

Capillaroscopy in Rheumatology

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A 40-year-old woman is referred to the rheumatology clinic for nailfold capillaroscopy. She has had Raynaud's phenomenon for 10 years, has no other relevant medical history, and is a non-smoker. She has three healthy children and no history of miscarriages. She does not take any medication. Family history is unremarkable, including the absence of Raynaud's phenomenon in any relatives. On history, she denies heartburn, shortness of breath, arthritis, or any other symptoms of connective tissue diseases. The physical exam is negative for sclerodactyly, neck sign, increased peribuccal folds, or skin thickening; however, she has two telangiectasias on her lower inner lip. Her anti-nuclear antibody was positive (1:160), with an anti-centromere pattern. Antibodies to extractable nuclear antigen, including anti-topoisomerase I antibodies, were negative. Nailfold videocapillaroscopy was performed (DS Medica, 200x magnification) and showed an active scleroderma pattern (Figure 1).

Does This Patient Have Scleroderma?

According to epidemiologic studies, the prevalence of Raynaud's phenomenon ranges from 2% to 22%, of which roughly 15% is associated with systemic sclerosis (SSc).¹⁻² Which patients with Raynaud's phenomenon are likely to progress to SSc? A twenty-year prospective study of 586 patients with Raynaud's phenomenon showed that

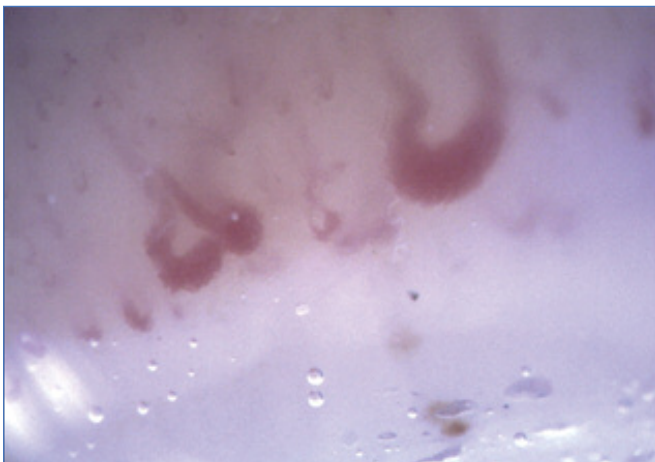


Figure 1. Giant capillaries are the hallmark of the scleroderma pattern. The presence of even one giant capillary is never normal and is characteristic of the scleroderma pattern. Other features of the scleroderma pattern include ectasias, capillary hemorrhages, capillary loss, neoangiogenesis, and disorganisation. More than 95% of SSc patients will have this pattern on videocapillaroscopy. Represented are two giant capillaries, one hemorrhage, and mildly diminished capillary density.

abnormal nailfold capillaroscopy at baseline, in the presence of an SSc-specific autoantibody (anti-centromere protein B [CENP-B], anti-topoisomerase I, anti-Th/To, or anti-RNA polymerase III), were excellent predictors for the development of definite SSc, whereas their absence practically ruled out this outcome. Indeed, subjects with both abnormalities at baseline were 60 times more likely to develop SSc compared to patients without these predictors; 80% of the patients with both abnormalities developed SSc over 20 years of followup. In contrast, only 2% of patients with Raynaud's phenomenon with normal capillaroscopy and absent SSc-specific auto-antibodies at baseline developed definite SSc in follow up.²

This landmark study² provided validation for the criteria proposed for early SSc in 2001 by Leroy and Medsger,³ that included Raynaud's phenomenon, SSc-specific autoantibodies (anti-centromere, anti-topoisomerase I, anti-fibrillarin, anti-PM/Scl or anti-RNA polymerase I or III) and a scleroderma pattern on capillaroscopy. Those criteria increased the sensitivity of the 1980 American College of Rheumatology (ACR) preliminary criteria⁴ for limited SSc from 33% to 92%.⁵ Nevertheless, we should keep in mind that 20% of the patients who fulfill those criteria will not develop SSc, at least with 20 years of follow-up.

In 2012, an ACR-European League Against Rheumatism (EULAR) committee was established to develop new classification criteria for SSc (Table 1).⁶ These criteria were expanded to include abnormal nailfold capillaries. A

Table 1
ACR-EULAR Criteria for the Classification of SSc

| Criteria | Sub-criteria | Weight |
|--|-----------------------------|--------|
| Skin thickening of the fingers of both hands extending proximal to the meta-carpophalangeal (MCP) joints <i>(sufficient criterion)</i> | | 9 |
| Skin thickening of the fingers <i>(only count the highest score)</i> | Puffy fingers; | 2 |
| | Whole finger, distal to MCP | 4 |
| Fingertip lesions <i>(count the highest of the two)</i> | Digital tip ulcers; | 2 |
| | Fingertip pitting scars | 3 |
| Telangiectasia | | 2 |
| Abnormal nailfold capillaries | | 2 |
| Pulmonary arterial hypertension and/or interstitial lung disease <i>(maximum score is 2)</i> | | 2 |
| Raynaud's phenomenon | | 3 |
| SSc-related antibodies (any of anti-centromere, anti-topoisomerase I, anti-Scl-70, anti-RNA polymerase III) <i>(maximum score is 3)</i> | | 3 |

A patient with a score of 9 or more is classified as SSc.

subject with a score of 9 or more is classified as having SSc. The case-study patient described above fulfills the criteria for definite SSc according to the new ACR-EULAR criteria. She has Raynaud's phenomenon (2 points), anti-centromere antibodies (3 points), SSc-capillaroscopy pattern (2 points), and telangiectasias (2 points), for a total of 9 points. Capillaroscopy was therefore a very useful tool to make a diagnosis of SSc in the case of this patient.

Suggested Work-up

The next step in her investigation should be to determine whether internal organs are involved, including esophageal transit or barium swallow to rule out esophageal dysmotility, echocardiography to measure pulmonary arterial pressures, and chest x-ray and pulmonary function tests to rule out interstitial lung disease. Hand x-rays could also be considered to determine the presence of calcinosis or acro-osteolysis. This patient had a normal work-up, barring the fact that her esophageal transit was compatible with moderate esophageal dysmotility.

Treatment

The treatment for Raynaud's phenomenon remains symptomatic. Non-pharmacologic interventions include smoking cessation, warm clothes, and minimizing cold exposure. Calcium channel blockers are used as first-line

treatment when pharmacotherapy is considered.⁷ Proton-pump inhibitors (PPIs) should be considered, even in asymptomatic patients, to prevent complications resulting from gastric reflux. Such complications may include esophagitis, esophageal strictures and Barrett's esophagus. The importance of aggressive treatment of esophageal dysmotility has been highlighted by recent studies which showed a relationship between asymptomatic micro-aspiration secondary to acid reflux and interstitial lung disease in SSc.⁸⁻⁹ Of note, 70% to 90% of SSc patients have esophageal involvement, and 50% of these patients are asymptomatic.⁷

Conclusion

Nailfold capillaroscopy is a rapid, non-invasive, and easy-to-perform test that should be considered as part of the evaluation of individuals with Raynaud's phenomenon, to facilitate the diagnosis of SSc, and to reassure those with negative autoantibodies and normal capillaries. The devices presently available for nailfold capillaroscopy include the dermatoscope (10X magnification), ophthalmoscope (20X magnification), widefield microscope (50X magnification), and videocapillaroscope (200X magnification). Although the dermatoscope and ophthalmoscope are available in the clinic, the better resolution of widefield microscopy and videocapillaroscopy is preferable

to identify all of the features of the SSc-pattern. The diagnostic and prognostic value of capillaroscopy in other rheumatologic diseases is still being investigated, in particular in the myositides where a scleroderma-like pattern has been described. No specific pattern for other connective tissue diseases has been described. The presence of the SSc-pattern in those diseases suggests an overlap with SSc.

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