Nailfold capillaroscopy and classification criteria for systemic sclerosis

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Introduction

In 1980, the American College of Rheumatology (ACR, formerly American Rheumatism Association) classification criteria for systemic sclerosis (SSc) were proposed with the intent "to establish a standard for definite disease in order to permit comparison of groups of patients from different centers" and not for diagnostic purposes (1). However, these criteria have been used by clinicians for more than 2 decades as diagnostic criteria (2, 3).

In 1988, SSc was classified in subsets by LeRoy *et al*. (4) and divided in limited SSc – with skin involvement up to the elbow and knees with the face – and in diffuse SSc – with skin involvement also including the trunk. In this classification, a capillaroscopic evaluation clearly describing the microvascular involvement was also included.

In the limited subset, capillaroscopic modifications needed to classify the subset were reported as "dilated capillary loops usually without capillary drop out" while in the diffuse subset they were reported as "nailfold capillary dilatations and capillary drop out". Therefore, capillaroscopy was used in practice at least to subset SSc patients.

In the present work in this issue, after having used the ARA criteria for diagnosis, SSc patients were classified in subsets following the new criteria proposed by Leroy and Medsger in 2001 (5, 6). These criteria represent a revised form, slightly different from those of 1988: the main concept of early SSc is introduced here, as well as that of limited Ssc, with a different definition.

However, the important contribution of the present work is the fact that it introduces, through the new subsetting of Leroy and Medsger, capillaroscopy in the diagnosis of early SSc.

It is well-known that the ACR criteria are not sensitive enough to identify patients with early SSc: in fact, it has been observed that ACR criteria exclude certain patients who have been diagnosed by experienced clinicians as having definite SSc (7).

Therefore, given that the ACR criteria were published 27 years ago, several investigators, during the last years, including the authors of the study in this issue, were eager to verify whether the addition of more recently described SSc features, such as nailfold capillary microscopy features, could increase their sensitivity (7, 8)

Nailfold capillaroscopy and sensitivity of the classification criteria

In 2001, Lonzetti *et al*. clearly reported that the sensitivity of the ACR criteria to identify patients with limited disease improved with the addition of nailfold capillary abnormalities and visible telangiectasias (from 34% to 89%) (9). Nailfold capillary abnormalities in that study were identified using a widefield stereomicroscope. That technique is not easily accessible to most rheumatologists.

However, scleroderma-specific findings in nailfold capillary microscopy were confirmed to be really sensitive and predictive for evolving disease.

More recently, in the study presented in this issue, with the same intent, 101 SSc patients were included, most of whom were women with a mean age of 59 (±13). Of these, 68 (67%) met the ACR classification criteria. The sensitivity of the criteria increased from 67% to 99% with the addition of nailfold capillary abnormalities identified using a dermatoscope and visible telangiectasias (6).

Even if the results clearly confirmed, once again, that capillaroscopic analysis increases the sensitivity of the ACR criteria, one of the major limitations of the study was the absence of scoring capillary abnormalities and the lack of definition of the SSc patterns observed.

However, since classification and early diagnosis of SSc may be difficult if disease expression is oligosymptomatic (undifferentiated), presenting with only Raynaud's phenomenon or limited scleroderma, recently an algorithm presented for the classification and diagnosis of SSc has been suggested which uses clinical, capillaroscopic and serologic criteria (10).

Nailfold capillaroscopy and early diagnosis of systemic sclerosis

Capillaroscopic observations, even in childhood rheumatic diseases and

healthy controls, have confirmed their usefulness in early recognition and monitoring scleroderma spectrum disorders (11).

In addition, in childhood Raynaud's phenomenon, nailfold capillaroscopy is a non-invasive examination, enabling early diagnosis of "systemic scleroderma sine scleroderma" (12).

More recently, children and adolescents who developed scleroderma spectrum disorders showed a sclerodermatous type of capillary changes 6 months before the expression of the disease, indicating that this type of capillary changes in children and adolescents with Raynaud's phenomenon highly correlated with further development of scleroderma spectrum disorders (13).

On the other hand, in a six-year follow-up study, nailfold capillaroscopy was confirmed to have a prognostic value in patients with Raynaud's phenomenon and scleroderma-pattern abnormalities (14).

As a matter of fact, nailfold videocapillaroscopy is a tool that enables us to distinguish between primary and secondary RP and that allows, through recognition of an "early" microvascular pattern, the suspicion of early SSc (15).

However, specific microvascular alterations are recognized by capillaroscopic analysis in other connective tissue diseases (*i.e.*, dermatomyositis, mixed connective tissue disease [MCTD], and systemic lupus erythematosus) (16, 17).

Scleroderma capillaroscopic patterns and Raynaud's phenomenon

Distinct morphologic patterns on nailfold videocapillaroscopy and a significant and gradual increase in these microvascular abnormalities are observed during the progression of SSc and seem to reflect the possible development of the pathophysiologic process (18).

The three different scleroderma patterns of microvascular damage, including the "Early", the "Active", and the "Late", have been found to correlate with the duration of the disease, and are possibly linked to the evolution of the microangiopathy (Fig. 1).

A scoring system to quantify the specific capillary abnormalities, as observed using the capillary microscopy was found to be of great interest to monitor the microangiopathy during the time, above all when a variation of the major SSc capillaroscopic patterns was not evident (19).

Very recently, the nailfold capillaroscopic morphological aspects were analyzed in 129 subjects initially referred to the videocapillaroscopic analysis as affected by primary Raynaud's phenomenon (20).

Based on the appearance of the well-assessed patterns on nailfold videocapillaroscopy, 14.6% of these patients were classified as having secondary Raynaud's phenomenon over a mean ± SD follow-up of 29.4 ± 10 months.

Interestingly, 4.6% of these patients had exhibited a normal nailfold videocapillaroscopy pattern at baseline (transition from normal to altered pattern observed in a mean SD of 42 ± 30 months) and 10% had minimal and nonsignificant microvascularchanges at baseline (transition to altered pattern observed in 25 ± 15 months). The duration of Raynaud's phenomenon from baseline to the transition to secondary Raynaud's phenomenon was 58 ± 10 months and 29 ± 10 months, respectively, in the 2 groups that were formed by 80% of SSc patients showing the well-assessed "scleroderma pattern". Positivity for antinuclear antibody was observed later during the follow-up (29.4 ± 10 months) in almost 85% of the SSc patients.

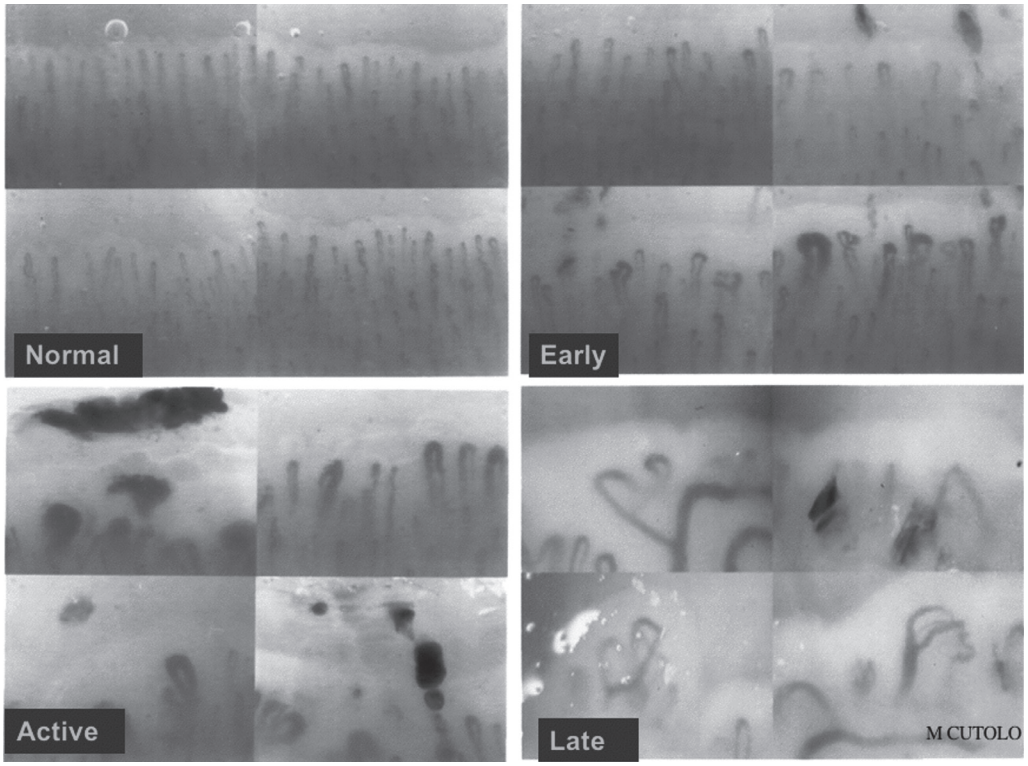

Fig. 1. The patterns identified within the "scleroderma pattern" include: 1) "Early" NVC pattern: few enlarged/giant capillaries, few capillary haemorrhages, relatively well-preserved capillary distribution, no evident loss of capillaries; 2) "Active" NVC pattern: frequent giant capillaries, frequent capillary haemorrhages, moderate loss of capillaries, mild disorganisation of the capillary architecture, absent or mild ramified capillaries; 3) "Late" NVC pattern: irregular enlargement of the capillaries, few or absent giant capillaries and haemorrhages, severe loss of capillaries with extensive avascular areas, disorganisation of the normal capillary array, ramified/bushy capillaries (magnification 200x, cutolo m).

In a previous study, almost 10% all patients affected by primary Raynaud's phenomenon who underwent transition to secondary during a follow-up of more then 10 years, were found affected by SSc (5). On the other hand, in another recent study, it was found that "clinically significant" Raynaud's phenomenon affects almost 1% of the population and early stages of scleroderma spectrum disorder were detected using either anticentromere autoantibody or scleroderma capillary pattern (21). Using the capillaroscopic analysis, the prevalence of SSc was found to be higher than expected.

All the studies confirmed that capillaroscopy is an essential imaging technique used in the evaluation of microcirculation and one of the best diagnostic tools for the early detection of systemic sclerosis and related conditions (22).

Conclusions

Despite the increasing interest in capillary microscopy and its clear diagnostic usefulness in SSc, there is still a surprising discrepancy between its potential application and its still too limited use in rheumatological practice. This contrast is surprising because few diagnostic techniques can combine all the positive features typical of capillaroscopy (low cost, uninvasiveness, repeatability, high sensitivity, good specificity, easy interpretation of results).

In conclusion, nailfold capillaroscopy seems the most efficient tool for the early diagnosis of SSc through the detection of specific microvascular alterations that allows distinguishing the primary from the secondary Raynaud's phenomenon, as well as, later, the progression of the disease (23). Therefore, the study reported in the present issue confirms that the ACR classification criteria for SSc lack sensitivity for the diagnosis of early SSc, that may be, however, significantly improved by easily identified clinical variables such as the detection of well-recognized nailfold capillary abnormalities (scleroderma patterns).

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