

# Four generations of rare familial lymphedema–Milroy Disease

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## ▲ Introduction

Lymphedema is a form of chronic tissue swelling due to impaired lymphatic drainage, often presenting as pedal swelling. The congenital forms of lymphedema are uncommon (1). We report a case of Milroy disease, a rare cause of congenital lymphedema and a familial condition with a strong genetic predisposition. To the best of our knowledge, this is the first reported case with 4 generations of family members being affected.

## Case Details and Discussion

A 28year Female, born of non consanguineous marriage, presented with 'Oedema of both lower limbs since birth'. Her medical history and clinical examination was unremarkable.

A detailed evaluation including blood counts, metabolic panel and imaging studies ruled out secondary causes of lymphedema. Radionuclide study (lymphoscintigraphy) to evaluate lymphatic drainage in the lower extremities, showed decreased uptake of radioactive tracer in proximal lymph nodes (inguinal nodes), suggesting impaired lymphatic drainage in the lower extremities. She mentioned that a few of her family members had similar symptoms. None of them had any other associated symptom other than asymptomatic bilateral pedal oedema.

A detailed family pedigree was charted, as far as the 4th generation. This was a case of the occurrence of lymphedema in multiple family members. By early adulthood, almost all the family members had lymphedema up to the shin or calves. However, there is some variability in phenotypic expression. Also, there is variability in the degree and severity of lymphedema. Genetic testing was not possible due to lack of availability and financial resources. She was reassured about the potential benign yet familial nature of this condition. The minimal-to-no

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uptake of radioactive tracer in proximal lymph nodes in proband indicates 'functional' failure of lymphatic channels in the lower extremities (1, 2).

Genetic testing in Milroy Disease has revealed a wide spectrum of involved genes in pathophysiology (3). The primary defect is thought to be the altered microarchitecture and function of small lymphatics causing impaired absorption of lymphatic fluid, accumulation in interstitial space and, thus, swelling (4, 5). It is of paramount importance to exclude other causes of secondary lymphedema before making the diagnosis of

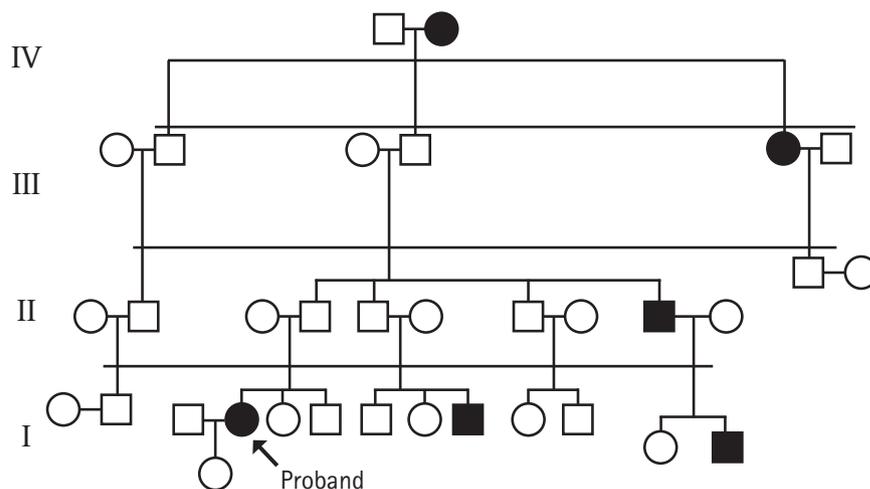


Abb. 1: Pedigree chart – Milroy disease showing 4 generations.

primary lymphedema. The important secondary causes include infections (filariasis), obstruction from a proximal mass such as intraabdominal tumor or postradiation lymphatic obstruction seen in patients undergoing radiation therapy for treatment of cancers.

Primary lymphedema presenting at birth is Milroy disease, unlike Meigs syndrome and lymphedema tarda

which present at a later age (6, 7). In a recently proposed comprehensive classification of primary lymphedema; importance of thorough clinical evaluation and identifying meticulous phenotypic patterns to guide molecular testing in subjects with primary lymphedema is stressed (8). The main consequences of lymphatic failure are swelling, recurrent infection such as cellulitis and, very rarely, a malignant transformation to lymphangiosarcoma (9).

## Summary

Hereditary lymphedemas are developmental disorders of the lymphatics resulting in oedema of the extremities due to altered lymphatic flow. Primary congenital lymphedema (Milroy disease) is a rare autosomal dominant condition and constitutes less than 10% of primary lymphedema cases, with less than 200 cases reported in the literature.

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