidney disease) maps to chromosome 2p. *Nat Genet* 1993; 3:342-5.
  13. Hildebrandt F, Singh-Sawhney I, Schnieders B, et al. Mapping of a gene for familial juvenile nephronophthisis: confirmation of linkage to chromosome 2 and definition of flanking markers. *Am J Hum Genet* 1993;53:1256-61.