Proteus syndrome

Description

Proteus syndrome is a rare condition characterized by overgrowth of the bones, skin, and other tissues. Organs and tissues affected by the disease grow out of proportion to the rest of the body. The overgrowth is usually asymmetric, which means it affects the right and left sides of the body differently. Newborns with Proteus syndrome have few or no signs of the condition. Overgrowth becomes apparent between the ages of 6 and 18 months and gets more severe with age.

In people with Proteus syndrome, the pattern of overgrowth varies greatly but can affect almost any part of the body. Bones in the limbs, skull, and spine are often affected. The condition can also cause a variety of skin growths, particularly a thick, raised, and deeply grooved lesion known as a cerebriform connective tissue nevus. This type of skin growth usually occurs on the soles of the feet and is hardly ever seen in conditions other than Proteus syndrome. Blood vessels (vascular tissue) and fat (adipose tissue) can also grow abnormally in Proteus syndrome.

Some people with Proteus syndrome have neurological abnormalities, including intellectual disability, seizures, and vision loss. Affected individuals may also have distinctive facial features such as a long face, outside corners of the eyes that point downward (down-slanting palpebral fissures), a low nasal bridge with wide nostrils, and an open-mouth expression. For reasons that are unclear, affected people with neurological symptoms are more likely to have distinctive facial features than those without neurological symptoms. It is unclear how these signs and symptoms are related to abnormal growth.

Other potential complications of Proteus syndrome include an increased risk of developing various types of noncancerous (benign) tumors and a type of blood clot called a deep venous thrombosis (DVT). DVTs occur most often in the deep veins of the legs or arms. If these clots travel through the bloodstream, they can lodge in the lungs and cause a life-threatening complication called a pulmonary embolism. Pulmonary embolism is a common cause of death in people with Proteus syndrome.

Frequency

Proteus syndrome is a rare condition with an incidence of less than 1 in 1 million people worldwide. Only a few hundred affected individuals have been reported in the medical literature.

Researchers believe that Proteus syndrome may be overdiagnosed, as some individuals with other conditions featuring asymmetric overgrowth have been mistakenly diagnosed with Proteus syndrome. To make an accurate diagnosis, most doctors and researchers now follow a set of strict guidelines that define the signs and symptoms of Proteus syndrome.

Causes

Proteus syndrome results from a mutation in the *AKT1* gene. This genetic change is not inherited from a parent; it arises randomly in one cell during the early stages of development before birth. As cells continue to grow and divide, some cells will have the mutation and other cells will not. This mixture of cells with and without a genetic mutation is known as mosaicism.

The *AKT1* gene helps regulate cell growth and division (proliferation) and cell death. A mutation in this gene disrupts a cell's ability to regulate its own growth, allowing it to grow and divide abnormally. Increased cell proliferation in various tissues and organs leads to the abnormal growth characteristic of Proteus syndrome. Studies suggest that an *AKT1* gene mutation is more common in groups of cells that experience overgrowth than in the parts of the body that grow normally.

In some published case reports, mutations in a gene called *PTEN* have been associated with Proteus syndrome. However, many researchers now believe that individuals with *PTEN* gene mutations and asymmetric overgrowth do not meet the strict guidelines for a diagnosis of Proteus syndrome. Instead, these individuals actually have condition that is considered part of a larger group of disorders called *PTEN* hamartoma tumor syndrome. One name that has been proposed for the condition is segmental overgrowth, lipomatosis, arteriovenous malformations, and epidermal nevus (SOLAMEN) syndrome; another is type 2 segmental Cowden syndrome. However, some scientific articles still refer to *PTEN*-related Proteus syndrome.

Learn more about the gene associated with Proteus syndrome

- AKT1

Inheritance

Because Proteus syndrome is caused by *AKT1* gene mutations that occur during early development, the disorder is not inherited and does not run in families.

Other Names for This Condition

- PS

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Proteus syndrome (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0085261/)

Genetic and Rare Diseases Information Center

- Proteus syndrome (https://rarediseases.info.nih.gov/diseases/7475/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Proteus syndrome%22)

Catalog of Genes and Diseases from OMIM

- PROTEUS SYNDROME (https://omim.org/entry/176920)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28Proteus+Syndrome%5BMAJR%5D%29+AND+%28Proteus+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

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