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SHORT REPORTS

Regional Differences in Microvascular Responses in Generalized Scleroderma

Johannes Kjeldstrup Kristensen

Department of Dermatology, Rigshospital, 9 Blegdamsvej, DK-2100 Copenhagen, Denmark

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Abstract. In 7 patients suffering from generalized scleroderma of the acrosclerosis type, a decreased reactivity towards changes in vascular transmural pressure was observed in subcutaneous tissue of finger, as compared with arm. Clinically, the fingers were regularly found to be more severely involved in the sclerodermal process, and the pathologic microvascular responses seem to parallel the tissue pathology.

Key words: Autoregulation; Vasoconstrictor reflex; Blood vessels; Generalized scleroderma

Autoregulation of blood flow, i.e. the tendency towards the maintenance of constant blood flow during changes in arterial perfusion pressure, has been demonstrated in normal human subcutaneous tissue (2). In previous studies, it was shown that in generalized scleroderma, blood flow in *cutaneous* tissue of hand and fingers depends mainly on arterial perfusion pressure, because of defects in the vascular reactions underlying the autoregulatory response (4). In *subcutaneous* tissue, autoregulation was demonstrated on the back of the hand, but was absent—or almost so—from more distally located areas (4), thus suggesting a deterioration of responsiveness from hand to fingers and from subcutaneous to cutaneous tissue.

When normal limbs were lowered, corresponding to an increase in vascular transmural pressure of 25 mmHg or more, a decrease in blood flow by 30 to 50% was observed in subcutaneous tissue of arm, hand and fingers (1, 4). This phenomenon is attributed to "the vasoconstrictor response" which is dependent on local nervous mechanisms involving sympathetic adrenergic fibres—probably a sympathetic axon reflex (1). The increase in pre- to postcapillary resistance ratio governed by the reflex will counteract any increase in capillary hydrostatic pressure and, together with the autoregulatory response, act as oedema protection factors (1). In previous studies, it was observed tha "the vasoconstrictor response" is severely reduced or abolished in subcutaneous tissue on the dorsum of the hand or fingers affected by generalized scleroderma (4).

The aim of the present study was to compare in one and the same patient the microvascular responsiveness of a distal, clearly sclerodermic area, in relation to that of a more proximal and less severely involved area.

PATIENTS AND METHODS

Informed consent was obtained before each experiment. Seven patients suffering from generalized scleroderma of the acrosclerosis type were investigated, their ages ranging from 26 to 75 years and the disease duration from 2 to 15 years. All had a history of Raynaud's phenomenon. During the experiments, room temperature was kept con-

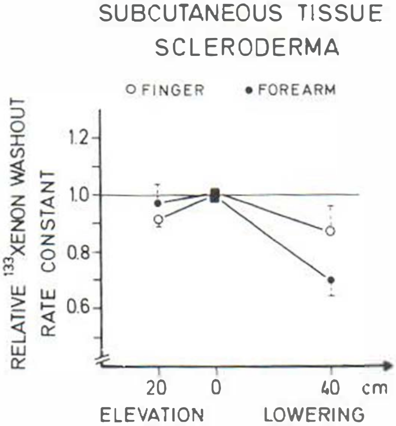

Fig. 1. Relative blood flow (or relative ^{133}Xenon washout rate) during elevation and lowering of arm or hand with respect to heart level.

stant at 24°±1°C. Blood flow in subcutaneous tissue on the dorsum of the proximal finger phalanx and in subcutaneous tissue just proximal to the wrist was estimated by the local ^{133}Xenon washout technique (5). Subcutaneous injections of 0.1 ml ^{133}Xenon dissolved in sterile isotonic saline were performed 30 to 60 minutes before the experiments were started. The patients were seated on an adjustable chair, with their legs hanging, and the arm and hand resting at heart level. The set-up provided complete immobilization during changes in position of the arm (constant counting geometry). For each ^{133}Xenon depot, washout constants (k) were measured (i) with the depot at heart level ($k_{(\mathrm{ref.}_1)}$); (ii) with the depot lowered by 40 cm ($k_{(l)}$); (iii) at heart level ($k_{(\mathrm{ref.}_2)}$); (iv) elevated 20 cm ($k_{(e)}$); and finally (v) at heart level ($k_{(\mathrm{ref.}_3)}$). At each level, measurements lasted about 5 min. Mean perfusion coefficient, (f), can be calculated from the rearranged Kety kormula (3): $f=k \cdot \lambda \cdot 100$ ml/100 g·min, where k denotes the washout rate constant in min^{-1} and λ the subcutaneous tissue to blood partition coefficient in ml/g·λ is not known for subcutaneous tissue (5), but relative changes in blood flow are uninfluenced by λ. For the same radioactive depot, where λ remains constant, relative blood flow equals relative ^{133}Xenon washout rate. Relative ^{133}Xenon washout rate during lowering was calculated as $k_{(l)}/\bar{k}/_{(\mathrm{ref.})}$ and during elevation as $k_{(e)}/\bar{k}_{(\mathrm{ref.})}$, where $\bar{k}_{(\mathrm{ref.})}$ is the mean value of the washout rate constants measured at reference level immediately before and after the test value. The washout rate constants were computed from the recorded counting activity, corrected for background activity, followed by logarithmic transformation as a function of time according to the least squares method.

Statistical testing for significance was performed by the Student's t-test for paired samples. As limit of significance, 0.05 was chosen.

RESULTS

In subcutaneous tissue of the arm, $\bar{k}_{(\mathrm{ref.})}$ was 0.00949 min^{-1}, while in the finger, the subcutaneous tissue value was 0.02276 min^{-1}. This difference probably reflects differences in lipid concentration in these areas, but some of the differences might represent different blood flow values.

During elevation by 20 cm, blood flow decreased by 8% in the finger ($0.1>p>0.05$, N.S.) and by 3% in the arm ($p>0.1$, N.S.). The difference between arm and finger was insignificant ($p>0.2$). During lowering, blood flow decreased by 13% in the finger ($p>0.1$, N.S.) and by 30% in the arm ($p<0.01$). The difference between arm and finger during lowering was statistically significant ($p<0.05$).

DISCUSSION

In this patient sample, normal responses to a decrease in arterial perfusion pressure (elevation) and increase in vascular transmural pressure (lowering) were registered in arm subcutaneous tissue. In finger subcutaneous tissue, autoregulation was present, as blood flow remained almost constant during both elevation and during lowering, while the vasoconstrictor reflex was absent from finger subcutaneous tissue. Oedema protection was thus not effective. The difference between arm and finger was significant, suggesting a deterioration of vascular responsiveness paralleling the degree of cutaneous sclerosis. Whether the suppression of the vasoconstrictor reflex is a sign of a sympathetic neuropathy or if the defect is in the vascular wall *per se*, cannot be definitely stated. It might be argued that a diseased vascular wall reacts differently when stimulated to dilatate (elevation) than when it is stimulated to contract (lowering). The results of the present study support the conclusion that contraction of digital arteries (during increase in vascular transmural pressure) is more easily obtained than dilatation (during decrease in arterial perfusion pressure head). In future experiments it is planned to investigate this problem.

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