Generalized Pustular Psoriasis

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Generalized pustular psoriasis (GPP) is a severe form of a skin disorder called psoriasis.

genetic conditions

1. Introduction

GPP and other forms of psoriasis are caused by abnormal inflammation. Inflammation is a normal immune system response to injury and foreign invaders (such as bacteria). However, when inflammation is abnormal and uncontrolled, it can damage the body's tissues and organs. Individuals with GPP have repeated episodes in which large areas of skin become red and inflamed and develop small pus-filled blisters (pustules). The skin problems can be accompanied by fever, extreme tiredness (fatigue), muscle weakness, an increased number of white blood cells, and other signs of inflammation throughout the body (systemic inflammation). The inflammation problems subside and reappear often. Episodes can be triggered by infection, exposure to or withdrawal from certain medications, menstruation, or pregnancy, although the trigger is often unknown. GPP can be life-threatening if not treated.

While many affected individuals have features only of GPP (called GPP alone), some develop features of another skin condition called psoriasis vulgaris (PV), either before or after GPP appears. PV, the most common form of psoriasis, is characterized by red, scaly patches of skin (plaques) on parts of the body.

2. Frequency

GPP is the rarest form of psoriasis. Although the worldwide prevalence of GPP is unknown, the condition is estimated to affect 2 per million people in Europe. It also occurs in approximately 0.6 per million people each year in Japan.

3. Causes

Mutations in several genes, including *IL36RN* and *CARD14*, increase the risk of developing GPP. These two genes provide instructions for making proteins that play roles in regulating inflammation, particularly in the skin. The IL-36Ra protein, produced from the *IL36RN* gene, blocks the activity of specific proteins that trigger signaling pathways to promote skin inflammation. *IL36RN* gene mutations involved in GPP reduce the amount of IL-36Ra protein in the skin. Without control by IL-36Ra, signaling pathways that promote inflammation are overly active.

Conversely, the CARD14 protein normally turns on inflammation signaling. The *CARD14* gene mutations associated with GPP increase the activity of the CARD14 protein, leading to uncontrolled inflammation signaling in the skin. Enhancement of these signaling pathways results in abnormal inflammatory reactions, which contribute to the skin problems and systemic inflammation characteristic of GPP.

IL36RN gene mutations are most often associated with GPP alone and are only rarely found in individuals who also have PV. Mutations in this gene appear to be the most common genetic risk factor for GPP alone. *CARD14* gene mutations are more frequently found in individuals with both GPP and PV, although changes in this gene have also been found in individuals with GPP alone.

Many people with GPP do not have a mutation in the *IL36RN* or *CARD14* gene. Mutations in other genes, some of which have not been identified, may also be associated with the condition. Having a gene mutation in one of the associated genes does not mean an individual will have GPP. Researchers suspect that environmental or other genetic factors help determine whether an individual will develop the condition.

3.1. The genes associated with Generalized pustular psoriasis

- CARD14
- IL36RN

4. Inheritance

When associated with *IL36RN* gene mutations, risk of GPP is typically 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.

When associated with *CARD14* gene mutations, GPP risk is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to increase the risk of the disorder. In some cases, an affected person inherits the mutation from one parent. Other cases result from new (de novo) mutations in the gene.

People with mutations in either the *IL36RN* or *CARD14* gene inherit an increased risk of GPP, not the condition itself. Not all people with this condition have mutations in one of these genes, and not all people with a mutation in one of these genes will develop the disorder.

5. Other Names for This Condition

- acute generalised pustular psoriasis
- deficiency of the interleukin-36 receptor antagonist

- DITRA
- generalized pustular psoriasis of von Zumbusch
- GPP
- von Zumbusch psoriasis

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