

Nailfold capillaroscopy in children and adolescents with rheumatic diseases

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ABSTRACT

Objective: To assess nailfold capillaroscopy in children and adolescents with autoimmune rheumatic diseases (juvenile idiopathic arthritis, systemic lupus erythematosus, juvenile dermatomyositis, scleroderma and mixed connective tissue disease) and relate it to clinical and laboratory findings and disease activity. **Methods:** Cross-sectional study assessing 147 patients by use of nailfold capillaroscopy as follows: 60 with juvenile idiopathic arthritis; 30 with systemic lupus erythematosus; 30 with juvenile dermatomyositis; 20 with localized scleroderma; four with systemic sclerosis; and three with mixed connective tissue disease. Clinical and laboratory tests and nailfold capillaroscopy were performed in all patients. The nailfold capillaroscopy was performed with an optical microscope (at 10- and 16-time magnifications) by the same observer. **Results:** Most patients (76.2%) had normal nailfold capillaroscopy. The major changes in nailfold capillaroscopy, characterizing the scleroderma pattern, were observed in patients with juvenile dermatomyositis, systemic scleroderma and mixed connective tissue disease. There was no association between nailfold capillaroscopy and disease activity in patients with juvenile idiopathic arthritis, systemic lupus erythematosus and localized scleroderma. Disease activity and capillaroscopy were associated in patients with juvenile dermatomyositis. **Conclusion:** Nailfold capillaroscopy is a useful method to diagnose autoimmune rheumatic diseases and monitor disease activity.

Keywords: diagnostic equipment, juvenile rheumatoid arthritis, dermatomyositis, child, systemic scleroderma.

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INTRODUCTION

Nailfold capillaroscopy (NFC) plays an important role in the assessment of autoimmune rheumatic diseases (AIRD) with vascular structural changes. It is easily performed, applicable, non-traumatic, and of low cost, being thus useful for the diagnosis and follow-up of those diseases. It is also used to distinguish primary from secondary Raynaud's phenomenon (RP), to predict the prognosis of AIRD (such as in systemic scleroderma – SSc), and to assess disease activity (such as in dermatomyositis).¹⁻³

NFC has proved to be very useful in the diagnosis of the scleroderma spectrum disorders in adults and children. The scleroderma pattern (SD-pattern), characterized by capillary dilation and avascular areas (vascular deletion), resulting in

a reduction in the number of capillaries, is found in approximately 80% of the patients with SSc, but can also be seen in patients with dermatomyositis and mixed connective tissue disease (MCTD).⁴⁻⁶

This study aimed at characterizing NFC in children and adolescents with AIRD [juvenile idiopathic arthritis (JIA), systemic lupus erythematosus (SLE), juvenile dermatomyositis (JDM), SSc, and MCTD] and at assessing its relationship to clinical and laboratory changes and disease activity.

METHODS

This study assessed 147 children and adolescents cared for at the pediatric rheumatology outpatient clinic from March 2008 to November 2009. It was a convenience sample composed

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as follows, according to the respective diagnostic or classification criteria:⁷⁻¹² 60 patients with JIA (oligoarticular, 20; polyarticular, 20; and systemic, 20); 30 patients with SLE; 30 patients with JDM; 20 patients with localized scleroderma; four patients with SSc; and three patients with DMTC. Patients up to the age of 21 years accepting to participate in the study and with satisfactory nailfold conditions to undergo NFC were included.

Anamnesis and physical examination were performed on the day of NFC, focusing on the following: cutaneous changes (skin thickening, Gottron's sign, heliotrope rash, photosensitivity and periungual hyperemia); calcinosis; digital ulcers; RP; arthritis/arthritis; esophageal and pulmonary changes (dysphagia and dyspnea, respectively); assessment of muscle strength in JDM, by use of the Childhood Myositis Assessment Scale (CMAS);¹³ assessment of disease activity in JIA,¹⁴ in localized scleroderma,¹⁵ and in SLE (by use of the Systemic Lupus Erythematosus Disease Activity Index – SLEDAI).¹⁶

Laboratory assessment comprised complete blood count, acute-phase tests [erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)], serum levels of muscle enzymes [glutamic-oxaloacetic transaminase (GOT), glutamic-pyruvic transaminase (GPT), creatine kinase (CK), and lactic dehydrogenase (LDH)], autoantibodies [antinuclear antibody (ANA), anti-double stranded DNA antibody (anti-ds-DNA), extractable nuclear antigen antibody (ENA), rheumatoid factor (RF), anti-DNA topoisomerase-1 antibody (anti-Scl 70), anti-polymyositis-scleroderma antibody (anti-PM-Scl), anti-cardiolipin immunoglobulin G and immunoglobulin M (ACL IgG and ACL IgM, respectively)], and hemolytic complement (CH100 and C2). Pulmonary function test (PFT), echocardiography and esophagogastroduodenography (EGD) were performed in patients with SSc and MCTD.

NFC was performed by the same examiner (MTRAT) using an optical microscope (at 10- and 16-time magnifications), equipped with a graded ruler coupled with the right objective, allowing counting the number of capillaries per millimeter. The patients were instructed not to remove their fingernail cuticles for one month to avoid microtraumas that could jeopardize the exam. The fingers were examined (except for the thumbs). On semiquantitative analysis, according to the method proposed by Andrade et al.,¹⁷ the following parameters were assessed: integrity of the nailfold; number of micro-hemorrhages and their distribution pattern (focal or diffuse); number of capillaries per millimeter; vascular deletion score (avascular areas); atypical capillaries, such as dilated, 'giant', crossed, bushy and bizarre capillaries; subpapillary

venous plexus visualization score; and predominant capillary pattern.¹⁷

Capillaries were considered dilated when the loops were widened in all three branches (afferent, transition and efferent), with calibers ranging from four to nine times the normal dimension. 'Giant' capillary loops were defined as extremely widened loops, with calibers 10 or more times greater than those of the normal adjacent loops. For recording dilated and 'giant' capillaries, the mean number of capillaries in each finger with those changes was calculated. Deletion was defined as the absence of two or more successive capillaries. To quantify the degree of focal deletion or avascular area, a 0–3 scale was used according to the extension of the lesions:¹⁸ 0: no deletion area; 1: one or two discontinuous deletion areas; 2: more than two discontinuous deletion areas; 3: extensive and confluent avascular areas. The vascular deletion score was calculated by adding the scores of each finger and then dividing by the number of fingers with deletion.

NFC was considered normal in the presence of parallel non-dysmorphic capillaries and lack of deletion areas. Unspecific microangiopathy was defined as dilated capillaries and other morphological changes in the absence of deletion areas. The SD-pattern was characterized by dilated or 'giant' capillary loops and vascular deletion areas.

All participants provided written informed consent to participate in the study, which had been previously approved by the Ethics Committee of the Hospital São Paulo.

RESULTS

This study assessed 147 patients by use of NFC. Table 1 shows demographic data and the presence of RP. Table 2 shows the NFC findings and disease activity of the patients with AIRD. Most patients (76.2%) assessed had normal NFC.

Of the 20 patients with oligoarticular JIA, seven (35%) showed clinical activity, two (10%) had chronic anterior uveitis, and 12 (60%) were positive for ANA. Regarding NFC, all patients had normal results. Of the patients with polyarticular JIA, five (25%) had RP, seven (35%) were positive for ANA, 11 (55%) had clinical activity, most patients had normal NFC results, and only one patient had unspecific microangiopathy. Of the patients with systemic JIA, 12 (60%) showed clinical activity, 17 (85%) had normal NFC results, one (5%) had unspecific microangiopathy, one (5%) had the SD-pattern, and one (5%) was inconclusive due to poor visualization of the capillaries. Only two (10%) patients showed capillary tortuosity. No changes on NFC, such as tortuosity, were observed in

Table 1

Demographic data and presence of Raynaud's phenomenon in patients with autoimmune rheumatic diseases (n = 147)

Variables	JIA n = 60	SLE n = 30	JDM n = 30	LSc n = 20	SSc n = 4	MCTD n = 3
Female gender, n (%)	32 (53.3)	25 (83.3)	20 (66.6)	12 (60)	4 (100)	0
Caucasian race, n (%)	42 (70)	23 (76.7)	23 (76.7)	19 (95.0)	4 (100)	3 (100)
Current age (years), mean ± SD	11.5 ± 4.7	14.4 ± 3.3	10.7 ± 3.6	12.1 ± 3.3	11.2 ± 5.5	13.7 ± 1.5
Disease duration (years), mean ± SD	6.2 ± 4.3	4.4 ± 2.7	4.0 ± 3.3	5.5 ± 3.3	5.3 ± 3.6	8.7 ± 4.0
Raynaud's phenomenon, n (%)	12 (20)	11 (36.6)	6 (20)	8 (40)	4 (100)	3 (100)

JIA: juvenile idiopathic arthritis; SLE: systemic lupus erythematosus; JDM: juvenile dermatomyositis; LSc: localized scleroderma; SSc: systemic scleroderma; MCTD: mixed connective tissue disease.

Table 2

Nailfold capillaroscopy and disease activity in patients with autoimmune rheumatic diseases (n = 147)

	JIA n = 60	SLE n = 30	JDM n = 30	LSc n = 20	SSc n = 4	MCTD n = 3
Normal, n (%)	56 (93.3)	28 (93.4)	8 (26.7)	20 (100)	0	0
Unspecific microangiopathy, n(%)	2 (3.3)	1 (3.3)	0	0	0	0
SD-pattern, n (%)	1 (1.7)	1 (3.3)	22 (73.3)	0	3 (75)	3(100)
Inconclusive, n (%)	1 (1.7)	0	0	0	1 (25)	0
Disease activity, n (%)	30 (50)	6 (20)	26 (86.6)	7 (35)	4(100)	3 (100)
P	0.249	0.730	0.002	—	—	—

JIA: juvenile idiopathic arthritis; SLE: systemic lupus erythematosus; JDM: juvenile dermatomyositis; LSc: localized scleroderma; SSc: systemic scleroderma; MCTD: mixed connective tissue disease.

the oligoarticular and polyarticular subtypes. Twelve (20%) patients showed RP, which was associated with NFC changes ($P = 0.013$). In addition, no association of NFC with disease activity, presence of RF and ANA was observed in the three JIA subtypes (Table 2).

Of the 30 patients with SLE, six (20%) showed clinical and laboratory activity on the examination. Regarding NFC, only two (6.6%) patients showed changes (incipient SD-pattern and unspecific microangiopathy). Four patients positive for anti-RNP showed no changes on NFC. No elongated, tortuous, and crossed capillaries were observed. Nailfold capillaroscopy associated with neither SLEDAI nor RP presence (Table 2).

Of the 30 patients with JDM assessed, 26 (86.6%) were on the active phase of the disease. Regarding NFC, 22 of the 26 exams (84.6%) performed during the active phase of the disease showed the SD-pattern, while the four exams performed during disease remission were normal ($P = 0.002$) (Table 2). Thus, in 26 of the 30 patients (86.6%) assessed, the clinical and laboratory data were associated with the NFC findings. No association was observed between the NFC results and cutaneous changes, muscle weakness, increased levels of muscle enzymes, or acute phase tests.

Regarding NFC findings, the deletion score and number of dilated and bushy capillaries were statistically greater in the group with active disease ($P = 0.004$, $P = 0.001$, $P = 0.009$, respectively). No association was observed between the deletion score, number of dilated bushy capillaries and megacapillaries, and cutaneous and muscular changes, when the variables were assessed separately. The capillaroscopic changes and their association with disease activity are shown in Table 3.

Table 3

Distribution of the patients with juvenile dermatomyositis according to capillaroscopic changes and disease activity

Capillaroscopic changes (mean)	Active disease (n = 26)	Inactive disease (n = 4)	P
N. micro-hemorrhages ⁺	2.15	2.5	0.677
N. capillary dilation ⁺⁺	1.77	0.12	0.001*
N. megacapillaries ⁺⁺	0.18	0	0
N. bushy capillaries ⁺⁺	0.45	0.03	0.009*
Deletion score ⁺⁺⁺	2.06	0.5	0.004*

*Student *t* test. ⁺Sum of the number of hemorrhages/number of fingers with hemorrhage; ⁺⁺Sum of the number of changes/total number of fingers assessed; ⁺⁺⁺Sum of the deletion score/number of fingers with deletion.

All 20 patients with localized scleroderma had normal NFC. No association with disease activity was observed. Four patients with SSc were assessed. On clinical exam, all had RP, cutaneous thickening and sclerodactyly. Three (75%) had healed digital ulcers. No patient had fever, dyspnea, arthritis, or arthralgia. Two female patients reported dysphagia and had changes on EGD, and, on lung computed tomography, pulmonary fibrosis. All echocardiographies performed were normal. Three of four (75%) children showed the SD-pattern with reduced capillary density, severe capillary deletion, and 'giant' and dilated capillaries. In one female patient, NFC could not be performed because of poor visualization of the capillaries due to important skin thickening.

Three patients diagnosed with MCTD were assessed. All underwent echocardiography, PFT and EGD, which resulted normal. On NFC, the SD-pattern was observed with reduced capillary density, severe deletion and few dilated capillaries. All patients had active disease.

DISCUSSION

NFC has proved to be very useful for the diagnosis of the AIRD of the scleroderma spectrum. The SD-pattern is considered highly specific and sensitive to the diagnosis of SSc, being found in up to 80% of the patients, but can also be seen in patients with dermatomyositis and MCTD.⁴⁻⁶

The SD-pattern has not been described in JIA.¹⁹ Only non-specific changes, such as capillary tortuosity and elongation, increased subpapillary venous plexus visualization, and micro-petechiae, can be found. Those changes are more often found in patients with polyarticular JIA and positive for RF and ANA.^{19,20} In our study, those changes were not found, maybe because of the small amount of patients with those antibodies. However, patients with RP show more changes on NFC, indicating that they probably have vasculopathy.

SLE is a multisystemic disease that can affect all organs in the body. Vascular lesions are the pathological markers of that condition and comprise hemorrhages, digital infarctions, and cutaneous lesions. Several authors have described unspecific changes on NFC, such as elongated, tortuous, and crossed capillaries in approximately 30% of those patients. Such findings do not depend on the presence of the RP.²¹⁻²³ Reduced capillary density and increased capillary diameters occur more frequently in individuals with the RP.²⁴ The SD-pattern is rare and described in 5%–10% of the patients

with SLE. In our study no elongated, tortuous, and crossed capillaries were found; however, the NFC changes (SD-pattern and unspecific microangiopathy) were associated with the RP, as reported in the literature. In a study with children and adults, the SLEDAI and presence of anti-RNP antibodies were associated with changes on NFC.²⁵ In our study the four patients positive for anti-RNP showed no changes on NFC.

In JDM the SD-pattern is present in approximately 60% of the patients.⁶ Although usually undistinguishable from the changes found in scleroderma, the microangiopathy of dermatomyositis shows more bushy capillaries, with exuberant branching.²⁶ In addition, the changes seen in dermatomyositis usually have a more dynamic character than those from scleroderma, and can rapidly subside with disease control, as seen in our study. Several studies have reported that the intensity of the morphological changes on NFC correlate with the clinical course and the more severe forms of disease, such as ulcerative complications and calcinosis.²⁷⁻³⁰ In our study, disease activity was associated with capillaroscopic changes, indicating that NFC is an adequate method to monitor the course of JDM.

SSc is characterized by autoimmune changes, microvascular abnormalities and fibrosis of the skin and internal organs. The early diagnosis and assessment of the manifestations that indicate disease activity are not always easy to obtain; thus, NFC is a method that allows the early detection of microvascular changes, characterized in 90% of the patients as the SD-pattern.^{5,31} All our patients with SSc had the SD-pattern on NFC. An association with more severe deletion on NFC, pulmonary fibrosis, and digital ulcers in adults has been reported.³²⁻³⁴ However, because of the small number of patients, we could not assess that association in children.

Localized (cutaneous) scleroderma usually shows no changes on NFC, as reported in our study.³⁵ A study with 27 adults with localized scleroderma has reported that the only two patients with SD-pattern changes on NFC progressed to SSc.³⁶ In our study no patient progressed to the systemic form of the disease.

On NFC, MCTD shows the SD-pattern in approximately 60% of the adults.³¹ Most of those patients develop sclerodermic manifestations.³⁵ So far, studies have not been conducted with children. In our cohort all patients had the SD-pattern on NFC.

NFC proved to be an important method to aid the diagnosis of AIRD with vascular structural changes. It was also useful to

assess disease activity in JDM. Because it is relatively simple, easily performed and provides valuable information, the benefits easily overcome the costs. However, full training with an expert is required. Although the diagnostic criteria do not

include NFC, it is a complementary and useful test to assess the microcirculation of patients, being, thus, one more tool, along with clinical and laboratory findings, to aid rheumatologists in diagnosing AIRD.

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