Jan Mali (1918-1996)

Carine van der Vleuten, dermatoloog

Prof. dr. Jan W.H. Mali genoot zijn opleiding (1943-1946) in de (klassieke morfologische) dermatologie te Utrecht. Via zijn leermeesters, prof. dr. E. van Leeuwen en prof. dr. J.J. Zoon, had hij zijn wortels in de Franse school; de leer der primaire efflorescenties à la Darier was hem heilig.

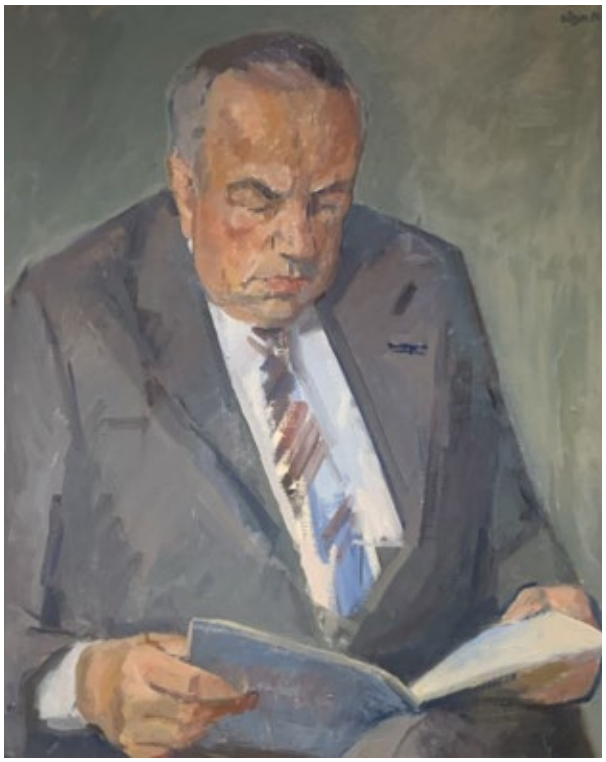
Hij vestigde zich als dermatoloog in 's-Hertogenbosch en aanvaardde in die tijd ook een parttime onderzoeksfunctie op de afdeling Fysiologie van de Rijksuniversiteit van Groningen met als focus het fysiopathologische gedrag van vaatgebieden en de daarmee samenhangende problemen rond de warmteregulatie. In zijn laatste Groningse jaar was hij als chef de clinique werkzaam op de afdeling Dermatologie bij prof. dr. M. Ruiter.

Vanuit die functie aanvaardde hij in 1957, tot zijn emeritaat in 1984, de benoeming tot hoogleraar en afdelingshoofd Dermatologie aan de Katholieke Universiteit van Nijmegen, gehuisvest in de dr. Veegerkliniek aan de Javastraat.

Vanuit zijn degelijke klinische dermatologische kennis bracht hij de primaire efflorescenties in verbinding met de dermatopathologie, fysiologie en biochemie. Mali was een verbinder van gedachten en van verschillende disciplines. Zijn denken ging niet over de bekende paden maar was origineel, gedurfd en met internationaal academisch élan.

De grote verdienste van Mali is dat hij gewerkt heeft aan een afdeling met een multidisciplinair team van clinici en niet-clinici. Aldus bouwde hij aan de banden van dermatologen met psychologen, fysiologen, farmacologen, moleculair biologen en fysici. Naast een goed lopende algemene polikliniek en kliniek, bloeide er een unit voor allergologie en arbeidsdermatologie, een unit voor flebologie en een researchlaboratorium.

Het ulcus cruris vormde een belangrijk klinisch thema waar Mali de interdisciplinaire benadering met de Medische Fysica heeft ontwikkeld. In deze context is samen met prof. dr. J.P. Kuiper het klinisch pathologisch fundament gegeven aan de flebologie. De eerste beschrijving van het dermatologisch ziektebeeld 'acro-angiodermatitis' (pseudo-Kaposi) als een uiting van veneuze insufficiëntie kan met recht de morbus Mali-Kuiper worden genoemd.



De verbondenheid tussen enerzijds de kliniek en anderzijds zowel het epidemiologisch als het celbiologisch onderzoek is ook in de huidige tijd een actueel thema, waarbij wij als dermatologen elke dag op zoek zijn naar innovaties voor de patient van nu en waarin wij blijven investeren voor de patiënt van morgen.

Acro-Angiodermatitis of the Foot

J. W. H. MALI, MD; J. P. KUIPER, MD;
AND A. A. HAMERS, MD, NIJMEGEN, THE NETHERLANDS

A peculiar form of angiodermatitis (angiodermite de Favre et Chaix) due to a chronic insufficiency of the venous network of the foot with typical lesions, localization, and evolution is described. Because of a certain conformity in histology the lesions may be misinterpreted as Kaposi's Sarcoma.

DURING THE treatment of patients with chronic venous insufficiency we noted that some of them showed peculiar purple maculae and plaques on the extensor side of the digits or the foot.[1] We believe it will be useful to draw attention to these lesions again, as their true nature is often unrecognized. Therapy-resistant, smaller or larger ulcerations, sometimes painful, were seen in these plaques. Histologically, proliferation of small blood vessels, fibroblasts, purpura, and hemosiderine were observed in the stratum papillare, more or less analogous with the picture one sees in the vicinity of an ulcus cruris (angiodermite de Favre et Chaix) (Fig 1).

Eighteen patients we saw in the past five years are tabulated in Table 1. Males form the majority, although chronic venous insufficiency is more frequent in females.

The beginning of the lesions most frequently occurs between the ages of 30 and 40 years. All patients are suffering from a major form of chronic venous insufficiency of long standing, with frequent thrombosis or surgical treatment in the anamnesis. The lesions may vary from some pinpoint-lesions on the large digit to a plaque the size of a hand on the back of the foot with a central ulceration (Figs 2, 3, and 4).

The small lesions vary from pinpoint to lentil, coinsized or even larger lesions. They are mostly flat, sometimes elevated or even papillomatous, and are of a characteristic eggplant color. They occur in places where no direct pressure from within or from without is exerted on the skin. The lesions on the extensor side of the digits, for instance, end abruptly at the places where the digits press against each other or against the shoe. The flexor sides of the end-phalanges are free, but the interdigital region may show lesions. If a wide vein traverses the plaque, the skin at this place is normal. The lesions appear mostly on the first and second digits, the extensor sides of the other digits, and in a triangular region with the ground-phalanges of the digits at the base and the tarsus at the top.

Many patients show, in addition, a boomerang-shaped, reticular pigmentation on either side of the ankles centered under the malleoli, fanning out to leg and digits. In these parts a large number of small atrophic spots or small ulcerations (atrophie blanche de Milian) are often present. The arteriae dorsales pedis and tibialis posticum are found to be pulsating normally. Edema on the ankle or the foot occurs quite frequently.

The interpretation of the lesions presented some problems because roentgenologic investigation by phlebography and arteriography met with unexpected difficulties. Only when we got more experience in measuring the total arterial bloodflow through the limbs and the skin bloodflow using Whitney's and Hensel's method [2] and were able to measure, directly and indirectly, the venous pressure at different places in the limbs [3] it was found possible to collect sufficient arguments to consider the syndromes as special forms of chronic venous insufficiency extending to the foot. We shall demonstrate the result of these investigations in the case of one patient.

Report of Cases

A German, forty-five years-old, who had fought in the Russian campaign and had been a prisoner in

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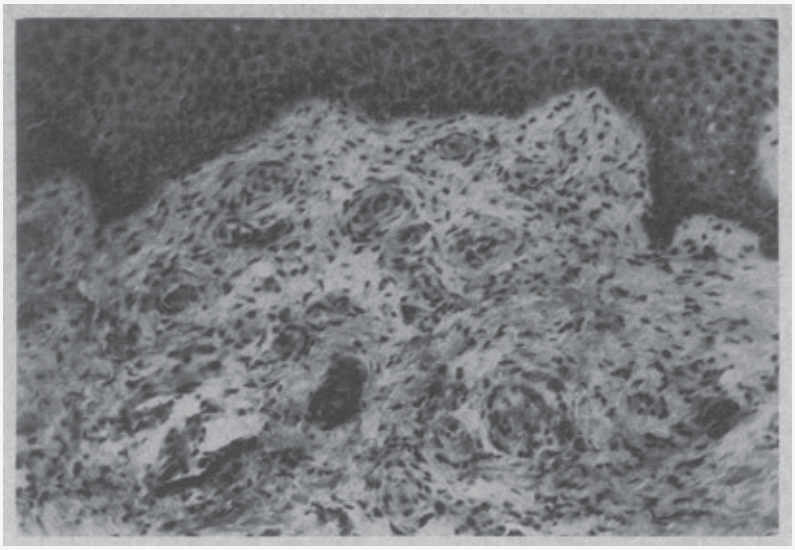


Fig 1.—Histology of acro - angiodermatitis, showing acanthosis of epidermis, proliferation of small vessels with swollen endothelium and thick walls, and proliferation of fibroblasts (Hemosiderin).

Russia until 1950, had been suffering from thrombosis and ulcerations in both legs. On the extensor side of the first toe digits of the right foot the typical purple coloring was found, extending to the back of the foot (Fig 5). In the interdigital area and on the lateral side of the first digit, a granular defect with elevated rim was found. The patient handed us a report of a histological investigation of the lesion, describing the purpura and proliferation of blood vessels and fibroblasts. The report concluded the case to be Kaposi's sarcoma.

In view of this diagnosis we were asked if amputation was to be considered. On further inspection it appeared that the digits of the other foot showed the same lesion, although to a lesser degree. In addition the patient had varices in the interior saphenous veins of both legs with insufficient perforators at knee and ankle level. There was no edema. At the back of both feet, small atrophic lesions and hyperpigmentations were visible. Both feet also showed the boomerang-shaped pigmentation around the ankles.

The arteriae dorsalis pedis and tibiale posticum were found to be pulsating normally. Internal and hemological investigations showed no abnormalities.

Special Investigations.—Measuring the total arterial blood-flow of the legs at mid-level at the ankles by venous occlusion, phlethysmography with Whitney's strain-gauges presented normal values.

Fig 2.—Acro-angiodermatitis of the extensor faces of two digits.

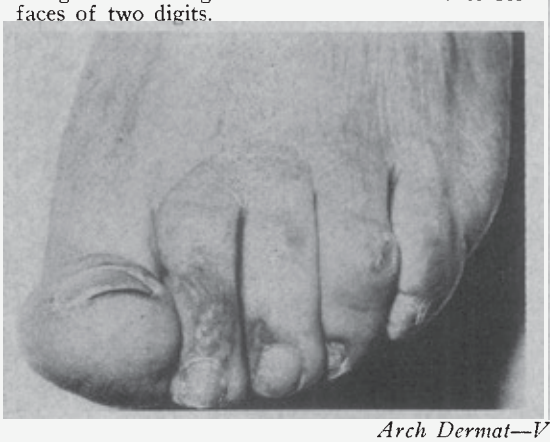
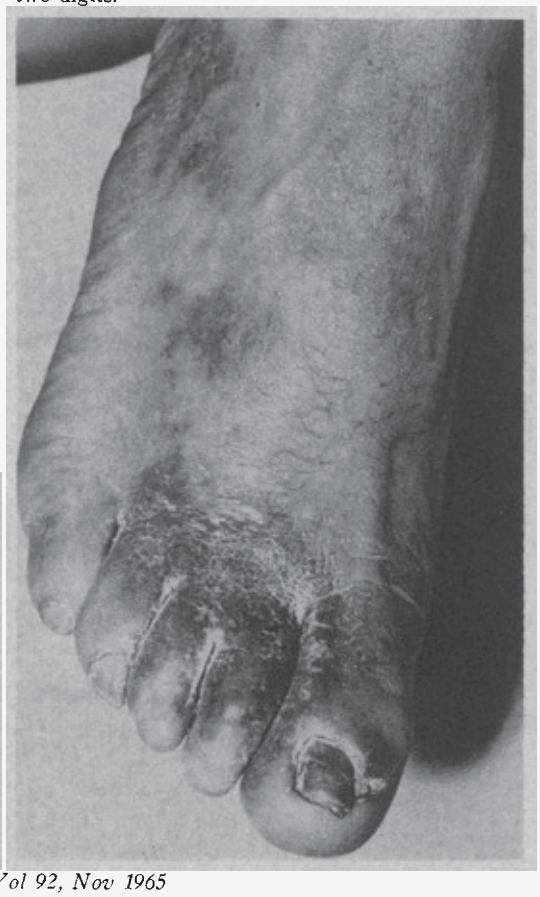


Fig 3.—Acro-angiodermatitis of digits with extension to fore-foot. Disappearance of nails from two digits.



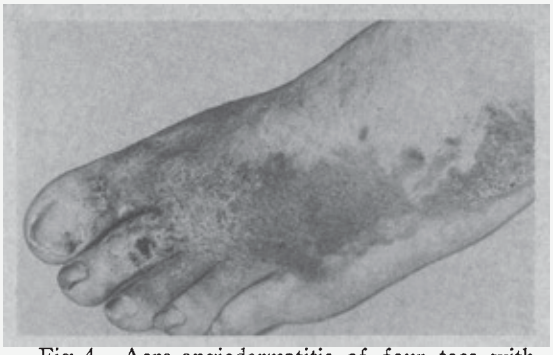
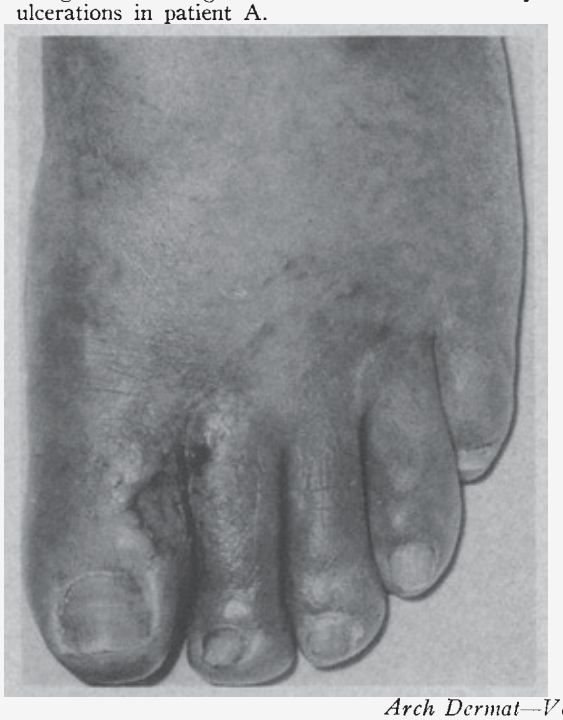


Fig 4.—Acro-angiodermatitis of four toes with extension to the forefoot, also showing pigmentation and atrophic changes.

Measuring the local skin flow at normal and purpuric skin of the ankle and with special appliers on the digits also showed essentially normal values. Reactive hyperemia after total occlusion of the leg above the systolic pressure sometimes yielded higher values for the lesions than for the normal skin. Measuring the venous pressure in a vein at the dorsum of the feet demonstrated a total insufficiency of the superficial and deep venous system of the leg, which could not be alleviated by occluding the insufficient perforators at either knee or ankle level.

Finally the venous pressure was measured at different levels of the leg, feet, and digits by measuring the volume changes with Whitney's method and converting them into venous pressure.[3] While in normal persons the venous pressure in the digits by rhythmical elevation on the toes is reduced from 100 mm Hg to 20 mm Hg, in our patient the pressure remained as high as 74 mm Hg. Moreover it remained higher in the toe than in the forefoot, in contrast with normal situations.

Fig 5.—Acro-angiodermatitis with secondary ulcerations in patient A.



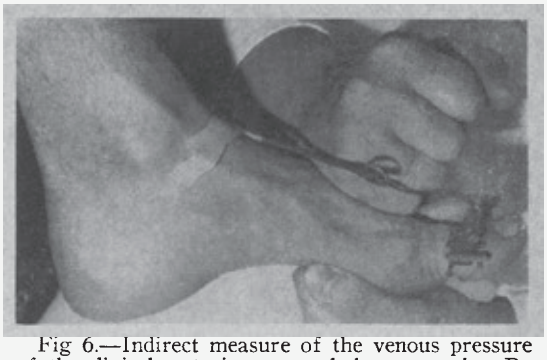


Fig 6.—Indirect measure of the venous pressure of the digit by strain-gauge plethysmography. By rhythmical movement of the fists by the investigator the blood is removed from the venous vessels of the foot resulting in diminution of pressure of the digit.

The insufficiency of the pumping system can also be demonstrated if the investigator pumps the foot artificially with both fists (Fig 6).

In normals it is possible to reduce the tension in the (sitting) subject with 45 mm Hg from 65 to 20 mm Hg (Fig 7*B*). In our patient the decrease in venous pressure to be obtained in this manner was not more than 22 mm Hg (Fig 7*A*). In some of the patients it was impossible to obtain any reduction of the venous pressure of the digit in this manner.

From our investigations it follows that the arterial circulation in legs and feet is normal, but that the superficial and deep venous system of legs and feet is totally deficient. Whereas, normally, the legs have a sufficient pumping system as the leading veins are, as it were, embedded in the muscles, the venous system of the feet flowing out into the deep system of the legs, is much less organized. As

Symptom of Patients With Chronic Venous Insufficiency

Sex	Age	Age of Onset	Symptoms of Venous Insufficiency (CVI *)
M	35	16	Postthrombotic CVI
M	66	22	"
M	51	16	"
M	47	13	" (+ arteriosclerosis)
M	51	18	" (+ lymphangitis)
M	36	14	" (posttraumatic)
M	37	14	" (+ arteriosclerosis)
M	54	38	"
M	46	19	"
M	47	12	" (+ arteriosclerosis)
M	57	11	" (pes excavatus)
M	37	5	" (posttraumatic)
M	51	15	"
M	53	11	"
F	57	10	"
F	58	24	"
F	50	15	"
F	68	20	" (diabetes)

* CVI indicates chronic venous insufficiency.

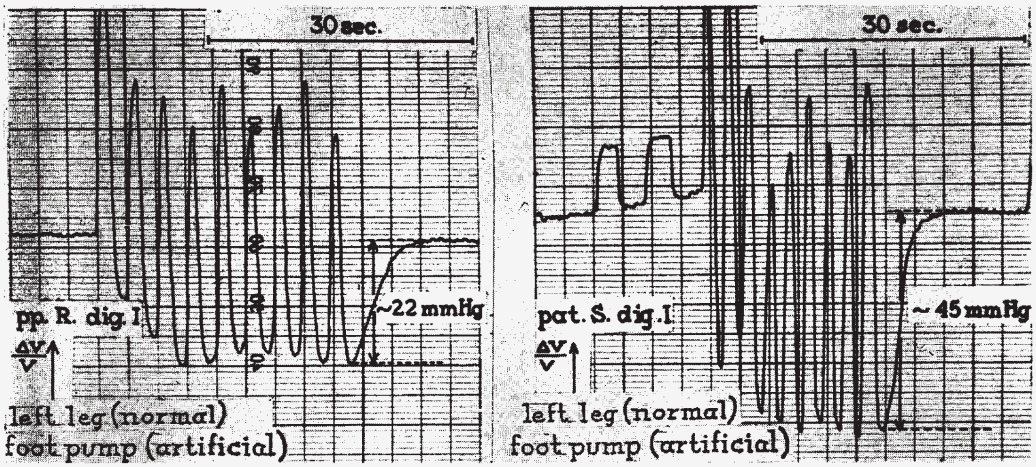


Fig 7.—Graphs of the volume changes of the digit (recalculated in pressure difference) by passive pumping of the feet. a) Patient A b) Normal subject.

the skin vessels do contain all kinds of anastomes, it must be assumed that, normally, the pumping system in the feet is kept going by the walking movement which, together with the tight structure of the foot tissue, enables the venous blood to reach the deep venous system of the leg.

Comment

Clinical and functional investigations and the effect of therapy, together form rather stringent arguments to consider the syndrome here described as a peculiar manifestation of chronic venous insufficiency. The pathological-anatomical investigation shows a picture which is very much Favre's and Chaix's angiodermatitis.[4] One has, however, the impression that the proliferation of bloodvessels is more outspoken than in the manifestations of the angiodermite of the legs in the vicinity of an ulcus cruris. This may be due to the peculiar anatomy of the blood vessels of the akra with their preponderance of arterio-venous anastomoses. As chronic edema of the ankles results in a proliferation of fibroblasts and collagen, it may be possible that the same factor causes proliferation of small blood vessels in the akra. This consideration may gain weight as one considers that other dermatological lesions of the akra (chondrodermatitis nodularis helicis, clavus, granuloma teleangiëctaticum) show analogous proliferation. Moreover, the relatively high oxygen content of the blood may play a role, analogous to what happens in retrolental fibroplasia.

It is understandable that with this histological picture a pathologist, who does not know the clinical lesions of the patient, will, in these cases, consider the diagnosis of Kaposi's sarcoma. We believe it happened in six of 16 cases of so-called "Kaposi's sarcoma" which have been demonstrated since 1900 in clinical meetings of the Netherland's Association of Dermatologists. However, if the histological picture is considered as only one element of the whole syndrome, it is evident that one should, at the most, speak of a "Kaposiform" lesion, due to a chronic venous insufficiency of the feet.

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