Andersen-Tawil syndrome

Andersen-Tawil syndrome is a disorder that causes episodes of muscle weakness (periodic paralysis), changes in heart rhythm (arrhythmia), and developmental abnormalities. Periodic paralysis begins early in life, and episodes last from hours to days. These episodes may occur after exercise or long periods of rest, but they often have no obvious trigger. Muscle strength usually returns to normal between episodes. However, mild muscle weakness may eventually become permanent.

In people with Andersen-Tawil syndrome, the most common changes affecting the heart are ventricular arrhythmia, which is a disruption in the rhythm of the heart’s lower chambers (the ventricles), and long QT syndrome. Long QT syndrome is a heart condition that causes the heart (cardiac) muscle to take longer than usual to recharge between beats. The irregular heartbeats can lead to discomfort, such as the feeling that the heart is skipping beats (palpitations). Uncommonly, the irregular heartbeats can cause fainting (syncope), and even more rarely, sudden death.

Physical abnormalities associated with Andersen-Tawil syndrome typically affect the face, other parts of the head, and the limbs. These features often include a very small lower jaw (micrognathia), dental abnormalities (such as crowded teeth), low-set ears, widely spaced eyes, fusion (syndactyly) of the second and third toes, and unusual curving of the fingers or toes (clinodactyly). Some affected people also have short stature and an abnormal side-to-side curvature of the spine (scoliosis).

The signs and symptoms of Andersen-Tawil syndrome vary widely, and they can be different even among affected members of the same family. About 60 percent of affected individuals have all three major features (periodic paralysis, cardiac arrhythmia, and physical abnormalities).

Frequency

Andersen-Tawil syndrome is a rare genetic disorder. Its exact prevalence is unknown, although it is estimated to affect 1 in 1 million people worldwide. About 200 affected individuals have been described in the medical literature. Researchers believe that Andersen-Tawil syndrome accounts for less than 10 percent of all cases of periodic paralysis.

Genetic Changes

Mutations in the KCNJ2 gene cause about 60 percent of all cases of Andersen-Tawil syndrome. When the disorder is caused by mutations in this gene, it is classified as type 1 (ATS1).
The \textit{KCNJ2} gene provides instructions for making channels that transport positively charged potassium ions across the membrane of muscle cells. The movement of potassium ions through these channels is critical for maintaining the normal function of muscles used for movement (skeletal muscles) and cardiac muscle. Mutations in the \textit{KCNJ2} gene alter the usual structure and function of these potassium channels. These changes disrupt the flow of potassium ions in skeletal and cardiac muscle, leading to the periodic paralysis and irregular heart rhythm characteristic of Andersen-Tawil syndrome.

Researchers have not determined the role of the \textit{KCNJ2} gene in bone development, and it is not known how mutations in the gene lead to the skeletal changes and other physical abnormalities often found in Andersen-Tawil syndrome.

In the 40 percent of cases not caused by \textit{KCNJ2} gene mutations, the cause of Andersen-Tawil syndrome is usually unknown. These cases are classified as type 2 (ATS2). Studies suggest that variations in at least one other potassium channel gene may underlie the disorder in some of these affected individuals.

\textbf{Inheritance Pattern}

This condition is inherited in an autosomal dominant pattern, which means one copy of an altered gene in each cell is sufficient to cause the disorder. When the condition results from a mutation in the \textit{KCNJ2} gene, an affected individual may inherit the mutation from one affected parent. In other cases, the condition results from a new (de novo) mutation in the \textit{KCNJ2} gene. These cases occur in people with no history of the disorder in their family.

\textbf{Other Names for This Condition}

- Andersen syndrome
- ATS
- long QT syndrome 7
- LQT7

\textbf{Diagnosis & Management}

\textbf{Formal Treatment/Management Guidelines}

- Periodic Paralysis International: Hospital Management Guidelines for Patients with Andersen-Tawil Syndrome
  \url{http://hkpp.org/patient/hospital-management/ATS}
  \url{https://www.sads.org/Living-with-SADS/Sports-Exercise#WqaksOdG1aQ}
Genetic Testing

- Genetic Testing Registry: Andersen Tawil syndrome

Other Diagnosis and Management Resources

- GeneReview: Andersen-Tawil Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1264

- GeneReview: Long QT Syndrome

- Periodic Paralysis International: Anaesthesia and Peri-Operative Care in the Primary Periodic Paralysis Disorders
  http://hkpp.org/node/181

- Sudden Arrhythmia Death Syndromes (SADS) Foundation Physician Referral Network
  https://www.sads.org/living-with-sads/Find-a-Physician#.WqakjudG1aQ

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html

- Drug Therapy
  https://medlineplus.gov/drugtherapy.html

- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html

- Palliative Care
  https://medlineplus.gov/palliativecare.html

- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Arrhythmias
  https://medlineplus.gov/ency/article/001101.htm

- Health Topic: Arrhythmia
  https://medlineplus.gov/arrhythmia.html

- Health Topic: Congenital Heart Defects
  https://medlineplus.gov/congenitalheartdefects.html
Genetic and Rare Diseases Information Center

- Andersen-Tawil syndrome

Additional NIH Resources

- National Heart, Lung, and Blood Institute
  https://www.nhlbi.nih.gov/health-topics/long-qt-syndrome

Educational Resources

- Centre for Genetics Education (Australia)

- Disease InfoSearch: Andersen Tawil Syndrome
  http://www.diseaseinfosearch.org/Andersen+Tawil+Syndrome/431

- KidsHealth from the Nemours Foundation: Arrhythmias

- MalaCards: MalaCards: andersen syndrome
  http://www.malacards.org/card/andersen_syndrome


- Orphanet: Cardiodysrhythmic potassium-sensitive periodic paralysis
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=37553

- Periodic Paralysis International: Physician’s Summary: Andersen-Tawil Syndrome
  http://hkpp.org/physicians/ATS

Patient Support and Advocacy Resources

- American Heart Association
  http://www.heart.org/

- Muscular Dystrophy Association: Periodic Paralyses
  https://www.mda.org/disease/periodic-paralyses

- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/andersen-tawil-syndrome/

- National Organization for Rare Disorders (NORD): International Long QT Syndrome Registry
  https://rarediseases.org/organizations/international-long-qt-syndrome-registry/

- Periodic Paralysis Association
  https://www.periodicparalysis.org/
Periodic Paralysis International  
http://hkpp.org/

Resource List from the University of Kansas Medical Center: Heart/Cardiology Conditions  
http://www.kumc.edu/gec/support/conghart.html

Sudden Arrhythmia Death Syndromes (SADS) Foundation  
https://www.sads.org/What-is-SADS/Long-QT-Syndrome#.Vds6vpdGdD8

GeneReviews  
- Andersen-Tawil Syndrome  
https://www.ncbi.nlm.nih.gov/books/NBK1264  
- Long QT Syndrome  

ClinicalTrials.gov  
- ClinicalTrials.gov  
https://clinicaltrials.gov/ct2/results?cond=%22Andersen-Tawil+syndrome%22+OR+%22Long+QT+Syndrome%22

Scientific Articles on PubMed  
- PubMed  
https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28andersen-tawil+syndrome%5BTI%5D%29+OR+%28andersen+syndrome%5BTI%5D%29+OR+%28andersen's+syndrome%5BTI%5D%29+OR+%28lqt7%5BTI%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D

OMIM  
- ANDERSEN CARDIODYSRHYTHMIC PERIODIC PARALYSIS  
http://omim.org/entry/170390

MedGen  
- Andersen Tawil syndrome  

Sources for This Summary  
Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/28024840

Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16540748
   Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24383070

   Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11371347

   Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301441

   Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20306271

Reprinted from Genetics Home Reference:

Reviewed: April 2018
Published: April 11, 2018

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services