



Senior-Løken Syndrome

(Juvenile Nephronophthisis with Retinal Dystrophy)

Senior-Løken syndrome refers to a disorder in which there is the combination of nephronophthisis with retinal dystrophy. In some individuals, Senior-Løken syndrome can occur as part of a group of genetic conditions that result from an abnormality in the part of the brain called the cerebellar vermis. These disorders that share this cerebellar malformation are known as Joubert syndrome and related disorders (JSRD). These conditions have some characteristics in common, but there is a spectrum of symptoms and abilities in affected individuals. For additional information regarding this family of conditions, please refer to the Joubert Syndrome & Related Disorders Foundation website at www.jsrdf.org.

Individuals diagnosed with Senior-Løken syndrome traditionally exhibit the following features:

- Renal insufficiency, particularly juvenile nephronophthisis. Initial symptoms of nephronophthisis include increased thirst and urination, and sometimes anemia (low blood count).
- Retinal dystrophy, particularly increased pigmentation of the retina or flattened electroretinogram (ERG) traces. Reduced ability to see well during low-light conditions (e.g., night-time) may be one of the first indications of retinal dystrophy.

While less common, the following features may also be present in some individuals:

- Underdevelopment (hypoplasia) or complete lack (aplasia/agenesis) of the cerebellar vermis, usually indicated by the “Molar Tooth” sign found on an axial view of a brain MRI scan.
- Developmental delays/mental retardation—variable severity.
- Difficulty coordinating voluntary muscle movements; uncoordinated movements (ataxia).
- Poor visual function accompanied by rapid, involuntary movements of the eyes (nystagmus), sluggish pupillary responses, intolerance to light (photophobia), and far-sightedness (hyperopia)
- Repeated eye rubbing, poking, and pressing (symptoms of severe visual impairment, or Leber congenital amaurosis)
- Decreased muscle tone (hypotonia).
- Abnormal breathing pattern with episodes of rapid breathing or panting (hyperpnea), which may be followed by pauses in breathing (apnea).
- Difficulty processing and reacting to information received through any of their five senses.
- Facial features may be abnormal in appearance (eyes far set from each other, small ear lobes, broad forehead, arched eyebrows, broad mouth)
- Vascular hypertension, as a result of the affected kidneys
- Other conditions not listed here may also be observed

Explanation of features:

Some individuals diagnosed with Senior-Løken may have an absence or underdevelopment of part of the brain called the cerebellar vermis which controls balance and coordination. The severity of the resulting ataxia (uncoordinated movements) varies from person to person. Some individuals with Senior-Løken syndrome do not have any cerebellar abnormalities or ataxia.

Decreased muscle tone may occur in children with Senior-Løken. As a result of the poor muscle tone, developmental delay (usually in gross motor, fine motor and speech areas) can occur. Some children have also been noted to have abnormal eye and tongue movements.

Developmental delays, when present, may be treated through physical therapy, occupational therapy, speech therapy, and infant stimulation. Most children are able to achieve standard milestones, although some may do so at a later age. Retinal dystrophy may impact vision and cause difficulty with developmental skills that rely on normal vision.

Some individuals experience difficulties resulting from an inability to appropriately process information received through the five senses - hearing, seeing, tasting, touching, and smelling - as well as from their poor sense of

balance and muscle movement. Some families have found that sensory integration therapy can help to minimize these sensory issues.

Renal insufficiency known as juvenile nephronophthisis may develop during childhood. Initial symptoms may include excessive thirst and urination, and kidney failure may result.

Mild to moderate mental retardation may be present, but overall health and growth are not known to be severely affected by this condition unless significant vision loss or kidney failure occurs.

Management and treatment:

Presently, there is no cure for Senior-Løken syndrome. It is recommended that individuals with Senior-Løken syndrome see the appropriate specialists necessary to help monitor their various clinical features. Suggested specialists include a nephrologist (kidney specialist), ophthalmologist (eye doctor), geneticist, and neurologist, as well as any others recommended by your doctor.

Screening for some of the complications associated with Senior-Løken, such as those related to vision or kidney involvement that may become progressive over time, is recommended on an annual basis. Kidney failure usually develops in childhood or early adulthood, and management may require medications, dialysis, and/or renal transplantation. Retinal dystrophy can be relatively stable or it can progress slowly, and may not have onset until after age 10 years. Please refer to the Joubert Syndrome Foundation and Related Cerebellar Disorders website's "Evaluation Recommendations" link for a complete listing of recommended annual tests.

Inheritance and recurrence:

Senior-Løken syndrome is passed down from parents to offspring as an autosomal recessive trait, which means that both parents have one altered copy of the gene responsible for this disorder in their DNA. (In order for a child to be born with this disorder, both the egg and the sperm must contain the same altered gene in question). The odds of having a child born with Senior-Løken syndrome to parents who carry the altered gene involved are 1 in 4, or 25%, in each pregnancy that they share.

Genetic cause:

A number of genes responsible for Senior-Løken syndrome have been identified, and some of these genes are altered in those individuals who have associated features of a cerebellar malformation and/or developmental delays. Three such genes associated with Joubert syndrome and complications of retinal dystrophy and/or nephronophthisis are *NPHP1*, *AHI1* and *CEP290*. However, these do not explain all cases of Senior-Løken syndrome, and the genetics of these disorders remain complex. It is likely that other genes that cause this condition exist.

Research is currently underway to assist medical professionals in developing a greater understanding about this disorder. For more information about genetic research, please contact the Joubert Syndrome Foundation and Related Cerebellar Disorders.

Additional resources for families:

- Joubert Syndrome & Related Disorders Foundation: www.jsrdf.org
- American Liver Foundation: www.liverfoundation.org/
- National Association for the Visually Handicapped: www.navh.org
- National Kidney Foundation: www.kidney.org
- National Eye Institute: www.nei.nih.gov

Resources used in the creation of this document:

- Gleeson, J.G. et al. (2003). Molar Tooth Sign of the Midbrain-Hindbrain Junction: Occurrence in Multiple Distinct Syndromes. *American Journal of Medical Genetics*, 125A, 125-134.
- Joubert Syndrome & Related Disorders Foundation website: www.jsrdf.org
- Parisi, M.A. and Glass, I. A. "Joubert Syndrome" GeneReviews, Online publication of expert-authored disease reviews: www.genereviews.org
- ORPHANET database on rare diseases and orphan drugs: www.orphanet.net
- Satran, D, Pierpont, M. M., & Dobyns, W. B. (1999). Cerebello-Oculo-Renal Syndromes Including Arima, Senior-Løken, and COACH Syndromes: More Than Just Variants of Joubert Syndrome. *American Journal of Medical Genetics*, 86, 459-469.

The information presented is intended to summarize this condition as it is presently understood by medical professionals. The statements included in this document are for information only and should not be considered as medical advice. Please always consult your physician for medical advice.