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Capillaroscopic pattern in inflammatory arthritis

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ABSTRACT

Background: There are limited data about the role of nailfold capillaroscopy in inflammatory arthritis.
Objectives: To study the role of capillaroscopy in inflammatory arthritis — rheumatoid arthritis (RA), psoriatic arthritis (PsA) and early arthritis.
Methods: Patients from the following groups were included in the study: 62 patients with RA; 34 patients with PsA with involvement of the joints of the hands; 9 women with early arthritis. Nailfold capillaroscopy was performed with videocapillaroscope.
Results: Raynaud's phenomenon (RP) was found in 30.6% (19/62) of RA patients, in 32.4% (11/34) of PsA patients and 44.4%, (4/9) of cases with early arthritis. The most frequent found capillaroscopic changes in RA patients were presence of elongated capillaries in 58% of cases (36/62) and prominent subpapillary plexus in 69% (43/62). Dilated capillaries were found in 78.9% (15/19) of patients with secondary RP and in 62.8% (27/43) of those without RP. "Scleroderma-like" capillaroscopic pattern was observed with low frequency in RA patients (14.5%/9/62). "Scleroderma-like" capillaroscopic pattern was also found in 11.1% (1/9) in the group of patients with early arthritis. The low frequency of the last type of capillaroscopic pattern in RA requires patients with such changes to be observed during regular follow-up for the development of systemic rheumatic disease different from inflammatory arthritis. In patients with PsA capillaries with specific morphology (tight terminal convolutions) were found in 58.8% (20/34) of cases.
Conclusions: Results from the present study confirm the necessity for inclusion of the nailfold capillaroscopy in the diagnostic algorithm in patients with inflammatory arthritis.

Introduction

Capillaroscopic pattern in rheumatoid arthritis

In rheumatology specific capillaroscopic pattern is found in systemic sclerosis (SSc), which is characterized by presence of dilated and giant capillaries, hemorrhages, avascular areas and neoangiogenic capillaries. It has been described for the first time by Maricq et al. (1980) and is called "scleroderma" type capillaroscopic pattern (Beltran et al., 2007; Bollinger and Fagrell, 1990; Cutolo et al., 2000, 2003, 2004, 2005, 2006, 2007). It occurs in a high proportion of patients with SSc — more than 90%, which is explained with the high frequency of Raynaud's phenomenon (RP) in these patients — also in more than 90% of SSc patients. Similar changes are found in patients with dermatomyositis, mixed connective tissue disease, undifferentiated connective tissue disease and they are called "scleroderma-like" pattern". Such changes are not observed in patients with rheumatoid arthritis (RA).

The prevalence of RP in RA is not well-defined. Some authors consider that such an association is quite rare (Seibold and Steen, 1994). On the other hand, other authors include RA among the rheumatic diseases associated with RP (Block and Sequeira, 2001; Le Roy and Medsger, 1992). Grassi et al. (1994, Italy) found a low incidence of RP in RA — 4.6%, (19/411). The higher prevalence of RP in men with RA (7.5%) than in women (3.2%) was interesting. In comparison, in a cohort of 919 patients with osteoarthritis, a global tendency of a female predominance of RP was observed. The higher prevalence of RP in men with RA has been explained by the authors with a higher association of RA with secondary vasculitis in men (Grassi et al., 1994). These results are in agreement with the findings of Carrol et al. (1981, North Australia), who found a manifestation of RP in 2.7% of 141 patients with RA (Carrol et al., 1981). In a French population of RA patients, Saraux et al., 1996 found a higher prevalence of RP in RA (17.2%, 54/322). The contradictory literature data about the prevalence of RP in RA require future studies in different populations of RA patients. In 31 RA patients, Redisch and co-authors found the following abnormal capillaroscopic findings: elongated capillaries, increased tortuosity, prominent subpapillary plexus. A "scleroderma-like" pattern was not observed in RA patients (Grassi et al., 1989; Redisch, 1970).

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Psoriatic arthritis

The first observation of capillaroscopic findings in psoriatic arthritis (PsA) was performed by Redisch et al. (1970), using light microscope. The most frequent capillaroscopic changes were meandering capillaries and tight terminal convolutions (Redisch, 1970). In PsA patients with nail involvement, independent of presence or absence of arthritis of distal interphalangeal joints, a lower mean capillary density has been found as compared with healthy controls. In PsA patients with distal interphalangeal joint involvement, independent of the concomitant nail damage, a decreased diameter of the arterial and the venous limb of the capillary loop has been observed (Bhushan et al., 2000). In an Italian study, a decreased capillary diameter and length in RA-like form of PsA was reported (Salli et al., 1999).

Early arthritis

According to the EULAR recommendations (2007) for the management of early arthritis, exclusion of diseases other than RA requires careful medical history, clinical examination, and at least the following laboratory tests: complete blood cell count, urine analysis, transaminases and ANA test. These investigations are necessary to differentiate RA from other rheumatic diseases such as connective tissue disease, reactive arthritis etc. because of the different prognosis and treatment (Combe et al., 2007). The role of capillaroscopy in early arthritis has not been studied and discussed in the current rheumatologic literature including in the aforementioned EULAR recommendations.

Analysis of the current literature demonstrated, that there are limited data about the role of nailfold capillaroscopy in inflammatory arthritis.

Objectives

To study the role of capillaroscopy in inflammatory arthritis — rheumatoid arthritis (RA), psoriatic arthritis (PsA) and early arthritis.

Patients and methods

Patients from the following groups were included in the study: 62 patients with RA, mean age 62.8 ± 11.3 years; 34 patients with PsA with involvement of the joints of the hands, mean age 49 ± 12.5 years; 9 women with early arthritis, mean age 46.4 ± 13.8 years.

Diagnosis of RA was made according to the current ACR classification criteria, 1987 (Arnett et al., 1988) and the diagnosis PsA — according to the CASPAR criteria respectively (Taylor et al., 2006).

Patients with early arthritis at the time of their first referral to a rheumatologist, with duration of symptoms <6 months, who did not fulfill the criteria for a definite type of arthritis or connective tissue disease. Comparison of the capillaroscopic parameters was made with age- and sex-matched healthy controls without history of vasospasm, rheumatic or other known diseases, who do not take any medication were examined as a control group. The age- and sex distribution of the patients and the respective healthy volunteers are presented in Table 1.

Nailfold capillaroscopy was performed with videocapillaroscope Videocap 3.0 (DS Medica) in the Department of Rheumatology and Clinical Immunolgy, Bad Nauheim, Justus-Liebig University-Gießen, Germany. The following capillaroscopic parameters were evaluated: distribution, shape, width, length, mean capillary density, presence of avascular areas, hemorrhages, neoangiogenesis, visibility of subpapillary plexus. Nailfold capillaroscopy was performed using a high-end videocapillaroscope Videocap 3.0 (DS Medica, Italy). Measurements were performed with the software program of the device and all the measurements were made in mm, (0.001 mm = 1 μm).

Table 1
Number, age and sex of the included groups of patients and the age- and sex-matched controls.

RA, n = 62	62.8 ± 11.3	47 females, 15 males
Healthy controls, n = 62	61.16 ± 9.16 (p > 0.05)	20 females, 4 males (p > 0.05)
PsA, n = 34	49 ± 12.04	22 females, 12 males
Healthy controls, n = 43	49.30 ± 16.09 (p > 0.05)	34 females, 9 males (p > 0.05)
Early arthritis, n = 9	46.44 ± 13.8	9 females
Healthy controls, n = 22	47.27 ± 10.40 (p > 0.05)	22 females (p > 0.05)

As dilated were classified capillaries with a diameter of the arterial limb wider than 0.015 mm (= 15 μm) or a venous limb wider than = 0.020 mm (= 20 μm). As giant capillary loops were classified microvessels with diameter of either an arterial or a venous limb greater than 0.050 mm (= 50 μm). As elongated were classified capillary loops with lengths longer than 0.300 mm (= 300 μm). The hemorrhages are the extracapillary brown aggregations of erythrocytes. The mean capillary density was calculated as a number of capillary loops in the distal row per 1 mm. The avascular area was defined as a distance between two adjacent capillary loops from the distal rows greater than 0.5 mm (= 500 μm) or above 0.3 mm (300 μm) in the proximal area (Schmidt et al., 1997). Meandering capillaries, presence of more than one capillary loop in a single dermal papilla, ramified and bushy capillaries are the characteristic features of neoangiogenic capillaries and were classified respectively. All observations are performed with the subjects in a constant temperature setting (22° to 25°C).

For statistical analysis of the data, variational analysis, t-criterion of V. Goset (Student–Fisher) and -square test were used. Results are shown as mean value/average SD. The values of $p<0.05$ were considered as statistically significant. The study has been approved by the local ethical committee and all patients signed an informed consent.

Results

Capillaroscopic pattern in rheumatoid arthritis

RP was found in 30.6% (19/62) of the patients with RA, a vasculitis of peripheral vessels — in 3% (2/62) respectively. The most frequent findings at nailfold capillaroscopic examination were prominent subpapillary plexus in 69% (40/62) and elongated capillaries in 58% (36/62). They were found statistically significantly more frequent in RA patients as compared with healthy controls ($p<0.05$), (Fig. 1). The mean capillary length in RA patients (0.265 ± 0.086 mm) was significantly longer than those in healthy individuals (0.216 ± 0.081 mm),

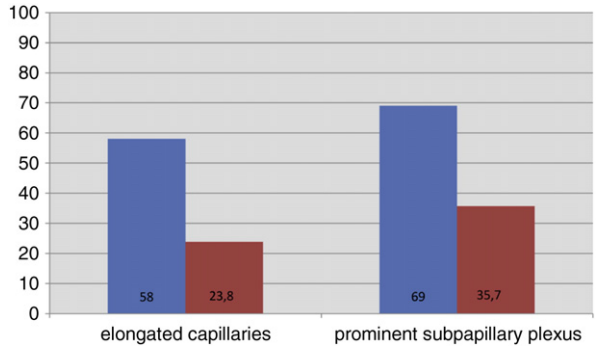

Fig. 1. Frequency of elongated capillaries and prominent subpapillary plexus in RA (blue column) in comparison with healthy volunteers (red column).

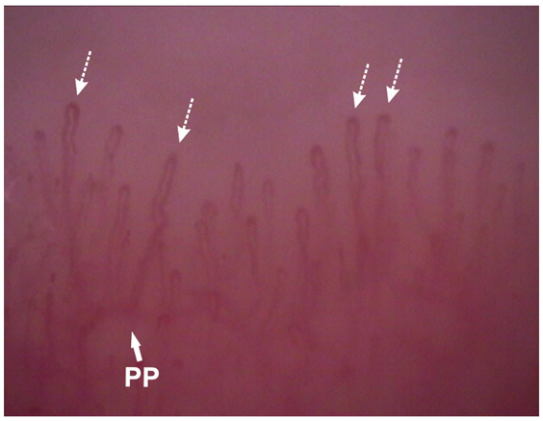

Fig. 2. Capillaroscopic pattern in RA patient without RP, magnification 200×; PP — prominent subpapillary plexus, dotted arrows — elongated capillaries.

Fig. 4. Capillaroscopic pattern in PsA patient with involvement of small joints of the hands, demonstrating tight terminal convolutions (arrows), magnification 200×.

($p<0.05$). The diameters of the arterial (0.018 ± 0.005 mm) and the venous limb of the capillary loops (0.028 ± 0.009 mm) in patients with RA and secondary RP were found to be significantly wider as compared with RA patients without RP (0,016 ± 0.003 mm for the arterial limb and 0.022 ± 0.005 for the venous limb), ($p<0.05$). On the other hand, dilated capillaries were found not only in RA patients with RP (78.9%; 15/19), but also in RA patients without clinical symptoms of vasospasm of peripheral vessels (62.8%; 27/43), ($p<0.05$), (Figs. 2 and 3). The diameters of the capillary loops of RA patients without secondary RP were also significantly wider than those of healthy controls ($p<0.05$), which may be associated with endothelial damage in different mechanisms in these patients. In 14.5% (9/62) of the RA patients, a "scleroderma-like" pattern was observed (2 males and 7 females). In one of these cases, an overlap of RA with SLE, secondary RP and secondary vasculitis was found. In the rest, 8/9 patients, no overlap with other CTD was evident. In all RA patients with "scleroderma-like" capillaroscopic pattern (9/9), a secondary RP was present, and in 2/9 a secondary vasculitis respectively.

Capillaroscopic pattern in psoriatic arthritis

In 30.2% (11/34) of the cases with PsA, RP was present. The mean capillary length in PsA patients (0.166 ± 0.09 mm) was found to be significantly lower as compared with healthy individuals (0.209 ± 0.07 mm), ($p<0.05$). The mean capillary density was significantly lower in PsA patients (8 ± 1 capillaries/mm) as compared with healthy individuals (10.2 ± 0.62 capillaries/mm), ($p<0.05$). In patients with PsA, capillaries with specific morphology — tight terminal convolutions were found in 58.8% (20/34) of the cases (Fig. 4). The finding is analogous to the vascular morphology in the psoriatic plaque (Figs. 5 and 6) and the type of vascular proliferation in the inflamed synovium in the knee joint of patients with PsA (Fiocco et al., 2001).

Capillaroscopic pattern in early arthritis

We have found RP in 44% (4/9) of the examined patients with early symmetric arthritis, who were diagnosed as RA at the follow-up (7 patients with CCP-positive and rheumatoid factor positive form of RA and 2 patients with seronegative RA). At the capillaroscopic examination, a normal capillaroscopic picture was observed in 66% (6/9) and moderately dilated capillaries in 22.2% (2/9). A "scleroderma-like" pattern was found in 11.1% (1/9) of the patients with early arthritis, who presented with complaints of RP. The low frequency of the last type of capillaroscopic pattern in RA requires patients with such changes to be observed during the regular follow-up for the development of systemic rheumatic disease different from inflammatory arthritis.

Discussion

Capillaroscopic pattern in rheumatoid arthritis

RP was found in 30.6% (19/62) of the patients with RA and in 3% (2/62) — a vasculitis of peripheral vessels. The most frequent findings

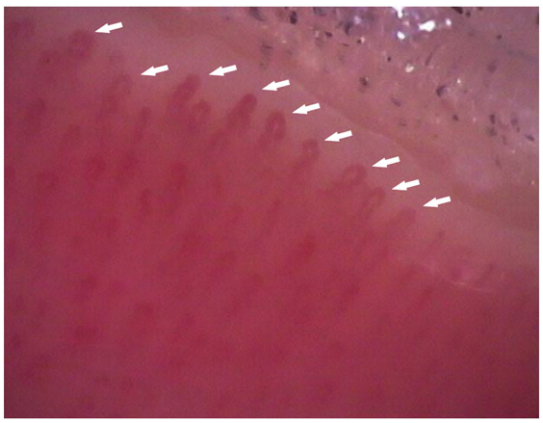

Fig. 3. Capillaroscopic pattern in RA with secondary RP, demonstrating presence of dilated capillaries (arrows), magnification 200×.

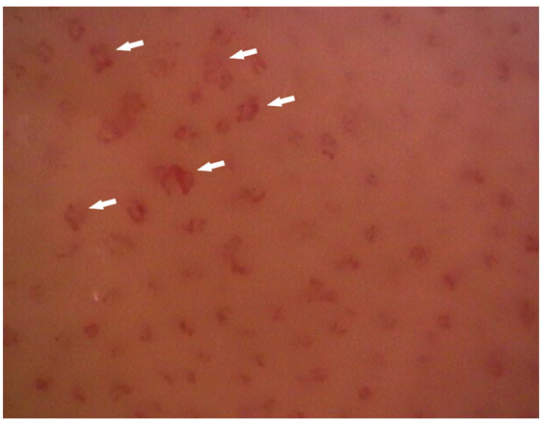

Fig. 5. Capillaries of the psoriatic plaque with terminal convolution, magnification 200×.

Fig. 6. Capillaries with normal morphology at a skin area unaffected from psoriatic lesions of the same patient, presented in Fig. 5, magnification 200×.

at nailfold capillaroscopic examination were prominent subpapillary plexus in 69% (40/62) and elongated capillaries in 58% (36/62). The diameters of the arterial and venous limb of the capillary loop were significantly wider in patients with RA and secondary RP as compared with RA patients without RP. On the other hand, dilated capillaries were found not only in RA patients with RP (78.9%, 15/19), but also in RA patients without clinical symptoms of vasospasm of peripheral vessels (62.8%, 27/43). The diameters of the capillary loops in RA patients without secondary RP were also significantly wider than those of healthy controls, which may be associated with endothelial damage in different mechanisms in these patients in the context of the chronic inflammation. Moreover a correlation between abnormal capillaroscopic pattern and increased levels of fibrinogen and other acute-phase reactants (CRP, ESR) could be found in patients with primary and secondary RP (Spengler et al., 2004). In 14.5% (9/62) of RA patients a "scleroderma-like" pattern was observed, 2 males and 7 females. Only in one of these cases an overlap of RA with SLE was found. A secondary RP and a secondary vasculitis were evident in this patient. In the rest patients with such capillaroscopic changes (8/9), no overlap with other CTD was found. In all the patients with "scleroderma-like" pattern (9/9), a secondary RP was present, and in 2/9 a secondary vasculitis respectively. This suggests that "scleroderma-like" capillaroscopic pattern may be observed in RA patients although with low frequency and its presence is not obligatory associated with overlap syndromes. These findings are not reported by other authors in the current rheumatologic literature.

Capillaroscopic pattern in psoriatic arthritis

In PsA patients, a significantly lower mean capillary length and mean capillary density was found as compared with healthy individuals. In patients with PsA, capillaries with specific morphology — tight terminal convolutions were present in a high proportion of the patients. This finding is analogous to the vascular morphology in the psoriatic plaque and the type of vascular proliferation in the inflamed synovium of the knee joint of patients with PsA [45]. The capillaroscopic examination of the uninvolved from psoriatic lesions skin, in the areas adjacent to the psoriatic plaques, showed normal capillary morphology. In contrast to the increased vascularity in the psoriatic plaque and the synovium in PsA, in the area of the nailfold the mean capillary density was found to be significantly lower as compared with healthy individuals.

Capillaroscopic pattern in early arthritis

The presence of RP in patients with early arthritis requires exclusion of SSc or SLE. In the group of patients with early arthritis, RP was present in 44% (4/9) of the examined patients with early symmetric arthritis, who were diagnosed as RA at the follow-up. A "scleroderma-like" pattern was found in 11.1% (1/9) of patients with early arthritis, who presented with RP. The low frequency of this type of capillaroscopic pattern in RA requires patients with such changes to be observed during regular follow-up for the development of systemic rheumatic disease different from inflammatory arthritis.

In conclusion, in patients with early arthritis capillaroscopic examination is helpful for the differential diagnosis.

Conclusion

This is the first extensive study of capillaroscopic pattern in RA with and without RP.

Nailfold capillaroscopy revealed characteristic changes in patients with RA both with and without RP. This is the first extensive study for evaluation the role of the capillaroscopy in patients with other inflammatory arthritis e.g., PsA, early arthritis. Nailfold capillaroscopy revealed characteristic changes in the RA-like form of PsA and in the subtype of the disease with involvement of the distal interphalangeal joints.

In patients with early arthritis, the capillaroscopic examination may facilitate differential diagnosis.

Results from the present study confirm the necessity for inclusion of the nailfold capillaroscopy in the diagnostic algorithm in patients with inflammatory arthritis.

Disclosure statement

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