Ophthalmo-acromelic syndrome

Ophthalmo-acromelic syndrome is a condition that results in malformations of the eyes, hands, and feet. The features of this condition are present from birth. The eyes are often absent or severely underdeveloped (anophthalmia), or they may be abnormally small (microphthalmia). Usually both eyes are similarly affected in this condition, but if only one eye is small or missing, the other eye may have a defect such as a gap or split in its structures (coloboma).

The most common hand and foot malformation seen in ophthalmo-acromelic syndrome is missing fingers or toes (oligodactyly). Other frequent malformations include fingers or toes that are fused together (syndactyly) or extra fingers or toes (polydactyly). These skeletal malformations are often described as acromelic, meaning that they occur in the bones that are away from the center of the body. Additional skeletal abnormalities involving the long bones of the arms and legs or the spinal bones (vertebrae) can also occur. Affected individuals may have distinctive facial features, an opening in the lip (cleft lip) with or without an opening in the roof of the mouth (cleft palate), or intellectual disability.

Frequency

The prevalence of ophthalmo-acromelic syndrome is not known; approximately 35 cases have been reported in the medical literature.

Causes

Mutations in the *SMOC1* gene cause ophthalmo-acromelic syndrome. The *SMOC1* gene provides instructions for making a protein called secreted modular calcium-binding protein 1 (SMOC-1). This protein is found in basement membranes, which are thin, sheet-like structures that support cells in many tissues and help anchor cells to one another during embryonic development. The SMOC-1 protein attaches (binds) to many different proteins and is thought to regulate molecules called growth factors that stimulate the growth and development of tissues throughout the body. These growth factors play important roles in skeletal formation, normal shaping (patterning) of the limbs, as well as eye formation and development. The SMOC-1 protein also likely promotes the maturation (differentiation) of cells that build bones, called osteoblasts.

SMOC1 gene mutations often result in a nonfunctional SMOC-1 protein. The loss of SMOC-1 could disrupt growth factor signaling, which would impair the normal development of the skeleton, limbs, and eyes. These changes likely underlie the anophthalmia and skeletal malformations of ophthalmo-acromelic syndrome. It is unclear how *SMOC1* gene mutations lead to the other features of this condition.

Some people with ophthalmo-acromelic syndrome do not have an identified mutation in the *SMOC1* gene. The cause of the condition in these individuals is unknown.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- anophthalmia-syndactyly
- anophthalmia-Waardenburg syndrome
- anophthalmos-limb anomalies syndrome
- anophthalmos with limb anomalies
- microphthalmia with limb anomalies
- OAS
- ophthalmoacromelic syndrome
- syndactyly-anophthalmos syndrome
- Waardenburg anophthalmia syndrome

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Anophthalmos with limb anomalies
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0599973/

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22ophthalmo-acromelic+syndrome%22+OR+%22Waardenburg+anophthalmia+syndrome%22+OR+%22anophthalmia-syndactyly%22+OR+%22anophthalmos+with+limb+anomalies%22+OR+%22microphthalmia+with+limb+anomalies%22+OR+%22Anophthalmos%22

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Webbing of the Fingers or Toes
  https://medlineplus.gov/ency/article/003289.htm
- Health Topic: Vision Impairment and Blindness
  https://medlineplus.gov/visionimpairmentandblindness.html

Genetic and Rare Diseases Information Center

- Anophthalmos with limb anomalies
  https://rarediseases.info.nih.gov/diseases/722/anophthalmos-with-limb-anomalies

Additional NIH Resources

- National Eye Institute: Facts About Anophthalmia and Microphthalmia
  https://nei.nih.gov/health/anoph/anophthalmia

Educational Resources

- American Society for Surgery of the Hand: Congenital Hand Differences
  http://www.assh.org/handcare/Anatomy/Details-Page/ArticleID/39392/Congenital-Hand-Differences
- MalaCards: anophthalmos with limb anomalies
  https://www.malacards.org/card/anophthalmos_with_limb_anomalies
- Minnesota Department of Health: Anophthalmia and Microphthalmia
  https://www.health.state.mn.us/diseases/cy/anophthalmia.html
- Orphanet: Microphthalmia with limb anomalies
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=1106
- Scottish Sensory Centre: Anophthalmia
  http://www.ssc.education.ed.ac.uk/resources/vi%26multi/eyeconds/Anoph.html

Patient Support and Advocacy Resources

- American Foundation for the Blind
  https://www.afb.org/
- Contact a Family (UK): Anophthalmia
  https://contact.org.uk/advice-and-support/medical-information/conditions/a/anophthalmia/
- Micro and Anophthalmic Children's Society
  https://macs.org.uk/

- Resource List from the University of Kansas Medical Center: Anophthalmia
  http://www.kumc.edu/gec/support/anopthal.html
- The International Children's Anophthalmia Network
  http://www.anophthalmia.org/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28ophthalmo-acromelic+syndrome%5BTIAB%5D%29+OR+%28anophthalmia-syndactyly%5BTIAB%5D%29+OR+%28anophthalmos+with+limb+anomalies%5BTIAB%5D%29+OR+%28microphthalmia+with+limb+anomalies%5BTIAB%5D%29+OR+%28ophthalmoacromelic+syndrome%5BTIAB%5D%29+OR+%28waardenburg+anophthalmia+syndrome%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D

Catalog of Genes and Diseases from OMIM

- MICROPHTHALMIA WITH LIMB ANOMALIES
  http://omim.org/entry/206920

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