Arthrogryposis, Distal, with Impaired Proprioception and Touch

Alternative Names
DAIPT

Record Category
Disease phenotype

WHO-ICD
Congenital malformations, deformations and chromosomal abnormalities > Congenital malformations and deformations of the musculoskeletal system

Incidence per 100,000 Live Births
Unknown

OMIM Number
617146

Mode of Inheritance
Autosomal recessive

Gene Map Locus
18p11.22-p11.21

Description
DAIPT is a neurologic disorder characterized by skeletal contractures and a marked decrease in the ability to perceive touch, vibration or proprioception. Affected individuals also suffer from sensory ataxia, walking difficulties, dysmetria, dysarthria, impaired fine motor skills, areflexia, hypotonia and muscle weakness. Neurological investigations reveal mild sensory axonal neuropathy and reduced amplitude of sensory nerve action potentials. Other symptoms include short stature, neonatal respiratory insufficiency, scoliosis, congenital hip dysplasia, hand and foot deformities, and facial dysmorphia such as a long nose with a wide nasal bridge, a thin upper lip, a high arched palate and myopathic facies.

The condition has an onset in the first decade of life. DAIPT is a rare disease and only a handful of cases have been reported thus far. There is hence limited knowledge on the prevalence and prognosis of the disorder. It is, however, a progressive condition, and symptoms such as skeletal contractures and neuropathy are expected to worsen over time.

The condition can be diagnosed based on clinical investigations such as an algometer to measure the pain threshold, an esthesiometer for skin tactile sensitivity and a Peltier-based thermode to measure the threshold for thermal pain detection. There is currently no cure for the disorder, and treatment is focused on symptomatic support.

Molecular Genetics
The disorder follows an autosomal recessive pattern of inheritance and is caused by homozygous or compound heterozygous mutations in the PIEZO2 gene. This gene encodes a component of a mechanosensitive cation channel and is essential for the rapid adaptation of mechanically-activated currents in somatosensory neurons. It plays a key role in perceiving touch and proprioception. Mutations in the gene associated with DAIPT mainly include nonsense variants and deletions that cause frameshift and premature truncation, often resulting in a non-functioning PIEZO2 protein.

Epidemiology in the Arab World
Saudi Arabia
Monies et al. (2017) outlined the findings of 1000 diagnostic panels and exomes carried out at a next generation sequencing lab in Saudi Arabia. One patient, a 12-year-old female from a consanguineous family, suffered from severe lower limb weakness, progressive scoliosis and suspected spinal muscular atrophy but did not have arthrogryposis. She also reported a family history of this phenotype. Using whole exome sequencing, a

homozygous mutation (c.273_279del, p.A91fs) was identified in exon 3 of the patient's PIEZO2 gene, associated with DAIPT. Given the atypical presentation of the patient, this case helped in the phenotypic expansion of the disorder.

References

Monies D, Abouelhoda M, AlSayed M, Alhassnan Z, Alotaibi M, Kayyali H, Al-Owain M, Shah A, Rahbeeni Z, Al-Muhaizea MA, Alzaidan HI, Cupler E, Bohlega S, Faqeih E, Faden M, Alyounes B, Jaroudi D, Goljan E, Elbardisy H, Akilan A, Albar R, Aldhalaan H, Gulab S, Chedrawi A, Al Saud BK, Kurdi W, Makhseed N, Alqasim T, El Khashab HY, Al-Mousa H, Alhashem A, Kanaan I, Algoufi T, Alsaleem K, Basha TA, Al-Murshedi F, Khan S, Al-Kindy A, Alnemer M, Al-Hajjar S, Alyamani S, Aldhekri H, Al-Mehaidib A, Arnaout R, Dabbagh O, Shagrani M, Broering D, Tulbah M, Alqassmi A, Almugbel M, AlQuaiz M, Alsaman A, Al-Thihli K, Sulaiman RA, Al-Dekhail W, Alsaegh A, Bashiri FA, Qari A, Alhomadi S, Alkuraya H, Alsebayel M, Hamad MH, Szonyi L, Abaalkhail F, Al-Mayouf SM, Almojalli H, Alqadi KS, Elsiesy H, Shuaib TM, Seidahmed MZ, Abosoudah I, Akleh H, AlGhonaium A, Alkharfy TM, Al Mutairi F, Eyaid W, Alshanbary A, Sheikh FR, Alsohaibani FI, Alsonbul A, Al Tala S, Balkhy S, Bassiouni R, Alenizi AS, Hussein MH, Hassan S, Khalil M, Tabarki B, Alshahwan S, Oshi A, Sabr Y, Alsaadoun S, Salih MA, Mohamed S, Sultana H, Tamim A, El-Haj M, Alshahrani S, Bubshait DK, Alfadhel M, Faquih T, El-Kalioby M, Subhani S, Shah Z, Moghrabi N, Meyer BF, Alkuraya FS. The landscape of genetic diseases in Saudi Arabia based on the first 1000 diagnostic panels and exomes. Hum Genet. 2017 Aug;136(8):921-939. PMID: 28600779.

Related CTGA Records

Piezo-Type Mechanosensitive Ion Channel Component 2 (OMIM 613629)

External Links

http://www.malacards.org/card/arthrogryposis_distal_with_impaired_proprioception_and_touch

Contributors

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