# Early-onset Lower Limb Edema

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*Received: 26 February 2024*

*Accepted: 3 April 2024*

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**DOI 10.5001/omj.2024.78**

A 7-year-old boy reported to the pediatric dermatology clinic with a chronic eczematous, pruritic eruption that had been present for several months, as well as persistent bilateral lower limb edema. Remarkably, the patient exhibited an absence of respiratory distress, tachycardia, or mucocutaneous discoloration, and denied any history of jaundice, hematuria, or periorbital edema. He maintained a healthy appetite without any reported weight loss, fatigue, or myalgia. The patient had not traveled to areas with unusual insect exposure or swampy environments. He was born late preterm, with a prenatal diagnosis of hydrops fetalis. Similar symptoms of lower limb edema were observed in his mother and younger brother. While the parents were not closely related, they shared the same tribal and village background. During the overall physical and systemic examination, no abnormalities were identified. However, upon focused examination, the patient exhibited bilateral lower limb edema extending proximally to the mid-thigh, in conjunction with eczematous lesions. The skin displayed scaliness, with erosions on the dorsum of both feet [Figure 1].

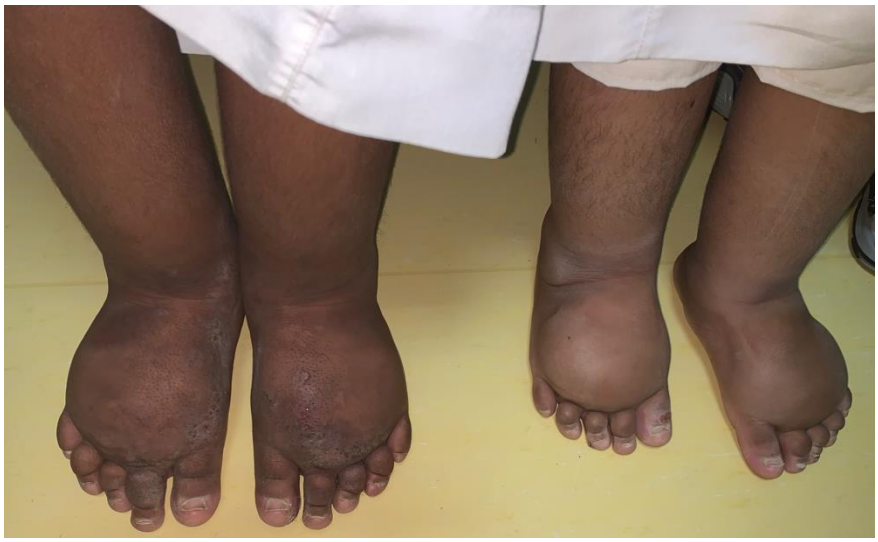

**Figure 1:** Patient and his sibling with bilateral lower limb edema. The patient (left) has an eczematous skin lesion over the dorsum of bilateral feet.

## *What is the diagnosis?*

A) Congestive heart disease

B) Cirrhosis

C) Milroy disease

D) Malnutrition

E) Elephantiasis

### *Answer*

C) Milroy diseases

## Discussion

Milroy disease, also known as congenital lymphedema, follows an autosomal dominant inheritance pattern.[1] This condition is characterized by underdeveloped or anomalous lymphatic vessels resulting from a mutation in the FLT-4 gene, encoding vascular endothelial growth factor receptor 3 (VEGFR-3). The mutation impedes proper lymphatic fluid drainage, leading to protein accumulation in the extracellular fluid. This accumulation stimulates fibroblasts, resulting in structured swelling and an increased vulnerability to lymphangiomas and recurrent skin infections.[2]

Milroy disease is characterized by lower-limb lymphedema, presenting as pedal swelling evident either at birth or shortly thereafter, with potential onset later in life. The severity of the swelling exhibits variation both within and among families, typically affecting both legs but with potential asymmetry. While the edema may progress, there are instances, especially in the early years, where improvement is observed. Additional features associated with Milroy disease include hydrocele (occurring in 37% of males), prominent veins below the knees (in 23% of cases), up-slanting toenails (in 14% of cases), papillomatosis (in 10% of cases), and urethral abnormalities in males (in 4% of cases).[1] Approximately 20% of individuals with this condition may experience cellulitis, which can further harm the lymphatic vessels, with males showing a higher susceptibility than females.[1]

Milroy disease diagnosis relies on genetic testing, primarily molecular genetic testing (MGT)for a specific FLT4 gene variant. This is crucial for individuals with early-onset lower-limb lymphedema. Alternatively, confirmation can be obtained through lymphoscintigraphy, revealing a distinctive lack of radioactive colloid absorption in ilioinguinal lymph nodes.1. Our patient MGT was done and detected a variant mutation in exon 19 of the FLT4 gene, c.2735T>G (p.Leu912Arg).

The treatment strategy for hereditary lymphedema is concentrated on the ultimate management of symptoms that can be divided into conservative and surgical approaches as well as the prevention of secondary complications.

Lower extremities lymphedema is the most frequent medical morbidity that is frequently seen by dermatologists. The initial main stain treatment is the prevention of lymphedema and the reduction of swelling through pneumatic compressions, well-fitting stockings, and supportive wear-foot along with adjuvant therapies including weight control, exercises, and massage.[1]

Prevention of the secondary complications in severe lymphedema such as stasis dermatitis, skin fissuring, and cellulitis can be reduced through good skin hygiene, moisturization, topical corticosteroids, prompt treatment of infections with antibiotics, and prophylactic antibiotics for recurrent episodes and active surveillance through regular follow-up in lymphedema-specialized clinics.[1]

The surgical approach is when conservative management becomes ineffective. Different surgical approaches have been described in the literature to treat hereditary lymphedema. Some studies described the microsurgery anastomosis approach where small lymphatic vessels are directly connected to the venous system. The reduction operation is another surgical approach through the removal of access fibrous tissue. Recently one study showed vascularized lymph node transfer (VLNT) with therapeutic lipoectomy is a reliable technique through which it provides an alternative pathway for lymph drainage, reducing the lymph node load and the excess subcutaneous adipose tissue.[3,4]

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