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The Role of Genetic Mutations in Gene *FLT4* in Milory Syndrome

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Abstract

Milory Syndrome is a genetic disorder that affects the normal functioning of the lymph system. The milroy syndrome comes with other features besides lymph nodes. Men with milory syndrome are sometimes born with fluid accumulation in the hydrocele. Some cases of milory syndrome are caused by the mutation of the *FLT4* gene, which is based on the long arm of chromosome number 5 as 5q35.3.

Keywords: Milory syndrome; Genetic disorder; Lymph system; *FLT4* gene; Hydrocele

Introduction

Generalizations of milory syndrome

Milory Syndrome is a genetic disorder that affects the normal functioning of the lymph system. The lymphatic system produces and transports fluids and immune cells throughout the body. Lymphatic drainage disorder causes lymphedema [1].

Signs and symptoms of milory syndrome

People with Milroy syndrome usually has lymph nodes on their legs and legs at birth or develops it in childhood. Lymph nodes are usually seen on both sides of the body and may get worse over time [2] (Figure 1).

The milroy syndrome comes with other features besides lymph nodes. Men with milory syndrome are sometimes born with fluid accumulation in the hydrocele. Men and women with this syndrome may develop symptoms such as deep wrinkles in the toes, growth of warts (papillomas) and prominent veins. Some people develop non-cutaneous infections called cellulitis, which can damage the capillaries carrying lymphatic fluid (lymphatic vessels). Cellulitis can cause more swelling in the lower extremities of milory syndrome [2] (Figure 2).

The causes of milory syndrome

Some cases of milory syndrome are caused by the mutation of the *FLT4* gene, which is based on the long arm of chromosome number 5 as 5q35.3 (Figure 3). The gene provides instructions for protein synthesis called the receptor 3 of the endothelial cell growth factor (VEGFR-3), which regulates the development and maintenance of the lymphatic system. Mutations in the *FLT4* gene interfere with the growth, movement and survival of cells that form lymph vessels (lymphatic endothelial cells). These mutations lead to the development of small lymph vessels or their lack of development. If the lymph fluid is not properly transported, it will accumulate abnormally in

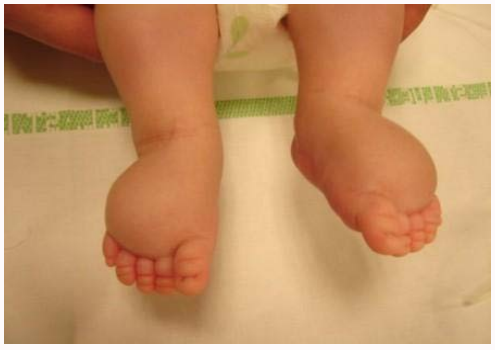

Figure 1: The legs of a child with milory syndrome accompanied by lymph nodes in the legs [1].

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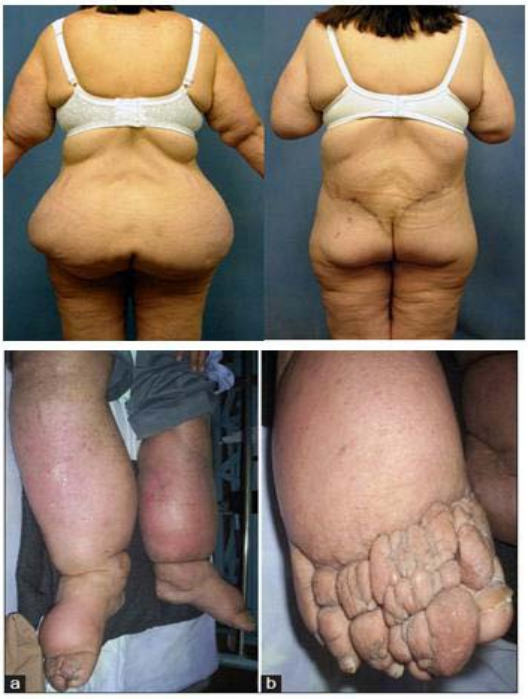

Figure 2: Images of the relevant disorders in milory syndrome [2].

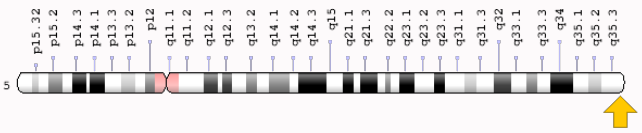

Figure 3: Schematic view of chromosome number 5 where the FLT4 gene is located in the long arm of this chromosome as 5q35.3 [3].

the tissues of the body, which causes lymphatic drainage. It is not yet known how the mutation in the *FLT4* gene results in other features of milory syndrome. Many people with milroy syndrome have no mutations in the *FLT4* gene, and the cause of the disorder is still unknown in these people [3].

Milory syndrome follows the dominant autosomal inheritance pattern. Therefore, to produce this syndrome, a copy of the mutated *FLT4* gene (parent or parent) is needed and the chance of having a child with this syndrome in the dominant autosomal state is 50% for each possible pregnancy [4].

Frequency of milory syndrome

Milory Syndrome is a rare genetic disorder whose frequency is not known in the world [4].

Diagnosis of milory syndrome

Milory Syndrome is diagnosed based on the clinical and clinical findings of the patients and some pathological examinations. The most accurate method for detecting this syndrome is the molecular genetic testing of the *FLT4* gene in order to investigate the presence of possible mutations [5] (Figure 4).

Milory syndrome treatment routes

The treatment and management strategy for milory syndrome is symptomatic and supportive. Treatment can be done by teaming up with a team of specialists, including pediatricians, gastroenterologists,

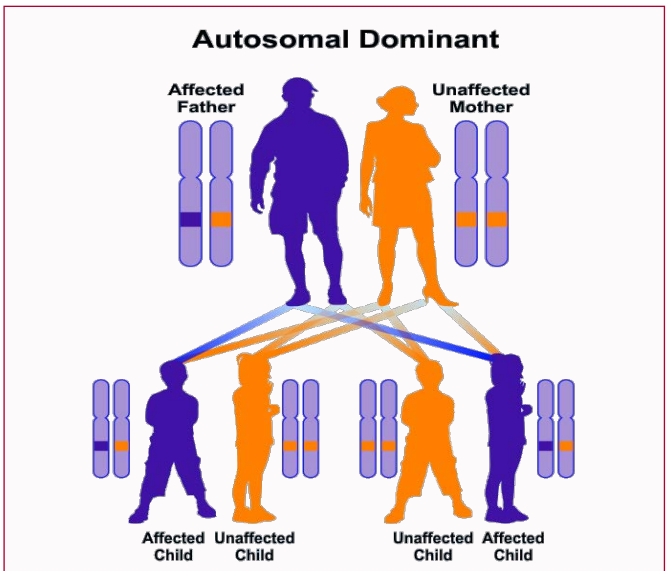

Figure 4: A schematic view of the dominant autosomal inheritance pattern that milory syndrome follows from this pattern [5].

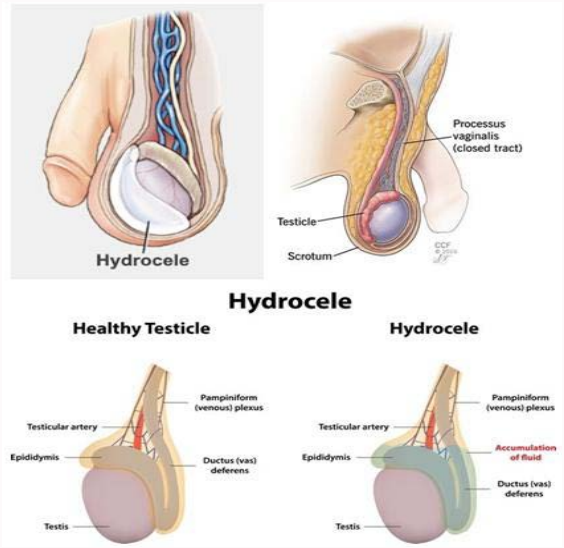

Figure 5: Schematic of hydrocele disorders in milory Syndrome tests [6].

dermatologists and other healthcare professionals. There is no valid treatment for this syndrome, and all clinical measures are needed to reduce the suffering of the sufferers. Genetic counseling is also important for all parents who want a healthy baby [6] (Figures 5-7).

Discussion and Conclusion

Milroy syndrome is a lymphatic disease that causes swelling (lymphedema) in the lower legs and feet. Lymphedema is usually present at birth or develops in infancy. It typically occurs on both sides of the body and can worsen over time. Other symptoms may include accumulation of fluid in the scrotum in males (hydrocele), upslanting toenails, deep creases in the toes, wart-like growths, prominent leg veins, and/or cellulitis. Milroy disease is sometimes caused by changes (mutations) in the *FLT4* gene and is inherited in an autosomal dominant manner. In many cases, the cause remains unknown. Treatment may include lymphedema therapy to improve function and alleviate symptoms. The symptoms and severity of

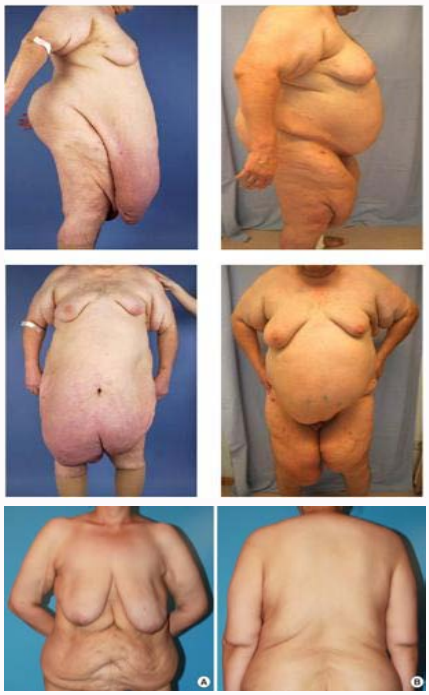

Figure 6: Another feature of lymphatic dysfunction in patients with milory syndrome [6].

Figure 7: Pictures of the oldest person with milory syndrome with lymphatic dysfunction in the legs [6].

Milroy disease can vary among affected people (even within the same family), so the long-term effects of the condition may be difficult to predict. Swelling varies in degree and distribution, and can be disabling and disfiguring. For some people the outlook depends on how chronic the lymphedema is, as well as whether complications arise. However, Milroy disease is rarely associated with significant complications [7].

The degree of edema sometimes progresses, but in some cases can improve (particularly in early years). Complications of lymphedema may include recurrent bouts of cellulitis and/or lymphangitis, bacterial and fungal infections, deep venous thrombosis, functional impairment, cosmetic embarrassment, and amputation.

Complications following surgery are common. It has also been reported that people with chronic lymphedema for many years may have a significantly higher risk to develop lymphangiosarcoma (a type of angiosarcoma). This type of tumor is highly aggressive and has a very poor prognosis [8].

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