Multiple Pterygium Syndrome

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Multiple pterygium syndrome is a condition that is evident before birth with webbing of the skin (pterygium) at the joints and a lack of muscle movement (akinesia) before birth. Akinesia frequently results in muscle weakness and joint deformities called contractures that restrict the movement of joints (arthrogryposis). As a result, multiple pterygium syndrome can lead to further problems with movement such as arms and legs that cannot fully extend.

Keywords: genetic conditions

1. Introduction

The two forms of multiple pterygium syndrome are differentiated by the severity of their symptoms. Multiple pterygium syndrome, Escobar type (sometimes referred to as Escobar syndrome) is the milder of the two types. Lethal multiple pterygium syndrome is fatal before birth or very soon after birth.

In people with multiple pterygium syndrome, Escobar type, the webbing typically affects the skin of the neck, fingers, forearms, inner thighs, and backs of the knee. People with this type may also have arthrogryposis. A side-to-side curvature of the spine (scoliosis) is sometimes seen. Affected individuals may also have respiratory distress at birth due to underdeveloped lungs (lung hypoplasia). People with multiple pterygium syndrome, Escobar type usually have distinctive facial features including droopy eyelids (ptosis), outside corners of the eyes that point downward (downslanting palpebral fissures), skin folds covering the inner corner of the eyes (epicanthal folds), a small jaw, and low-set ears. Males with this condition can have undescended testes (cryptorchidism). This condition does not worsen after birth, and affected individuals typically do not have muscle weakness later in life.

Lethal multiple pterygium syndrome has many of the same signs and symptoms as the Escobar type. In addition, affected fetuses may develop a buildup of excess fluid in the body (hydrops fetalis) or a fluid-filled sac typically found on the back of the neck (cystic hygroma). Individuals with this type have severe arthrogryposis. Lethal multiple pterygium syndrome is associated with abnormalities such as underdevelopment (hypoplasia) of the heart, lung, or brain; twisting of the intestines (intestinal malrotation); kidney abnormalities; an opening in the roof of the mouth (a cleft palate); and an unusually small head size (microcephaly). Affected individuals may also develop a hole in the muscle that separates the abdomen from the chest cavity (the diaphragm), a condition called a congenital diaphragmatic hernia. Lethal multiple pterygium syndrome is typically fatal in the second or third trimester of pregnancy.

2. Frequency

The prevalence of multiple pterygium syndrome is unknown.

3. Causes

Mutations in the *CHRNG* gene cause most cases of multiple pterygium syndrome, Escobar type and a smaller percentage of cases of lethal multiple pterygium syndrome. The *CHRNG* gene provides instructions for making the gamma (γ) protein component (subunit) of the acetylcholine receptor (AChR) protein. The AChR protein is found in the membrane of skeletal muscle cells and is critical for signaling between nerve and muscle cells. Signaling between these cells is necessary for movement. The AChR protein consists of five subunits. The γ subunit is found only in the fetal AChR protein. At about the thirty-third week of pregnancy, the γ subunit is replaced by another subunit to form adult AChR protein. The replacement of fetal AChR by adult AChR is the reason most people with multiple pterygium syndrome, Escobar type do not have problems with muscle movement after birth.

CHRNG gene mutations result in an impaired or missing γ subunit. The severity of the *CHRNG* gene mutation influences the severity of the condition. Typically, mutations that prevent the production of any γ subunit will result in the lethal type, while mutations that allow the production of some γ subunit will lead to the Escobar type. Without a functional γ subunit, the fetal AChR protein cannot be assembled or properly placed in the muscle cell membrane. As a result, the fetal AChR protein cannot function and the communication between nerve cells and muscle cells in the developing fetus is impaired. A lack of signaling between nerve and muscle cells leads to akinesia and pterygium before birth, and may result in many of the other signs and symptoms of multiple pterygium syndrome.

Mutations in other genes, most providing instructions for other AChR protein subunits, have been found to cause multiple pterygium syndrome. Changes in these genes can cause both the lethal and Escobar types of this condition, although they account for only a small number of cases. Some people with multiple pterygium syndrome do not have an identified mutation in any of the known genes associated with this condition. The cause of the disease in these individuals is unknown.

3.1. The Genes Associated with Multiple Pterygium Syndrome

- CHRNG
- RAPSN

3.1.1. Additional Information from NCBI Gene

- CHRNA1
- CHRND

4. Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

5. Other Names for This Condition

- Escobar syndrome
- familial pterygium syndrome
- pterygium syndrome

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