

Duane-radial Ray Syndrome

Subjects: Genetics & Heredity

Contributor: Nicole Yin

Duane-radial ray syndrome is a disorder that affects the eyes and causes abnormalities of bones in the arms and hands. This condition is characterized by a particular problem with eye movement called Duane anomaly (also known as Duane syndrome). This abnormality results from the improper development of certain nerves that control eye movement. Duane anomaly limits outward eye movement (toward the ear), and in some cases may limit inward eye movement (toward the nose). Also, as the eye moves inward, the eye opening becomes narrower and the eyeball may pull back (retract) into its socket.

Keywords: genetic conditions

1. Introduction

Bone abnormalities in the hands include malformed or absent thumbs, an extra thumb, or a long thumb that looks like a finger. Partial or complete absence of bones in the forearm is also common. Together, these hand and arm abnormalities are known as radial ray malformations.

People with the combination of Duane anomaly and radial ray malformations may have a variety of other signs and symptoms. These features include unusually shaped ears, hearing loss, heart and kidney defects, a distinctive facial appearance, an inward- and upward-turning foot (clubfoot), and fused spinal bones (vertebrae).

The varied signs and symptoms of Duane-radial ray syndrome often overlap with features of other disorders. For example, acro-renal-ocular syndrome is characterized by Duane anomaly and other eye abnormalities, radial ray malformations, and kidney defects. Both conditions are caused by mutations in the same gene. Based on these similarities, researchers suspect that Duane-radial ray syndrome and acro-renal-ocular syndrome are part of an overlapping set of syndromes with many possible signs and symptoms. The features of Duane-radial ray syndrome are also similar to those of a condition called Holt-Oram syndrome; however, these two disorders are caused by mutations in different genes.

2. Frequency

Duane-radial ray syndrome is a rare condition whose prevalence is unknown. Only a few affected families have been reported worldwide.

3. Causes

Duane-radial ray syndrome results from mutations in the *SALL4* gene. This gene is part of a group of genes called the SALL family. SALL genes provide instructions for making proteins that are involved in the formation of tissues and organs before birth. The proteins produced from these genes act as transcription factors, which means they attach (bind) to specific regions of DNA and help control the activity of particular genes. The exact function of the *SALL4* protein is unclear, although it appears to be important for the normal development of the eyes, heart, and limbs.

Mutations in the *SALL4* gene prevent cells from making any functional protein from one copy of the gene. It is unclear how a reduction in the amount of the *SALL4* protein leads to Duane anomaly, radial ray malformations, and the other features of Duane-radial ray syndrome and similar conditions.

3.1. The Gene Associated with Duane-radial Ray Syndrome

- *SALL4*

4. Inheritance

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered *SALL4* gene in each cell is sufficient to cause the disorder. In many cases, an affected person inherits a mutation from one affected parent. Other cases result from new mutations in the gene and occur in people with no history of the disorder in their family.

5. Other Names for This Condition

- DRRS
- Okihiro syndrome

References

1. Al-Baradie R, Yamada K, St Hilaire C, Chan WM, Andrews C, McIntosh N, Nakano M, Martonyi EJ, Raymond WR, Okumura S, Okihiro MM, Engle EC. Duane radial raysyndrome (Okihiro syndrome) maps to 20q13 and results from mutations in *SALL4*, a new member of the SAL family. *Am J Hum Genet*. 2002 Nov;71(5):1195-9.
2. Borozdin W, Boehm D, Leipoldt M, Wilhelm C, Reardon W, Clayton-Smith J, Becker K, Mühlendyck H, Winter R, Giray O, Silan F, Kohlhase J. *SALL4* deletions are a common cause of Okihiro and acro-renal-ocular syndromes and confirm haploinsufficiency as the pathogenic mechanism. *J Med Genet*. 2004 Sep;41(9):e113.
3. Borozdin W, Wright MJ, Hennekam RC, Hannibal MC, Crow YJ, Neumann TE, Kohlhase J. Novel mutations in the gene *SALL4* provide further evidence for acro-renal-ocular and Okihiro syndromes being allelic entities, and extend the phenotypic spectrum. *J Med Genet*. 2004 Aug;41(8):e102.
4. Kohlhase J, Chitayat D, Kotzot D, Ceylaner S, Froster UG, Fuchs S, Montgomery T, Rösler B. *SALL4* mutations in Okihiro syndrome (Duane-radial ray syndrome), acro-renal-ocular syndrome, and related disorders. *Hum Mutat*. 2005 Sep;26(3):176-83.
5. Kohlhase J, Heinrich M, Schubert L, Liebers M, Kispert A, Laccone F, Turnpenny P, Winter RM, Reardon W. Okihiro syndrome is caused by *SALL4* mutations. *Hum Mol Genet*. 2002 Nov 1;11(23):2979-87.
6. Kohlhase J, Schubert L, Liebers M, Rauch A, Becker K, Mohammed SN, Newbury-Ecob R, Reardon W. Mutations at the *SALL4* locus on chromosome 20 result in a range of clinically overlapping phenotypes, including Okihiro syndrome, Holt-Oram syndrome, acro-renal-ocular syndrome, and patients previously reported to represent thalidomide embryopathy. *J Med Genet*. 2003 Jul;40(7):473-8.
7. Kohlhase J. *SALL4*-Related Disorders. 2004 Aug 16 [updated 2015 Jan 15]. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, Amemiya A, editors. *GeneReviews*® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2020. Available from <http://www.ncbi.nlm.nih.gov/books/NBK1373/>
8. Miertus J, Borozdin W, Frezer V, Tonini G, Bertok S, Amoroso A, Miertus S, Kohlhase J. A *SALL4* zinc finger missense mutation predicted to result in increased DNA binding affinity is associated with cranial midline defects and mild features of Okihiro syndrome. *Hum Genet*. 2006 Mar;119(1-2):154-61.
9. Terhal P, Rösler B, Kohlhase J. A family with features overlapping Okihiro syndrome, hemifacial microsomia and isolated Duane anomaly caused by a novel *SALL4* mutation. *Am J Med Genet A*. 2006 Feb 1;140(3):222-6.

Retrieved from <https://encyclopedia.pub/entry/history/show/11361>