

Aplasia of Superficial Lymphatic Capillaries in Hereditary and Connatal Lymphedema (Milroy's Disease)*

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Summary

Four patients with hereditary lymphedema present at birth (Milroy's disease) have been studied by fluorescence microlymphography (1, 7). The video-microscopy technique failed to visualize any lymphatic capillary in the edematous part of their legs. In sporadic primary lymphedema with late manifestation, however, a well developed superficial capillary network is detected (1, 6). Three family members without lymphedema had normal microlymphatics.

Milroy's disease, at least in the family presented, is characterized by aplasia or extreme hypoplasia of both lymphatic capillaries and collectors whereas in the usual sporadic form of primary lymphedema aplasia or hypoplasia is confined to the larger trunks.

Introduction

The superficial lymphatic capillary network of the skin which is located at the level of the dermal papillae (9) may be visualized by a nearly atraumatic video-microscopy technique (fluorescence microlymphography, 1, 2, 6, 7). In patients with non hereditary and non-connatal primary lymphedema the capillary rete remains intact (1, 6, 7) in contrast to the larger trunks which are aplastic or hypoplastic (3, 8). In this report a family with hereditary lymphedema present at birth (Milroy's disease, 8, 10) is described. Aplasia of the lymphatic capillary network was found in the legs of the four family members affected by the disease.

Findings in the family

The family stems from the Emmental (Canton Berne, Switzerland). Four generations could be considered (Fig. 1). Among the numerous members of the last two generations four patients with congenital lymphedema present at birth were examined by clinical means, patent blue test and fluorescence microlymphography (1, 7). Three patients were women and one was a man.

Each of the four patients showed the typical picture of severe lymphedema of both legs. Indurated edema was marked at the foot, calf and distal thigh. It did not reverse during night's rest. Hyperkeratosis was present at the toes in two. Patent blue dye was injected in the usual way into the interdigital webs. In contrast to normals no superficial lymphatic vessels could be observed on the dorsum of the foot at the macroscopic level. The test result differed also from that usually found in primary lymphedema (3, 4, 8). The dye remained limited to a small portion of the skin and did not expand to larger areas within one hour. In one female patient conventional lymphography with contrast medium was tried in another hospital without success. No attempts for lymphography were made in the remaining patients.

Fluorescence microlymphography was performed as described earlier in detail (1). FITC-dextran 150'000 (Pharmacia) was injected by

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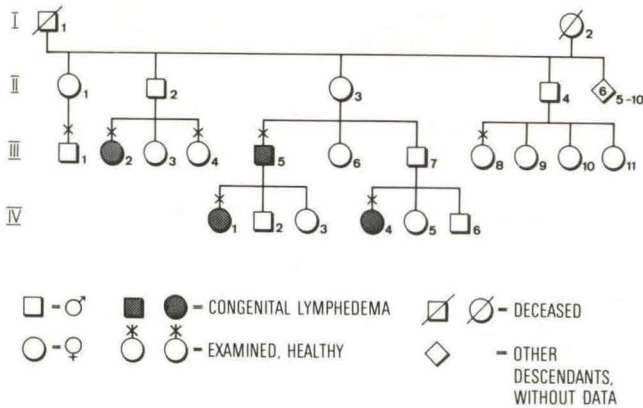


Fig. 1 Genealogical tree of the family with Milroy's disease

a steel microneedle (0.2 mm outer diameter) into the subepidermal layer of the skin near the medial ankle. Around the deposit visible below the fluorescence microscope no lymphatic capillaries were filled. In order to exclude a technical failure the injections were repeated 2–3 times by two experienced observers at different adjacent sites. Again no lymphatic microvessels could be detected (Fig. 2a). An injection at the upper part of the thigh in one female patient revealed a few meshes of superficial lymphatic capillaries emerging from the deposit of fluorescent dye. At this site no edema was found.

Three healthy family members were also examined. All were free from edema. Two showed a completely normal patent blue test with lymphatic vessels appearing at the dorsum of the foot whereas the third had an atypical relatively large and well delineated vessel leading to the lateral aspect of the ankle. Fluorescence microlymphography demonstrated normal lymphatic microvessels in all three subjects.

Discussion

The four patients with congenital and congenital lymphedema belong to a special subgroup of primary lymphedema called Milroy's disease (3, 8, 10). Genetic studies suggest that the entity is inherited as an autosomal dominant trait with incomplete

penetration and involving males and females almost equally (8).

In sporadic primary lymphedema with manifestation after puberty the superficial lymphatic network visualized by fluorescence microlymphography is intact (1, 6, 7). The extent of the rete filled by FITC-dextran 40'000 or 150'000 (Fig. 2b) is even significantly larger than in normals with rapid drainage of the tracer into the deeper channels (6). In some cases enlarged and tortuous microvessels are detected (1). Exceptionally, the diameter of the network meshes and of the lymphatic capillaries are both increased (6). In severe chronic venous insufficiency lymphatic microangiopathy with partial obliteration of the capillary network is observed (2).

Most of the patients with Milroy's disease have not only hypoplasia, a common finding in sporadic primary lymphedema, but aplasia of the large lymphatic trunks of the lower extremities (8). The same is true for the patients of the present family because patent blue did not fill any major vessel or conventional lymphography with contrast medium failed. Moreover, fluorescence microlymphography revealed in all four patients aplasia of the superficial capillary network in the medial ankle skin. The 3 non-affected members of the family, however, had normal lymphatic microvessels.

In the light of these observations the bad



Fig. 2a Original subepidermal deposit of FITC-dextran 150'000 in one of the family members with hereditary and connatal lymphedema. No lymphatic capillaries are filled by the dye (20 min after injection)

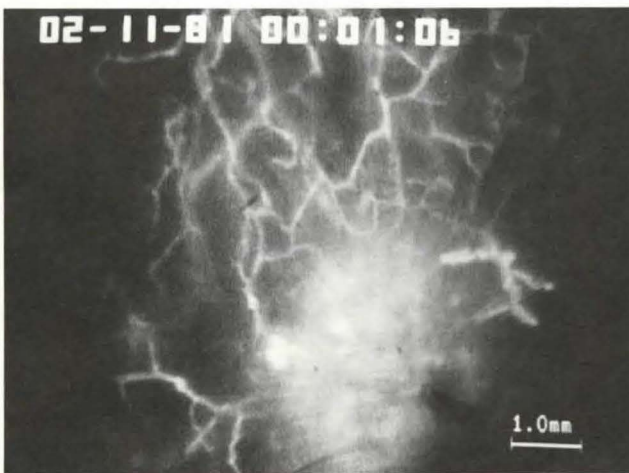


Fig. 2b Fluorescence microlymphography in a patient with non hereditary primary lymphedema and late manifestation. Originating from the dye deposit an extensive network of superficial lymphatic capillaries is visualized (1 min after injection)

prognosis of edema in Milroy's disease (8) might be explained by combined macro- and microvascular aplasia of the lymphatics whereas in sporadic primary lymphedema not present at birth aplasia or hypoplasia is confined to the larger trunks. This concept is supported by a recent observation in two cases of Milroy's disease in whom no lymphatics of the precollector size could be demonstrated by indirect lymphography with Iotasul (11). The slow expansion of patent blue on the dorsum of the foot of these patients during

many hours (5) would also suggest that there are no major preformed pathways for dye propagation. In usual primary and secondary lymphedema the area coloured by patent blue extends much faster, probably in the intact superficial capillary network (3, 4, 8). Nevertheless, the family presented in this report has been the only one studied by the new video-microscopy technique. Additional families have to be examined in order to confirm that the lack of skin lymphatic capillaries is characteristic for Milroy's disease.

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Addendum

Since submission of the manuscript two additional patients with connatal and hereditary lymphedema have been observed in another family. In 18-years-old twins, a girl and a boy, no lymphatic microvessels could be demonstrated in the edematous part of the legs. Normal capillaries were visualized in the unaffected parts.

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