Synonyms of MCT8-specific thyroid hormone cell transporter deficiency

- AHDS
- Allan-Herndon-Dudley syndrome
- Allan-Herndon syndrome
- MCT8-THCT deficiency
- mental retardation, X-linked, with hypotonia
- THCT deficiency

General Discussion

MCT8-specific thyroid hormone cell transporter deficiency (THCT deficiency) is an inherited disorder that is characterized by severe mental retardation, an impaired ability to speak, diminished muscle tone (hypotonia), and/or movement abnormalities.

With the exception of poor muscle tone, most affected infants appear to develop normally during the first months of life. However, by about two months of age, affected infants may seem weak and have an inability to hold up the head. Due to hypotonia, severely reduced motor development, and other abnormalities, affected children very rarely develop any ability to walk and when they do, it is with shuffling gait. Associated features often include underdevelopment (hypoplasia) and wasting (atrophy) of muscle tissue; weakness and stiffness of the legs (spastic paraplegia) with exaggerated reflexes (hyperreflexia); relatively slow, involuntary, purposeless, commonly dyskinetic (abnormal movement) attacks. Writhing movements (athetoid movements); and/or other movement abnormalities are less common. Affected individuals may also have abnormalities of the skull and facial (craniofacial) region. THCT deficiency is inherited as an X-linked genetic disorder.

Signs & Symptoms

THCT deficiency is primarily characterized by severe mental retardation, poor muscle tone (hypotonia), and movement abnormalities. As mentioned above, affected infants typically appear to develop normally (with the exception of hypotonia) until about 2 months of age, when they may seem to have generalized weakness and be unable to hold up their heads. Family members have described the latter feature as “limber neck.” Due to low muscle tone, weakness, severely reduced motor development, and/or other factors, affected children are unable to or may walk with great difficulty. Associated findings may include underdevelopment (hypoplasia) and wasting (atrophy) of various skeletal (voluntary) muscles; an impaired ability to coordinate certain voluntary movements (ataxia); weakness and stiffness of the legs (spastic paraplegia) with associated hyperreflexia and involuntary, rapid, repeated contractions and relaxations of the legs (clonus); involuntary. Movement abnormalities are common and include, most commonly, dyskinetic attacks or relatively slow, writhing movements (athetoid movements); and/or other movement abnormalities. Typical dyskinetic attacks last a few minutes or less and consist of body extension, opening of the mouth, and stretching or flexing of the limbs. They are usually triggered by physical (changing diapers...
or clothes) and emotional stimuli

As noted earlier, infants and children with the disorder are also affected by severe mental retardation and delays in the acquisition of skills requiring the coordination of muscular and mental activities (psychomotor retardation). In addition, affected children are unable to speak or rarely acquire garbled speech.

As adults, affected individuals may have generalized muscular wasting (atrophy), permanent fixation of multiple small and large joints in various fixed postures (joint contractures) and/or decreased reflex reactions (hyporeflexia).

Individuals with THCT deficiency may also have unusual craniofacial features and/or additional skeletal abnormalities. The head is usually of normal size but may be abnormally narrow at the temples (bitemporal narrowing). In addition, the face may appear abnormally long (elongated) and thin with large, poorly developed ears. In some cases, THCT deficiency may also be associated with abnormal side-to-side curvature of the spine (scoliosis); depression of the breastbone (“funnel chest” or pectus excavatum); and/or foot defects.

**Causes**

THCT deficiency is caused by an abnormality (mutation) in the MCT8 (SLC16A2) gene leading to alteration in the structure and function of the MCT8 protein. The abnormal protein is unable to transport thyroid hormone produced by the thyroid gland into the brain, thus affecting its development.

THCT deficiency is inherited as an X-linked genetic condition. X-linked genetic disorders are conditions caused by an abnormal gene on the X chromosome and manifests mostly in males. Females that have a defective gene present on one of their X chromosomes are carriers for that disorder. Carrier females usually do not display symptoms because females have two X chromosomes and one carries the defective gene. Males have one X chromosome that is inherited from their mother and if a male inherits an X chromosome that contains a defective gene he will develop the disease. Female carriers of an X-linked disorder have a 25% chance with each pregnancy to have a carrier daughter like themselves, a 25% chance to have a non-carrier daughter, a 25% chance to have a son affected with the disease and a 25% chance to have an unaffected son.

If a male with X-linked disorders is able to reproduce, he will pass the defective gene to all of his daughters who will be carriers. A male cannot pass an X-linked gene to his sons because males always pass their Y chromosome instead of their X chromosome to male offspring.

**Affected Populations**

THCT deficiency is a rare inherited disorder that manifests in males only. One hundred and forty four cases involving males from 56 separate families (kindreds) have been identified two thirds of whom have reported in the medical literature. They involves 49 distinct MCT8 gene mutations. The frequency of THCT deficiency in the general population with mental retardation is not known.

**Related Disorders**

Symptoms of the following disorders may be similar to those of THCT deficiency. Comparisons may be useful for a differential diagnosis:

Angelman syndrome (AS) is a rare genetic neurological disorder characterized by severe developmental delays and learning disabilities; the absence or near absence of speech; an inability to coordinate voluntary movements (ataxia) and tremulous, jerky movements of the arms and legs; and a distinct behavioral pattern characterized by a happy disposition and unprovoked episodes of laughter and smiling, often at inappropriate times. Additional symptoms may occur in some cases including seizures, sleep disorders and feeding difficulties. Some affected children may have distinctive facial features. AS is caused by deletion of or abnormal expression of the UBE3A gene that is located on
the long arm (q) of chromosome 15 (15q11-q13). Most cases of AS appear to occur spontaneously. (For more information on this disorder, choose “Angelman” as your search term in the Rare Disease Database.)

Juberg-Marsidi syndrome is an extremely rare X-linked genetic disorder that is fully expressed in males only, and is apparent at birth (congenital) or during the first few weeks of life. Affected children exhibit severe mental retardation; delays in reaching developmental milestones (e.g., crawling, walking, etc.); muscle weakness; diminished muscle tone (hypotonia); and/or delayed bone growth as well as growth retardation, resulting in short stature. Affected infants also exhibit hearing loss; underdevelopment of the genitals (microgenitalism); and/or abnormalities of the head and facial (craniofacial) area such as an abnormally small head (microcephaly), a flat (depressed) nasal bridge, eye (ocular) abnormalities, and/or, in some cases, additional physical abnormalities. The range and severity of symptoms may vary from case to case. (For more information on this disorder, choose “Juberg Marsidi” as your search term in the Rare Disease Database.)

Renpenning syndrome is one of the X-linked mental retardation disorders that affect males almost to the exclusion of females. It is characterized by mental retardation that can be severe, short stature, a smaller than normal head circumference (microcephaly), and small testes. The syndrome has been mapped to gene map locus Xp11.2-p11.4 and the term “Renpenning syndrome” should be limited to the condition that maps to this region.

L1 syndrome is a genetic condition occurring in males that usually includes hydrocephalus, mental retardation, spasticity of legs and clasped (adducted) thumbs. L1 syndrome is caused by an abnormality (mutation) in the L1CAM gene. The variable types of L1 syndrome were once thought to be different diseases, but all of the following conditions are caused by mutations in the L1CAM gene:

X-linked hydrocephalus with stenosis of aqueduct of Sylvius (HSAS) is characterized by severe hydrocephalus that often begins prenatally, adducted thumbs, spasticity and severe mental retardation. MASA syndrome (mental retardation, aphasia, spastic paraplegia adducted thumbs) is characterized by mild to moderate mental retardation, aphasia (delayed speech), hypotonia that progresses to spasticity, adducted (clasped) thumbs, and variable widening of the third ventricle in the brain. X-linked complicated hereditary spastic paraplegia type 1 is characterized by spastic paraplegia (shuffling gait), mild to moderate mental retardation and normal findings on MRI of the brain. X-linked complicated corpus callosum agenesis is characterized by variable spastic paraplegia, mild to moderate mental retardation and abnormalities in the corpus callosum of the brain. (For more information on this disorder, choose “L1 syndrome” as your search term in the Rare Disease Database.)

Pelizaeus-Merzbacher disease (PMD) is a rare X-linked genetic disorder affecting the central nervous system that is associated with abnormalities of the white matter of the brain. Symptoms develop due to lack of the fatty covering of nerve cells (myelin sheath). Many areas of the central nervous system may be affected, including the deep portions of the cerebrum (subcortical), cerebellum, and/or brain stem. Symptoms may include the impaired ability to coordinate movement (ataxia), involuntary muscle spasms (spasticity) that result in slow, stiff movements of the legs, delays in reaching developmental milestones, loss of motor abilities, and the slow progressive deterioration of intellectual function. Some individuals with THCT deficiency have been erroneously diagnosed as having PMD. PMD disease is associated with abnormalities (mutations) in the PLP1 gene. (For more information on this disorder, choose “Pelizeaus-Merzbacher” as your search term in the Rare Disease Database.)

There are additional congenital disorders that may be characterized by X-linked mental retardation and occur in association with movement abnormalities, psychomotor retardation, and/or other features similar to those associated with THCT deficiency. (For more information on these disorders, choose the exact disease name in question as your search term in the Rare Disease Database.)

Diagnosis

The diagnosis of THCT deficiency may be suspected in infants with diminished muscle tone (hypotonia) with poor head control that causes the head to droop (limber neck). Although hypotonia and muscle weakness may be obvious
during early infancy, other symptoms (e.g., Dyskinetic attacks, spastic paraplegia, etc.) may not become apparent until late infancy. Therefore, the disorder may not be diagnosed until childhood, based upon a thorough clinical evaluation, a detailed patient history, and specialized tests.

Thyroid hormone testing is necessary to determine if THCT deficiency is a possible diagnosis. If results elevated serum T3 and reduced reverse T3 concentrations, molecular genetic testing is indicated to determine if an abnormal MCT8 gene is present. In addition, serum T4 level has the tendency to be low and TSH may be slightly elevated.

**Standard Therapies**

**Treatment**

The treatment of THCT deficiency is directed toward the specific symptoms that are apparent in each individual. Treatment may require the coordinated efforts of a team of specialists. Pediatricians, surgeons, neurologists, specialists who assess and treat skeletal abnormalities (orthopedists), speech-language pathologists, physical therapists, and/or other health care professionals may need to systematically and comprehensively plan an affected child's treatment.

Specific therapies for the treatment of THCT deficiency are symptomatic and supportive. Affected individuals who have scoliosis may be treated with orthopedic braces, physical therapy, and/or other orthopedic measures. When abnormal depression of the breastbone (pectus excavatum) is present, corrective surgery may be recommended in some cases.

Early intervention is important to ensure that children with THCT deficiency reach their potential. Special services that may be beneficial include special remedial education, special social support, physical therapy, and/or other medical, social, and/or vocational services.

Genetic counseling is recommended for affected individuals and their families. Other treatment for this disorder is symptomatic and supportive.

**Investigational Therapies**

Propylthiouracil plus L-Thyroxine has been proposed as a possible treatment to improve the nutritional status of affected patients.

Information on current clinical trials is posted on the Internet at www.clinicaltrials.gov. All studies receiving U.S. Government funding, and some supported by private industry, are posted on this government web site.

For information about clinical trials being conducted at the NIH Clinical Center in Bethesda, MD, contact the NIH Patient Recruitment Office:

Tollfree: (800) 411-1222

TTY: (866) 411-1010

Email: prpl@cc.nih.gov

For information about clinical trials sponsored by private sources, contact:

www.centerwatch.com

**Resources**

(Please note that some of these organizations may provide information concerning certain conditions potentially
associated with this disorder [e.g., mental retardation, impaired speech, movement abnormalities, etc.]

Supporting Organizations

- **Genetic and Rare Diseases (GARD) Information Center**
  
  PO Box 8126  
  Gaithersburg, MD 20898-8126  
  Phone: (301) 251-4925  
  Toll-free: (888) 205-2311  
  Website: [http://rarediseases.info.nih.gov/GARD/](http://rarediseases.info.nih.gov/GARD/)

- **NIH/National Institute on Deafness and Other Communication Disorders**
  
  31 Center Drive, MSC 2320  
  Communication Avenue  
  Bethesda, MD 20892-3456  
  Phone: (301) 402-0900  
  Toll-free: (800) 241-1044  
  Email: [nidcdinfo@nidcd.nih.gov](mailto:nidcdinfo@nidcd.nih.gov)  
  Website: [http://www.nidcd.nih.gov](http://www.nidcd.nih.gov)

- **The Arc**
  
  1825 K Street NW, Suite 1200  
  Washington, DC 20006  
  Phone: (202) 534-3700  
  Toll-free: (800) 433-5255  
  Email: [info@thearc.org](mailto:info@thearc.org)  
  Website: [http://www.thearc.org](http://www.thearc.org)

References

**TEXTBOOKS**


**JOURNAL ARTICLES**


Friesema EC, Jansen J, Heuer H, et al. Mechanisms of disease: psychomotor retardation and high T3 levels caused...


FROM THE INTERNET


Years Published

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