Loeys-Dietz syndrome

Loeys-Dietz syndrome is a disorder that affects the connective tissue in many parts of the body.

There are five types of Loeys-Dietz syndrome, labelled types I through V, which are distinguished by their genetic cause. Regardless of the type, signs and symptoms of Loeys-Dietz syndrome can become apparent anytime from childhood through adulthood, and the severity is variable.

Loeys-Dietz syndrome is characterized by enlargement of the aorta, which is the large blood vessel that distributes blood from the heart to the rest of the body. The aorta can weaken and stretch, causing a bulge in the blood vessel wall (an aneurysm). Stretching of the aorta may also lead to a sudden tearing of the layers in the aorta wall (aortic dissection). People with Loeys-Dietz syndrome can also have aneurysms or dissections in arteries throughout the body and have arteries with abnormal twists and turns (arterial tortuosity).

Individuals with Loeys-Dietz syndrome often have skeletal problems including premature fusion of the skull bones (craniosynostosis), an abnormal side-to-side curvature of the spine (scoliosis), either a sunken chest (pectus excavatum) or a protruding chest (pectus carinatum), an inward- and upward-turning foot (clubfoot), flat feet (pes planus), or elongated limbs with joint deformities called contractures that restrict the movement of certain joints. A membrane called the dura, which surrounds the brain and spinal cord, can be abnormally enlarged (dural ectasia). In individuals with Loeys-Dietz syndrome, dural ectasia typically does not cause health problems. Malformation or instability of the spinal bones (vertebrae) in the neck is a common feature of Loeys-Dietz syndrome and can lead to injuries to the spinal cord. Some affected individuals have joint inflammation (osteoarthritis) that commonly affects the knees and the joints of the hands, wrists, and spine.

People with Loeys-Dietz syndrome may bruise easily and develop abnormal scars after wound healing. The skin is frequently described as translucent, often with stretch marks (striae) and visible underlying veins. Some individuals with Loeys-Dietz syndrome develop an abnormal accumulation of air in the chest cavity that can result in the collapse of a lung (spontaneous pneumothorax) or a protrusion of organs through gaps in muscles (hernias). Other characteristic features include widely spaced eyes (hypertelorism), eyes that do not point in the same direction (strabismus), a split in the soft flap of tissue that hangs from the back of the mouth (bifid uvula), and an opening in the roof of the mouth (cleft palate).

Individuals with Loeys-Dietz syndrome frequently develop immune system-related problems such as food allergies, asthma, or inflammatory disorders such as eczema or inflammatory bowel disease.

Case reports

Dahl RH, Farholt S, Hauerberg J, Poulsgaard L, Benndorf G. Management of a DAVF in a Patient with Loeys-Dietz Syndrome Type II : Case Report and Overview of the Literature. Clin Neuroradiol. 2021 May 12. doi: 10.1007/s00062-021-01007-3. Epub ahead of print. PMID: 33978775.

Skeletal overgrowth accompanied by de novo heterozygous activating mutations in PDGFRB (platelet-derived growth factor receptor beta), that is, p.Pro584Arg and p.Trp566Arg, defines Kosaki overgrowth syndrome (OMIM #616592). Emerging evidence suggests a role of PDGFRB in the genesis of cerebral aneurysms. The delineation of the range and progression of the vascular phenotype of Kosaki overgrowth syndrome is urgently needed. Herein, we conducted subsequent analyses of serial neurovascular imaging studies of two original patients with a de novo heterozygous mutation in PDGFRB, that is, p.Pro584Arg. The analysis showed the progressive dilation of basilar and vertebral arteries and coronary arteries commencing during the teenage years and early 20s. The radiographic appearance of the basilar vertebral aneurysms showed signs of arterial wall dilation, compatible with the known vascular pathology of vascular-type Ehlers-Danlos syndrome and Loeys-Dietz syndrome. The dolichoectasia in cerebrovascular arteries can lead to fatal complications, even with neurosurgical interventions. To prevent the progression of artery dilation, preventative and therapeutic medical measures using tyrosine kinase inhibitors may be necessary in addition to optimal control of the systemic blood pressure. Kosaki overgrowth syndrome is a clinically recognizable syndrome that can exhibit progressive dilatory and tortuous vascular changes in basilar/vertebral and coronary arteries as early as in the teenage years. We recommend careful counseling regarding the risk of future vascular complications, optimal blood pressure control, and regular systemic vascular screening during follow-up examinations [1)].

Uehara M, Ito K, Kosho T, Kuraishi S, Oba H, Hatakenaka T, Ikegami S, Takizawa T, Munakata R, Kubota M, Takahashi J. Posterior spinal fusion for severe kyphoscoliosis in a Loeys-Dietz syndrome patient with a large syringomyelia. J Clin Neurosci. 2020 Jun;76:211-213. doi: 10.1016/j.jocn.2020.04.017. Epub 2020 Apr 21. PMID: 32327376.

LoPresti MA, Ghali MZ, Srinivasan VM, Morris SA, Kralik SF, Chiou K, Du RY, Lam S. Neurovascular findings in children and young adults with Loeys-Dietz syndromes: Informing recommendations for screening. J Neurol Sci. 2020 Feb 15;409:116633. doi: 10.1016/j.jns.2019.116633. Epub 2019 Dec 12. PMID: 31862516; PMCID: PMC7239372.

Pending classification

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