McCune-Albright Syndrome

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McCune-Albright syndrome is a disorder that affects the bones, skin, and several hormone-producing (endocrine) tissues.

Keywords: genetic conditions

1. Introduction

People with McCune-Albright syndrome develop areas of abnormal scar-like (fibrous) tissue in their bones, a condition called polyostotic fibrous dysplasia. Polyostotic means the abnormal areas (lesions) may occur in many bones; often they are confined to one side of the body. Replacement of bone with fibrous tissue may lead to fractures, uneven growth, and deformity. When lesions occur in the bones of the skull and jaw it can result in uneven (asymmetric) growth of the face. Asymmetry may also occur in the long bones; uneven growth of leg bones may cause limping. Abnormal curvature of the spine (scoliosis) may also occur. Bone lesions may become cancerous, but this happens in fewer than 1 percent of people with McCune-Albright syndrome.

In addition to bone abnormalities, affected individuals usually have light brown patches of skin called café-au-lait spots, which may be present from birth. The irregular borders of the café-au-lait spots in McCune-Albright syndrome are often compared to a map of the coast of Maine. By contrast, café-au-lait spots in other disorders have smooth borders, which are compared to the coast of California. Like the bone lesions, the café-au-lait spots in McCune-Albright syndrome may appear on only one side of the body.

Girls with McCune-Albright syndrome may reach puberty early. These girls often have menstrual bleeding by age 2. This early onset of menstruation is believed to be caused by excess estrogen, a female sex hormone, produced by cysts that develop in one of the ovaries. Less commonly, boys with McCune-Albright syndrome may also experience early puberty.

Other endocrine problems may also occur in people with McCune-Albright syndrome. The thyroid gland, a butterfly-shaped organ at the base of the neck, may become enlarged (a condition called a goiter) or develop masses called nodules. About 50 percent of affected individuals produce excessive amounts of thyroid hormone (hyperthyroidism), resulting in a fast heart rate, high blood pressure, weight loss, tremors, sweating, and other symptoms. The pituitary gland (a structure at the base of the brain that makes several hormones) may produce too much growth hormone. Excess growth hormone can result in acromegaly, a condition characterized by large hands and feet, arthritis, and distinctive facial features that are often described as "coarse." Excess growth hormone secretion may also lead to increased expansion of the fibrous dysplasia in the bones, most visibly in the skull. Rarely, affected individuals develop Cushing syndrome, an excess of the hormone cortisol produced by the adrenal glands, which are small glands located on top of each kidney. Cushing syndrome causes weight gain in the face and upper body, slowed growth in children, fragile skin, fatigue, and other health problems. In people with McCune-Albright syndrome, Cushing syndrome occurs only before age 2.

Problems in other organs and systems, such as noncancerous (benign) gastrointestinal growths called polyps and other abnormalities, can also occur in McCune-Albright syndrome.

2. Frequency

McCune-Albright syndrome occurs in 1 in 100,000 to 1 in 1,000,000 people worldwide.

3. Causes

McCune-Albright syndrome is caused by a mutation in the *GNAS* gene. The *GNAS* gene provides instructions for making one part of a protein complex called a guanine nucleotide-binding protein, or a G protein.

In a process called signal transduction, G proteins trigger a complex network of signaling pathways that ultimately influence many cell functions by regulating the activity of hormones. The protein produced from the *GNAS* gene helps stimulate the activity of an enzyme called adenylate cyclase. *GNAS* gene mutations that cause McCune-Albright syndrome result in a G protein that causes the adenylate cyclase enzyme to be constantly turned on (constitutively activated). Constitutive activation of the adenylate cyclase enzyme leads to over-production of several hormones, resulting in abnormal bone growth and other signs and symptoms of McCune-Albright syndrome.

3.1. The Gene Associated with McCune-Albright Syndrome

GNAS

4. Inheritance

McCune-Albright syndrome is not inherited. Instead, it is caused by a random mutation in the *GNAS* gene that occurs very early in development. As a result, some of the body's cells have a normal version of the *GNAS* gene, while other cells have the mutated version. This phenomenon is called mosaicism. The severity of this disorder and its specific features depend on the number and location of cells that have the mutated *GNAS* gene. Affected individuals may have reproductive cells (eggs or sperm) with the mutation. However, a resulting embryo would have the mutation in every cell, which is thought to be incompatible with life, so the condition is not passed to the next generation.

5. Other Names for This Condition

- Albright syndrome
- Albright's disease
- Albright's disease of bone
- Albright's syndrome
- Albright's syndrome with precocious puberty
- Albright-McCune-Sternberg syndrome
- Albright-Sternberg syndrome
- fibrous dysplasia with pigmentary skin changes and precocious puberty
- MAS
- osteitis fibrosa disseminata
- PFD
- POFD
- polyostotic fibrous dysplasia

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