Giant Congenital Melanocytic Nevus

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Giant congenital melanocytic nevus is a skin condition characterized by an abnormally dark, noncancerous skin patch (nevus) that is composed of pigment-producing cells called melanocytes. It is present from birth (congenital) or is noticeable soon after birth.

Keywords: genetic conditions

1. Introduction

Giant congenital melanocytic nevus may be small in infants, but it will usually grow at the same rate the body grows and will eventually be at least 40 cm (15.75 inches) across. The nevus can appear anywhere on the body, but it is more often found on the trunk or limbs. The color ranges from tan to black and can become darker or lighter over time. The surface of a nevus can be flat, rough, raised, thickened, or bumpy; the surface can vary in different regions of the nevus, and it can change over time. The skin of the nevus is often dry and prone to irritation and itching (dermatitis). Excessive hair growth (hypertrichosis) can occur within the nevus. There is often less fat tissue under the skin of the nevus; the skin may appear thinner there than over other areas of the body.

People with giant congenital melanocytic nevus may have more than one nevus (plural: nevi). The other nevi are often smaller than the giant nevus. Affected individuals may have one or two additional nevi or multiple small nevi that are scattered over the skin; these are known as satellite or disseminated nevi.

Affected individuals may feel anxiety or emotional stress due to the impact the nevus may have on their appearance and their health. Children with giant congenital melanocytic nevus can develop emotional or behavior problems.

Some people with giant congenital melanocytic nevus develop a condition called neurocutaneous melanosis, which is the presence of pigment-producing skin cells (melanocytes) in the tissue that covers the brain and spinal cord. These melanocytes may be spread out or grouped together in clusters. Their growth can cause increased pressure in the brain, leading to headache, vomiting, irritability, seizures, and movement problems. Tumors in the brain may also develop.

Individuals with giant congenital melanocytic nevus have an increased risk of developing an aggressive form of skin cancer called melanoma, which arises from melanocytes. Estimates vary, but it is generally thought that people with giant congenital melanocytic nevus have a 5 to 10 percent lifetime risk of developing melanoma. Melanoma commonly begins in the nevus, but it can develop when melanocytes that invade other tissues, such as those in the brain and spinal cord, become cancerous. When melanoma occurs in people with giant congenital melanocytic nevus, the survival rate is low.

Other types of tumors can also develop in individuals with giant congenital melanocytic nevus, including soft tissue tumors (sarcomas), fatty tumors (lipomas), and tumors of the nerve cells (schwannomas).

2. Frequency

Giant congenital melanocytic nevus occurs in approximately 1 in 20,000 newborns worldwide.

3. Causes

NRAS gene mutations cause most cases of giant congenital melanocytic nevus. Rarely, mutations in the *BRAF* gene are responsible for this condition.

The proteins produced from these genes are involved in a process known as signal transduction by which signals are relayed from outside the cell to the cell's nucleus. Signals relayed by the N-Ras and BRAF proteins instruct the cell to grow and divide (proliferate) or to mature and take on specialized functions (differentiate). To transmit signals, these

proteins must be turned on; when the proteins are turned off, they do not relay signals to the cell's nucleus.

The *NRAS* or *BRAF* gene mutations responsible for giant congenital melanocytic nevus are somatic, meaning that they are acquired during a person's lifetime and are present only in certain cells. These mutations occur early in embryonic development during the growth and division (proliferation) of cells that develop into melanocytes. Somatic *NRAS* or *BRAF* gene mutations cause the altered protein in affected cells to be constantly turned on (constitutively active) and relaying signals. The overactive protein may contribute to the development of giant congenital melanocytic nevus by allowing cells that develop into melanocytes to grow and divide uncontrollably, starting before birth.

3.1. The genes associated with Giant congenital melanocytic nevus

- BRAF
- NRAS

4. Inheritance

This condition is generally not inherited but arises from a mutation in the body's cells that occurs after conception. This alteration is called a somatic mutation. A somatic mutation in one copy of the *NRAS* or *BRAF* gene is sufficient to cause this disorder.

5. Other Names for This Condition

- congenital giant pigmented nevus of skin
- congenital melanocytic nevus syndrome
- giant congenital melanocytic nevi
- giant congenital pigmented nevus
- giant pigmented hairy nevus
- GMN
- GPHN

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