Kindler Syndrome

Subjects: Genetics & Heredity

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Kindler syndrome is a rare type of epidermolysis bullosa, which is a group of genetic conditions that cause the skin to be very fragile and to blister easily.

genetic conditions

1. Introduction

From early infancy, people with Kindler syndrome have skin blistering, particularly on the backs of the hands and the tops of the feet. The blisters occur less frequently over time, although repeated blistering on the hands can cause scarring that fuses the skin between the fingers and between the toes. Affected individuals also develop thin, papery skin starting on the hands and feet and later affecting other parts of the body. Other skin abnormalities that occur with Kindler syndrome include patchy changes in skin coloring and small clusters of blood vessels just under the skin (telangiectases), a combination known as poikiloderma. In some affected individuals, the skin on the palms of the hands and soles of the feet thickens and hardens (hyperkeratosis). Kindler syndrome can also cause people to be highly sensitive to ultraviolet (UV) rays from the sun and to sunburn easily.

Kindler syndrome can also affect the moist lining (mucosae) of the mouth, eyes, esophagus, intestines, genitals, and urinary system, causing these tissues to be very fragile and easily damaged. Affected individuals commonly develop severe gum disease that can lead to early tooth loss. The moist tissues that line the eyelids and the white part of the eyes (the conjunctiva) can become inflamed (conjunctivitis), and damage to the clear outer covering of the eye (the cornea) can affect vision. Narrowing (stenosis) of the esophagus, which is the tube that carries food from the mouth to the stomach, causes difficulty with swallowing that worsens over time. Some affected individuals develop health problems related to inflammation of the colon (colitis) or damage to the mucosa in the vagina, the anus, or the tube that carries urine from the bladder out of the body (the urethra).

Kindler syndrome increases the risk of developing a form of cancer called squamous cell carcinoma. This type of cancer arises from squamous cells, which are found in the outer layer of skin (the epidermis) and in the mucosae. In people with Kindler syndrome, squamous cell carcinoma occurs most often on the skin, lips, and the lining of the mouth (oral mucosa).

2. Frequency

Kindler syndrome appears to be rare. About 250 cases have been reported worldwide.

3. Causes

Kindler syndrome results from mutations in the *FERMT1* gene. This gene provides instructions for making a protein known as kindlin-1. This protein is found in epithelial cells, which are the cells that line the surfaces and cavities of the body. In the skin, kindlin-1 plays a critical role in specialized cells called keratinocytes, which are the major component of the epidermis. Kindlin-1 is involved in several important cell functions, including cell growth and division (proliferation), the attachment of cells to the underlying network of proteins and other molecules (cell-matrix adhesion), and the movement (migration) of cells.

Most mutations in the *FERMT1* gene prevent the production of any functional kindlin-1. A lack of this protein disrupts many essential cell functions. For example, keratinocytes without kindlin-1 have an abnormal structure and cannot grow or divide normally. They are also less able to attach the epidermis to the underlying layer of skin (the dermis). These changes make the skin fragile and prone to blistering. Similarly, a lack of kindlin-1 in epithelial cells of the mucosae causes damage that makes these tissues extremely fragile. It is unclear how a shortage of kindlin-1 is related to squamous cell carcinoma in people with Kindler syndrome.

3.1. The gene associated with Kindler syndrome

- FERMT1

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

- congenital bullous poikiloderma
- Kindler's syndrome
- poikiloderma of Kindler

References

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