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The Study of Genetic Mutations in Gene *IKBKG* in Bloch-Siemens Syndrome

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Abstract

The Bloch-Siemens syndrome is a genetic dermatological disorder affecting the skin, hair, teeth, and central nervous system. Progressive skin changes occur in four stages, the first of which appear in early infancy or can be present at birth. This syndrome is an X-linked dominant genetic disorder caused by mutations in the *IKBKG* gene.

Keywords: Bloch-Siemens syndrome; Genetic dermatological disorder; Mutations in the *IKBKG* gene

Introduction

Generalizations of the Bloch-Siemens syndrome

The Bloch-Siemens syndrome is a genetic disorder that can affect many body systems, especially the skin. The syndrome is more common in women than in men [1].

Clinical signs and symptoms of Bloch-Siemens syndrome

Skin disorders appear in children with a childhood, adolescence, or youth. Many newborns with this syndrome reveal mild rashes at birth, which are later recovered and subsequently grow into warts in the skin. In the early days of childhood, the skin produces gray and brown plates that occur in a rotating pattern. These plaques disappear over time, and adults with this syndrome reveal unusual skin lines (hypopigmentation) on the arms and legs [1] (Figure 1).

The other Symptoms and Signs Bloch-Siemens syndrome can include hair loss (alopecia) that affects the scalp and other parts of the body, dental disorders (such as minor teeth or dental congestion) and eye disorders that can lead to lose sight. Most people with Bloch-Siemens syndrome have normal intelligence. However, Bloch-Siemens syndrome may also affect the brain. Brain-related problems in the Bloch-Siemens syndrome can include delay in the development of mental skills, intellectual disability, seizure and other neurological problems [2-5] (Figure 2).

Etiology of the Bloch-Siemens syndrome

The Bloch-Siemens syndrome is caused by the mutation of the *IKBKG* gene that is based on the Xq28 long arm of the X chromosome X. The gene provides instructions for protein synthesis that helps to regulate the kappa factor B nuclear factor. The Kappa B nuclear factor is a group of regulatory proteins that help protect certain cells from suicide (apoptosis) in response to certain signals [6-8] (Figure 3).

Approximately 80% of people with Bloch-Siemens syndrome have a knockout mutation in the *IKBKG* gene that removes some genetic material from the gene. This knockout mutation probably leads to the production of *IKBKG* abnormal and short-acting pterothene. Other people with Bloch-Siemens syndrome have mutations that prevent the production of IKBKG proteins. Without this protein, the Kappa B nuclear factor is not properly regulated and the cells become sensitive to signals that lead them to suicide. Researchers believe that this abnormal cell death leads to signs and symptoms of the Bloch-Siemens syndrome [9] (Figure 4).

The Bloch-Siemens syndrome follows the predominant X-dominant hereditary pattern. Therefore, to produce this syndrome, a mutation version of the *IKBKG* gene (parent or parent) is required, and the chance of having a child with a Bloch-Siemens syndrome is 50% for each pregnancy [9] (Figure 5).

Frequency of Bloch-Siemens syndrome

The Bloch-Siemens syndrome is an unusual skin disorder that has been reported in medical

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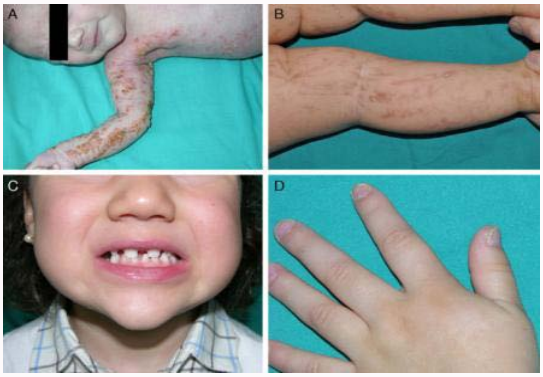

Figure 1: Images of disorders related to the Bloch-Siemens syndrome.

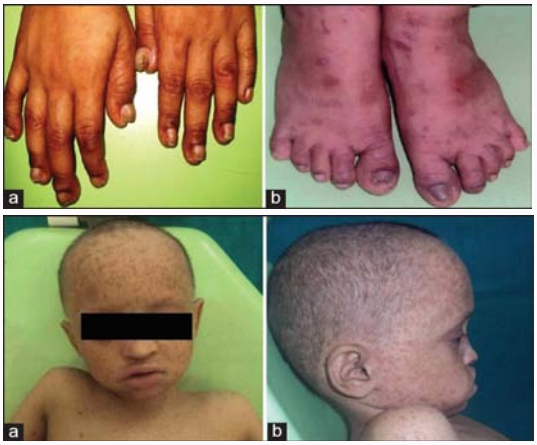

Figure 2: Other images of patients with Bloch-Siemens syndrome associated with skin and fingernail disorders.

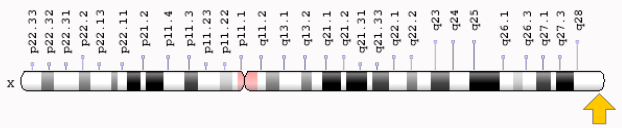

Figure 3: Schematic view of the X-chromosome X that the *IKBKG* gene deployed in the long arm of this chromosome is Xq28.

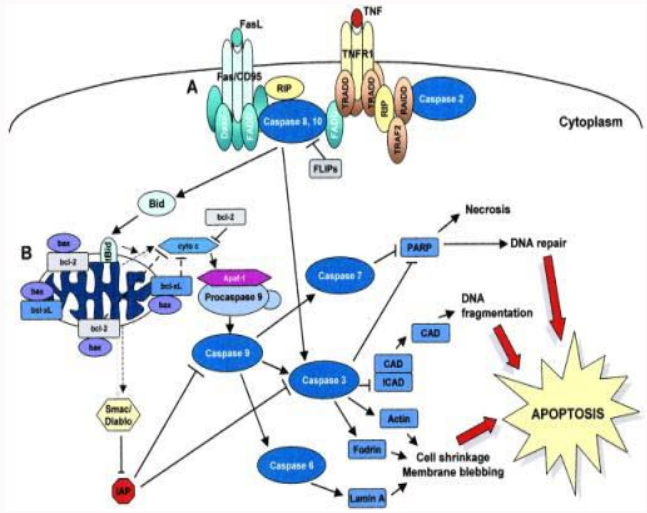

Figure 4: Schematic of the molecular pathway of cellular physiological death (apoptosis).

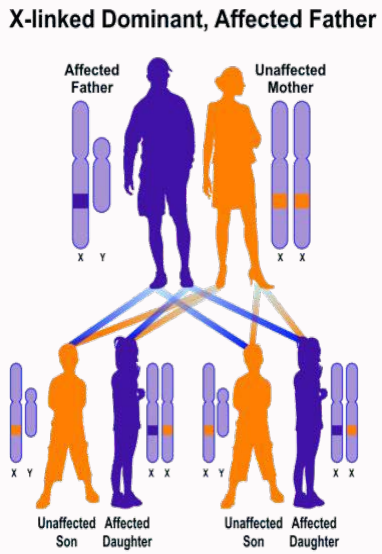

Figure 5: Schematic representation of the dominant X dominant heredity pattern (patient father) that follows the Bloch-Siemens syndrome.

literature for about 900 to 1200 people worldwide. It is worth noting that most people with Bloch-Siemens syndrome are women [10].

Diagnosis of Bloch-Siemens syndrome

The Bloch-Siemens syndrome is diagnosed based on the clinical and physical findings of the patients and some pathological tests. The most definite diagnostic method for this syndrome is the molecular genetic testing of the *IKBKG* gene to investigate the presence of possible mutations. Prenatal diagnosis is also possible by using the PGD technique and amniocentesis fluid or by sampling the embryo's chorionic pelvis. The diagnosis of Bloch-Siemens syndrome is based on clinical evaluation, detailed patient history, and molecular genetic testing for mutation in the *IKBKG* gene. *IKBKG* is the only gene known to be associated with Bloch-Siemens syndrome. 65 percent of patients have a specific deletion within the gene. Another 20 percent or so have mutations found by gene sequencing. A skin biopsy to confirm the diagnosis in a female is now rarely needed given the widespread availability and sensitivity of molecular genetic testing. Nonetheless, skin biopsy may be helpful in confirming the diagnosis in a female with borderline or questionable findings in whom molecular genetic testing has not identified a disease-causing mutation [11] (Figure 6).

Treatment routes for the Bloch-Siemens syndrome

The treatment and management strategy of Bloch-Siemens syndrome is symptomatic and supportive. Treatment may be done by a team of professionals, including pediatricians, dermatologists, dental practitioners, eye specialists and other healthcare professionals. Skin abnormalities characteristic of Bloch-Siemens syndrome usually disappear by adolescence or adulthood without any treatment.

Cryotherapy and laser photocoagulation may be used to treat affected individuals with retinal neovascularization that predisposes to retinal detachment.

Dental abnormalities can often be treated effectively by dentists who may provide dental implants in childhood as needed. Also if dental abnormalities interfere with chewing and/or speech, assistance from a speech pathologist and/or pediatric nutritionist may be

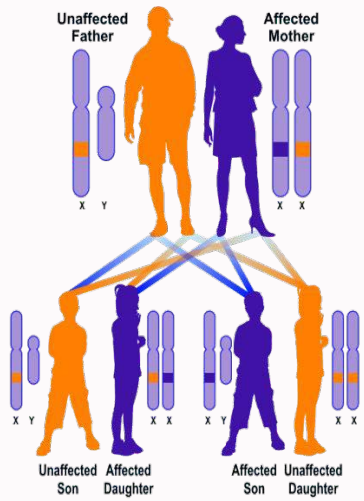

Figure 6: A schematic view of the X-dominant hereditary pattern (the patient's mother), which also follows Bloch-Siemens syndrome.

Figure 7: Dr. Bruon Bloch (right) and Dr. Marion Sulzberger (left) Explorers of the Bloch-Siemens syndrome.

necessary.

Hair problems may require the attention of a dermatologist in some cases, although they are usually not severe. Neurological symptoms such as seizures, muscle spasms or mild paralysis may be controlled with various drugs and/or medical devices [11].

There is no definite treatment for this syndrome and all clinical measures are needed to reduce the suffering of the infected person. Genetic counseling is also a special place for all parents who want a healthy baby [11].

Discussion and Conclusion

The Bloch-Siemens syndrome was named based on the appearance of the skin under the microscope during the later stages of the condition. The Bloch-Siemens syndrome is a genetic dermatological disorder affecting the skin, hair, teeth, and central nervous system. Progressive skin changes occur in four stages, the first of which appear in early infancy or can be present at birth. This syndrome is an X-linked dominant genetic disorder caused by mutations in the *IKBKG* gene. There is no definite treatment for this syndrome and all clinical measures are needed to reduce the suffering of the infected person. Genetic counseling is also a special place for all parents who want a healthy baby.

History of the Bloch-Siemens Syndrome

The Bloch-Siemens syndrome was first reported in 1926 by Dr. Bruno Bloch, a dermatologist from Switzerland, and in 1928 by Dr. Marion Sulzberger, a dermatologist from the United States [11] (Figure 7).

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