

Fibrodysplasia Ossificans Progressiva

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Fibrodysplasia ossificans progressiva (FOP), sometimes referred to as **Stone Man Syndrome**, is an extremely rare disease of the connective tissue. A mutation of the body's repair mechanism causes fibrous tissue (including muscle, tendon, and ligament) to be ossified when damaged. It is characterized by malformation of the great toes during embryonic skeletal development and by progressive heterotopic (or extra-skeletal) endochondral ossification (HEO) postnatally, which leads to the formation of a second skeleton of heterotopic bone. Injuries can cause joints to become permanently frozen in place and surgical removal of the extra bone growths has been shown to cause the body to "repair" the affected area with more bone.

Genetics behind this disease

FOP is caused by an autosomal dominant allele on chromosome 2q23-24. The allele has variable expressivity, but complete penetrance. The mutation in the gene encoding **ACVR1** (also known as ALK2), a **bone morphogenetic protein (BMP) type I receptor** changes codon 206 from **arginine** to **histidine**. The ACVR1 protein is found in many tissues of the body including skeletal muscle and cartilage. It helps to control the growth and development of the bones and muscles, including the gradual replacement of cartilage by bone (ossification) that occurs in normal skeletal maturation from birth to young adulthood. As a result of this mutation, the receptor may be constantly turned on. Constitutive activation of the receptor causes overgrowth of bone and cartilage and fusion of joints, resulting in the signs and symptoms of fibrodysplasia ossificans progressiva. This mutation affects approximately 1 in every 2 million people.

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. Most cases occur due to new mutations in the gene and generally there are no known cases in the family. In rare cases the mutation is inherited by one affected parent.

Symptoms

Children born with FOP have deformed big toes, possibly missing a joint or simply presenting with a notable lump at the minor joint. The malformed big toes (short, bent, and sometimes curved inward) are always associated with the condition and can be observed at birth, thus making this one of the first major signs of this disease. The first "flare-up" that leads to the formation of FOP bones usually occurs before the age of 10. FOP often begins in the neck and shoulders and progresses along the back, trunk, and limbs of the body. Specifically, FOP involvement is typically seen first in the dorsal, axial, cranial and proximal regions of the body. Later the disease progresses in the ventral, appendicular, caudal and distal regions of the body. However it does not necessarily occur in this order due to injury-caused flare-ups. Often, the tumor-like lumps that characterize the disease appear suddenly.

Rather than crawl on their hands and knees, most kids with FOP scoot on their buttocks; then get up and walk. The reason that most cannot crawl is because the facet joints in the back of the neck have not formed properly or have fused, thus limiting movement.

Although FOP is congenital, meaning that FOP starts before birth, the extra bone does not form before birth instead it begins during the first two decades of life.

Because the disease is so rare, the symptoms are often misdiagnosed as cancer or fibrosis. This leads doctors to order biopsies, which can actually exacerbate the growth of these lumps.

Treatment

There is no known cure for FOP. Attempts to surgically remove the bone result in more robust bone growth. While under anesthesia, patients with FOP may face problems, which include difficulties with intubation, restrictive pulmonary disease, and changes in the electrical conduction system of the heart. Activities that increase the risk of falling should be avoided, as injuries from falling can provoke the growth of bone.

External Links

KAPLAN, FS – CHAKKALAKAL, SA. Fibrodysplasia ossificans progressiva: mechanisms and models of skeletal metamorphosis. *Dis Model Mech.* 2012, y. 2012, vol. 5(6), p. 756-62, ISSN 010280. PMID: 23115204 (<http://www.ncbi.nlm.nih.gov/pubmed/23115204>).

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International Fibrodysplasia Ossificans Progressiva Association. *FOP Symptoms* [online]. [cit. 2012-12-04]. <<http://www.ifopa.org/en/what-is-fop/symptoms.html>>.

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