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REVIEW ARTICLE

The current role of capillaroscopy in vasculitides

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Abstract

Nailfold capillaroscopy (NFC) has gained remarkable interest among rheumatologists because of its utility in both clinical practice and research activity. Nevertheless, there has been scarce attention on its potential in other rheumatic disorders such as vasculitis. We perform a systematic review of literature on NFC in noninfectious vasculitides, with the aim to provide an overview of the main NFC changes described, to discuss the current evidence supporting its clinical impact and applications in daily practice and to provide future research fields.

Keywords Capillaroscopy · Nailfold · Vasculitis

Introduction

Vasculitides are a heterogeneous group of diseases characterized by inflammation of blood vessels and subsequent ischemia and damage to the organs supplied by these vessels [1]. Vasculitides may be classified by cause (broadly dichotomized into infectious vasculitis versus noninfectious vasculitis), location (localized or systemic), and size of vessel.

Currently, noninfectious vasculitides are nosologically divided on the basis of the size of vessel predominantly affected, following Chapel-Hill nomenclature that was recently updated [2].

Nailfold capillaroscopy (NFC) is an in vivo, non-invasive, and inexpensive imaging technique that allows the direct observation of the capillary network in living tissue throughout the skin [3]. It has gained remarkable interest among rheumatologists because of its utility in both clinical practice and research activity [4–6].

Although to date, several studies have demonstrated the diagnostic and prognostic role of NFC in rheumatic disorders, especially in systemic sclerosis (SSc), dermatomyositis (DM), and Raynaud phenomenon (RP) [7–9], there has been scarce attention on its potential in other rheumatic disorders such as vasculitis.

Vasculitis may hypothetically offer an ideal scenario for the use of NFC due to its active involvement of vessels including capillaries. This induces to consider that NFC may play a key role in providing useful information for the management of patients with vasculitis. On this light, the aim of this review is to provide an overview of the main NFC changes described in

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noninfectious vasculitis in order to discuss the current evidence supporting its clinical impact and applications in daily practice and to provide future research fields.

Methods

Research strategy

To identify all available studies, a detailed research pertaining to the topic of review was conducted according to PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines [10]. A systematic research was performed in the electronic databases (PubMed and EMBASE), using the following search terms in all possible combinations: capillaroscopy, videocapillaroscopy, nailfold capillary, capillary microscopy, vasculitis, Takayasu arteritis, giant cell arteritis, polyarteritis nodosa, Kawasaki disease, ANCA-associated vasculitis, microscopic polyangiitis, granumalomatosis with polyangiitis, eosinophilic granulomatosis, crioglobulinemic vasculitis, IgA vasculitis, Behçet disease, Cogan's syndrome, lupus vasculitis, rheumatoid vasculitis, sarcoid vasculitis. Also the old nomenclature was included in research: Wegener's vasculitis, Churg-Strauss vasculitis, Schönlein-Henoch vasculitis.

The Boolean operators "AND" and "OR" were used in combining more key words to increase the specificity and reduce the sensitivity of our search. In addition, the reference lists of all retrieved articles were manually reviewed. In case of missing data, study authors were contacted by e-mail to try to retrieve original data. Two independent authors (CB and SG) analyzed each article and performed the data extraction independently. In case of disagreement, a third investigator was consulted (MG). Discrepancies were resolved by consensus.

Inclusion and exclusion criteria

All relevant literature in the field of NFC and vasculitis published in the last 40 years has been systematically reviewed (a large period of review was considered since there are not previous reviews in this topic). We included original articles concerning studies in humans, published between January 1978 and March 2018. We excluded from this review the following types of publications: articles not published in English, case reports, letters to the editor, and/or non-human studies.

Articles non-available on web archives were also excluded. Infectious vasculitis, or vasculitis caused by the invasion of vessel walls by pathogens, were not comprised in the review. Research results were screened to avoid duplicates. Titles, abstracts, and full reports of articles identified were systematically screened with regard to inclusion and exclusion criteria.

Results

Sixty publications were identified in PubMed and EMBASE databases. Manual research leads to find seven additional articles. At the end of the selection process, 13 articles were included in the present review. The results of the research strategy are illustrated in Fig. 1. Details and characteristics of the studies included in the review are illustrated in Table 1. Technical aspects are reported in Table 2. Table 3 shows the NFC alterations described and relations with activity and clinical characteristics.

IgA vasculitis

Greenberg et al. [11] described in a cross-sectional study, 28 patients with IgA vasculitis (IAV)—formerly Schönlein-Henoch purpura—and 76 healthy controls (HC). The patients' group was observed in a time comprised from 34 to 161 months from IAV diagnosis. Normal capillaries were found in 46% of IAV patients with respect to 94% of HC. The main NFC abnormality was the loop dilation that was found in 51% of patients vs 11% of HC, with an optimal visibility of venous plexuses. No significant correlation between NFC abnormalities and organ involvement or disease activity was found in this cohort.

Martino et al. [17] reported a longitudinal observation (16 months) of 31 cases of IAV, including 48 HC. In the acute phase of IAV, the authors found NFC alterations such as tortuosity of capillaries, edema, derangement of capillaries, branching, and sludging of hematic column (granular flux). These NFC abnormalities remain unchanged during the 16-month follow-up.

Zampetti et al. [20] observed 31 patients with IAV in the acute phase of disease and after 6 months. Twenty HC were also recruited. They found density reduction in the 40% of patients, disarrangement with avascular areas and neoangiogenesis in 20% of patients, morphologic alteration in 46.7% of patients, increased capillary length in 40% of patients, and microhemorrhagias in 10% of patients and macrohemorrhagias in 10% of patients. Edema was severe in 74.2% of patients, moderate in 22.6%, and mild in 3.2%. To the contrary to Greenberg et al., they had not reported enlarged capillaries.

A significant difference between IAV patients with acute phase of disease and HC in loop density, length, and shape was reported ($p < 0.01$). Furthermore, in the 6-month follow-up, they observed the normalization of most of the NFC parameters (except minimal architectural and shape abnormalities in 10% of patients) but persistence of edema (severe in 25%, moderate in 55%, and mild in 20% of patients), contrarily to Martino et al.

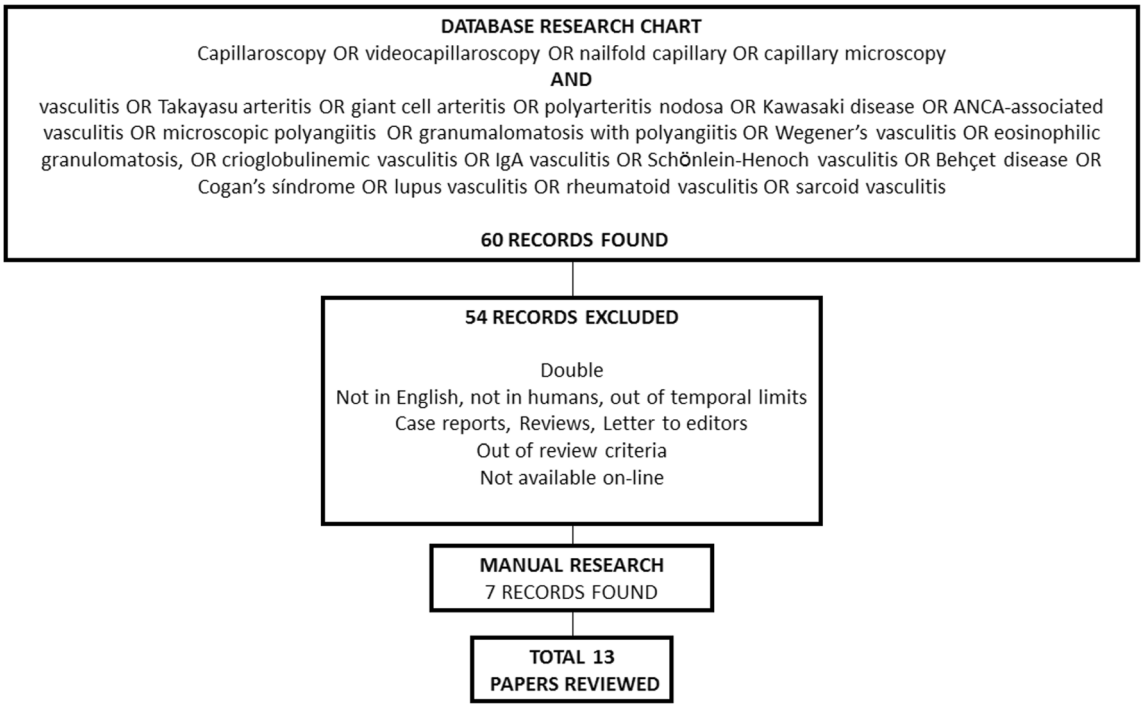

Fig. 1 Research strategy

Kawasaki disease

There was a single article regarding Kawasaki disease (KD) conducted by Huang et al. [21] involving 64 patients with KD (31 in subacute, afebrile phase and 33 in convalescent phase of disease) and 36 HC.

NFC changes in the morphology of capillaries were detected in KD patients with respect to HC. Larger diameters of arterial and venous limbs, higher intercapillary distance, and decrease in the loop numbers were the main NFC changes reported. Abnormal loops and intercapillary distance improved from subacute (afebrile) to convalescent phase.

Behçet disease

Vaioupoulos et al. [13] described 33 patients with Behçet disease (BD) and 40 HC in a cross-sectional study. The NFC alterations were graduated by severity in the following stages: 0 = normal; A = slightly dilated vessel; B = diameter > 3 times

Table 1 Characteristics of studies included in the review

Year	Author	Disease	No. of patients	No. of controls	Sex of patients F/M	Patient's age in years mean ± SD (range)
1983	Greenberg [11]	IAV	28	76	NS	(3–19 months)
1995	Vaiopoulos [13]	BD	33	40	14/19	38 ± 11
1996	Kuryliszn-Moskal [12]	RA vasculitis	79	30	63/16	52 ± 12
1998	Kuryliszn-Moskal [14]	RA vasculitis	80	30	63/17	52 ± 12
2000	Anders [16]	GPA and TAO	19 *	46	NS	34.3 ± 15
2002	Martino [17]	IAV	31	48	15/16	(8–9)
2003	Witkowska [18]	RA vasculitis	37	18	37/0	49 (21–20)
2004	Rossi [15]	MC	29	NO	19/10	66.05 (40–83)
2009	Movasat [19]	BD	128	NO	50/63	37 ± 10
2009	Zampetti [20]	IAV	31	20	14/18	7.5 ± 3.4
2012	Huang [21]	KD	64	36	47/53	4.09 ± 1.24 afebrile, 3.72 ± 1.3 convalescent
2014	Aytekin [22]	BD	40	40	15/5	34 ± 10
2016	Alan [23]	BD	82	82	34/48	36.95 ± 11.80

IAV IgA vasculitis, *RA* rheumatoid arthritis, *BD* Behçet disease, *CM* mixed crioglobulinemia, *GPA* granulomatosis with polyangiitis, *TAO* tromboangiigtis obliterans, *KD* Kawasaki disease, *NS* not specified, *part of a study on multiple rheumatic diseases

Table 2 Technical characteristics of studies

Year	Author	Instrument	Magnification	Site
1983	Greenberg [11]	Microphotography	NS	NS
1995	Vaiopoulos [13]	Stereomicroscope + camera	× 250	10 fingers and toes
1996	Kuryliszn-Moskal [12]	Stereomicroscope	NS	8 fingers
1998	Kuryliszn-Moskal [14]	Stereomicroscope	NS	8 fingers
2000	Anders [16]	Stereomicroscope	NS	10 fingers
2002	Martino [17]	NS	NS	NS
2003	Witkowska [18]	NS	NS	8 fingers
2004	Rossi [15]	VCP	NS	NS
2009	Movasat [19]	Microscopy	× 3.2	8 fingers
2009	Zampetti [20]	VCP	× 200	8 fingers
2012	Huang [21]	Stereomicroscope + video laser Doppler flowmetry	× 800	4 left finger
2014	Aytekin [22]	Videodermatoscope	× 30	10 fingers
2016	Alan [23]	VCP	× 200	8 fingers

VCP videocapillaroscopy, *NS* not specified

the normal size; widely dilated and indistinct capillaries; C = microhemorrhages, density < 10/mm.

The authors found capillary abnormalities in 75% of BD patients with respect to HC (7%). Interestingly, it was observed that a more severe stage of NFC microangiopathy was related with a longer disease duration. Curiously, pathergy test was more frequently positive in patients with stage B of NFC alterations (89%) with respect to stage 0 (25%), and globally associated with medium or severe capillary alterations. Eye lesions were present in 37% of patients in stage 0 of NFC alterations, 85% in stage A, 50% in stage B, and 50% in stage C. Skin lesions were present in all the patients in stage B or C versus 73% of patient in stages 0 and A together. Arthritis and arthralgia were more present in patients with low NFC stage (0 = 74%, A = 85%) with respect to more severe (B and C together = 44%).

Movasat et al. [19] included 128 patients in a prospective study. NFC abnormalities were found in 40% of patients. Enlarged capillaries were present in 26% of BD patients, microhemorrhages in 16%, and capillary loss in only one patient. The multivariate analysis showed an association between enlarged capillaries and lower age at disease onset ($p = 0.01$), high blood pressure ($p = 0.001$), and superficial phlebitis ($p = 0.03$).

Similarly, Aytekin et al. [22] studied 40 BD patients and 40 HC in a prospective case-control study showing capillary dilation in 35% of BD patients, microhemorrhages (15%), and avascular areas (7.5%). No NFC alterations were found in HC.

The presence of capillary dilation and microhemorrhages reached a statistical significance ($p < 0.05$), but not the presence of avascular areas and capillary density. No correlation was also found between NFC changes and both clinical findings and treatment.

Alan et al. [23] conducted a cross-sectional study including 82 BD patients and 82 age- and sex-matched HC. Among patients, 75 showed at least one capillary change including: tortuosity (91.5%), bizarre capillaries (9.8%), microhemorrhages (4.9%), and giant capillaries (2.4%).

The difference in tortuous and bizarre capillaries between BD patients and HC was significant ($p < 0.001$ and $p = 0.017$ respectively). Capillary density was significantly reduced with respect to HC (10.17 ± 1.23 and 11.45 ± 0.99 respectively, $p < 0.001$). Among patients, the disease duration was significantly longer in patients presenting tortuosity or any NFC alteration ($p = 0.01$).

Granulomatosis with polyangiitis and thromboangiitis obliterans

Anders et al. [16] in a prospective study reported 12 patients with granulomatosis with polyangiitis (GPA, formerly Wegener's vasculitis) and 7 with thromboangiits obliterans (TAO). NFC abnormalities detected were classified as enlarged capillaries, giant loops, avascular areas, tortuous capillaries, bushy capillaries, and hemorrhages.

In the GPA cohort, avascular areas were described in almost 92% of patients, crossed capillaries in 67%, bushy capillaries in 33%, and microhemorrhages in 50%. No relationship was found between avascular areas and digital vasculitis.

In the TAO cohort, all patients presented crossed capillaries whereas microhemorrhages were described in 71% of patients, enlarged capillaries in 29%. Only a single patient presented giant capillaries and bushy capillaries.

Cryoglobulinemic vasculitis

Rossi et al. [15] examined 29 patients with mixed cryoglobulinemia (MC), 28 of them secondary to hepatitis C virus infection, presenting with weakness (24 patients), arthralgia (24), purpura (16), peripheral neuropathy (20),

Table 3 Principal NFC alterations described and relationship of NFC picture with clinical characteristic of vasculitis

Author, year	NFC alteration (% of patients)	Relationship with activity	Relationship with clinical characteristic of vasculitis
IgA vasculitis			
Greenberg 1983 [11]	Loop dilation (50%) Visibility of subpapillary plexus	Not found	Not found
Martino 2002 [17]	Tortuosity (100%) Edema (60%) Disarrangement (50%) Branching (20%) Sludging flux (20%)	Not found	ND
Zampetti 2009 [20]	Density reduction (40%) Disarrangement (20%) Avascular areas (20%) Neangiogenesis (20%) Morphologic alterations (46.6%) Increased capillary length (40%) Microhemorrhagias (10%) Macrohemorrhagias (10%) Edema (100%)	Normalization of the most NFC parameters in 6 months	ND
Kawasaki disease			
Huang 2012 [21]	Larger diameters of arterial and venous limbs* Increased number of abnormal loop* Density reduction*	Abnormal loops and intercapillary distance improved from post-acute to convalescent phase	Red blood cell velocity was associated with increased coronary artery diameter ($p = 0.031$)
Behçet disease			
Vaiopoulos 1995 [13]	Enlarged capillaries microhemorrhages, reduced density (75%)	ND	NFC severity corresponded to larger disease duration (n.s) Pathergy test positivity associated with severe NCF alterations ($p = 0.01$) Eye lesions, arthritis and arthralgia associated with mild NFC alterations (n.s)
Movasat 2009 [19]	Enlarged capillaries (26%) Microhemorrhages (16%) Capillary loss (1 pt.)	ND	Enlarged capillaries associated with lower age at disease onset ($p = 0.01$) high blood pressure ($p = 0.001$) and superficial phlebitis ($p = 0.03$)
Aytekin 2014 [22]	Enlarged capillaries (35%) Microhemorrhages (15%) Avascular areas (7.5%)	ND	Not found
Alan 2016 [23]	Tortuosity (91.5%) Bizarre capillaries (9.8%) Microhemorrhages (4.9%) Giant capillaries (2.4%)	ND	Alteration associated with disease duration ($p = 0.01$)
Granulomatosis with poliangiitis			
Anders 2000 [16]	Avascular areas (92%) Crossed capillaries (67%) Bushy capillaries (33%) Microhemorrhages (50%)	ND	Not found
Tromboangiitis obliterans			
Anders 2000 [16]	Crossed capillaries (100%) Microhemorrhages (71%) Enlarged capillaries (29%) Giant capillaries (1 pt., 14%) Bushy capillaries (1 pt., 14%)	ND	ND
Mixed cryoglobulinemia			
Rossi 2004 [15]	Morphologic abnormalities § (93%) Altered orientation (62%) Shortened capillaries (59%)	ND	Glomerulonephritis associated with higher score of capillary alterations ($p = 0.01$)

Table 3 (continued)

Author, year	NFC alteration (% of patients)	Relationship with activity	Relationship with clinical characteristic of vasculitis
	Neoangiogenesis (69%) Evidence of subpapillary plexus (45%) Microhemorrhages (34%) Giant capillaries (2 pt., 7%) Avascular areas (2 pt., 7%)		
Rheumatoid arthritis vasculitis			
Kuryliszn-Moskal 1996 [12]	ND	ND	sICAM-1 elevated in patients with severe NFC alterations (n.s)
Kuryliszn-Moskal 1998 [14]	Tortuous or meandering loops (93.8%)	ND	The capillary score correlates with disease duration ($p < 0.05$), cutaneous vasculitis ($p < 0.001$), joint erosions ($p < 0.5$) and systemic vasculitis ($p < 0.05$)
Witkowska 2003 [18]	Abnormalities in all patients: morphologic changes, reduced density, and increased visibility of subpapillary plexus		sICAM-1 elevated in patients with severe NFC alterations

ND not determined, *pt.* patients, *n.s.* not statistically significant, *in post-acute vs convalescent phases and in patients vs controls, § morphologic abnormalities include tortuosity and apical enlargement

Raynaud phenomenon (8), and membranoproliferative glomerulonephritis (9) confirmed by renal biopsy. They registered capillary tortuosity, capillary orientation and length, presence of enlarged and giant capillaries, avascular areas, hemorrhages, disorganization of the vascular array, and angiogenesis (described as highly tortuous and arborized capillary loops). The sum of alterations was scored between 0 (absent) and 7 (severe). Twenty-seven patients (93%) showed morphological abnormalities, including tortuosity and apical enlargement; 18 (62%) had capillaries with deeply altered orientations; 17 (59%) had shortened capillaries and 20 (69%) had neoangiogenetic phenomena. Relatively common findings included evidence of deep venous plexuses (13 cases, 45%) and hemorrhages (10 cases, 34%). In two cases, giant capillaries were found, and other two patients presented avascular areas. Patients with glomerulonephritis had a significantly higher score of capillary alterations, respect to non-nephritic patients ($p = 0.01$). No relationship was found with the other clinical manifestations.

Rheumatoid arthritis

Kurylizyn-Moskal [12] examined 79 patients with rheumatoid arthritis (RA), 32 of them with clinical signs of vasculitis, 47 without signs of vasculitis and 30 HC. The aim was correlate capillary damage and levels of soluble intracellular adhesion molecule-1 (sICAM-1), a membrane-bond molecule highly expressed in inflammation.

The capillary changes were classified according a scoring between 0 and 3 (0 = no signs of capillary vasculitis, 1 = mild, 2 = moderate, 3 = severe changes), based on density, capillary morphology, visibility of sub-papillary plexus, and architectural derangement.

All RA-vasculitis patients showed moderate or severe NFC changes, whereas only 59% of RA patients without vasculitis demonstrated NFC changes. Seventy-five percent of patients with severe capillary alteration have sICAM-1 levels exceeding the cutoff value (not statistically significant).

The same authors described successively NFC changes of 80 RA patients (33 with signs of systemic vasculitis) and 30 HC [14] in a study focused to correlate cytokines and NFC. They registered abnormalities as tortuous or meandering loops in 93.8% of patients. The 0–3 previously reported scoring was adopted for classified the NFC findings. They described mild changes in 16.3% of patients, moderate in 56.3%, and severe in 21.2%. The capillary score correlates with disease duration ($p < 0.05$), cutaneous vasculitis ($p < 0.001$), joint erosion ($p < 0.5$), and systemic vasculitis ($p < 0.05$). Soluble CD4 (sCD4), soluble CD8, tumor necrosis factor-α, soluble interleukin-6 (IL-6), and soluble receptor for IL-6 were assessed. From those, only sCD4 resulted significantly associated with severe vascular changes ($p < 0.05$).

Witkowska et al. [18] compared sICAM-1 and selenium levels with NFC evaluation. They observed 37 patients and 18 HC. The alterations were scored with the system reported above. All the patients with RA showed capillary alterations. According to Kurylizyn-Moskal et al. [12] in the groups with

moderate and severe capillary alterations, the levels of sICAM-1 were elevated, whereas in the group with mild capillary changes, levels of molecule did not differ from the control group. Levels of selenium were not correlated with NFC score in a significant way.

Discussion

Despite the use NFC is increasing among the rheumatologists in daily clinical practice in different rheumatic disorders [2–9], there is a gap of knowledge regarding the potential utility in vasculitis. To the best of our knowledge, this is the first review exploring the current literature of NFC in vasculitis.

The results of the studies analyzed suggest to consider the NFC as a useful tool to add further valuable information in the workout of vasculitis patients.

As expected, vasculitis showed several and heterogeneous NFC changes which confirm the microvascular involvement in this group of diseases. However, the most of NFC abnormalities are classifiable as minor or nonspecific alterations (i.e.,: increased tortuosity, microhemorrhages, enlarged, bushy, and bizarre capillaries, see Fig. 2). An architectonic disarrangement was also a very frequent finding.

On the other hand, some vasculitides such as IAV, BD, GPA, TAO, and MC showed major or specific (typical of the scleroderma pattern) NFC changes, such as giant capillaries, avascular areas, or capillary loss, although these features were present only in few group of patients [15, 19, 20, 22]. These last findings are hard to interpret: it is possible that representing a deep capillary damage is due to primary vasculitis. In not possible to exclude, however, that in the observed populations were present some cases of overlap with a scleroderma-related disease (SSc, DM, or mixed connective tissue disease).

For example, in GPA [16], avascular areas were described in 90% of patients, other than nonspecific alterations such as crossed and bushy capillaries and microhemorrhages. Although the results need to be confirmed in more and larger studies, it suggests a severe microvascular involvement in GPA vasculitis which could depict a specific NFC sign of disease.

Regarding the nonspecific alterations, in BD, three papers reported the same type of alterations: enlarged capillaries, reduced density (in some case avascular areas), and microhemorrhages [13, 19, 22].

In RA studies, as reported previously, the NFC alterations described were mainly tortuous or meandering loops in the majority of patients [12, 14, 18].

In MC vasculitis, the author suggested that a cluster of "tortuous and short capillaries with abnormal orientations and with neoangiogenetic shapes" might be regarded as a typical finding [15].

In IAV, the NFC findings from the three studies are conflicting. All the studies reported NFC alterations, but the types of alterations are different. Greenberg et al. [11] reported enlargement of vessels, whereas Martino et al. [17] reported most frequently tortuosity and branching, and Zampetti et al. [20] described reduction of density with avascular areas.

Some papers described correlation between NFC alteration and clinical features. In BD, the NFC severity in BD was associated with disease duration [13, 23] and to the positivity of pathergy test; capillary ectasias were associated with high blood pressure and phlebitis; contrarily, arthralgia, arthritis, and eye involvement (features of early disease) were associate with less NFC alterations [13, 19].

In MC, vasculitis was described a significant relation between a sever NFC picture and the presence of glomerulonephritis, that may have a clinical relevance [15].

In the RA studies, the authors assumed the presence of NFC alterations as clue of systemic vasculitis. The NFC severity correlates with disease duration, cutaneous vasculitis, joint erosion and systemic vasculitis, and to sICAM-1 and pro-inflammatory cytokines [12, 14, 18].

The correlation between NFC picture and disease activity was explored in two diseases: in IAV, one author reports the

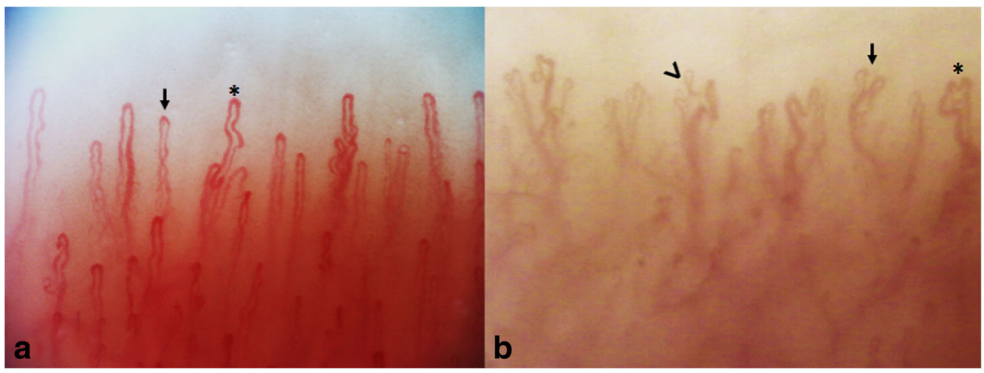

Fig. 2 Nailfold capillaroscopy (× 200). **a** Normal pattern characterized by a regular distribution, parallel orientation, regular shape (U-shaped capillaries and one slightly tortuous capillary, asterisk, and a single-crossed capillary, arrow). **b** Nonspecific NFC alterations in a patient with RA vasculitis. Note that in each dermal papilla are visible groups of three or more bushy (arrowhead), highly tortuous (asterisk), or multiple-crossed (arrow) capillaries. The orientation between capillaries is not parallel

normalization of the NFC picture in non-active phases [20], but the other two works have not confirmed the finding [11, 17]. The paper exploring KD describes amelioration of NFC picture in convalescence [21].

For the sum of results reviewed, the following consideration could be done.

First, NFC seems more useful in vasculitis affecting small vessels than vasculitis affecting large vessels. This aspect could be supported by the fact that NFC changes were most largely frequent in patients with vasculitis of small vessels. Anyway, the presence of NFC alterations in large vessel vasculitis may not be excluded, because the inflammation of large vessel did not exclude the involvement of microcirculation. Second, NFC may provide more useful information regarding organ involvement and disease activity. In fact, some works suggested that NFC alteration may be related to or disease characteristics [13, 15, 19] or disease activity [20, 21]. These observations open the doors to a perspective area of research regarding the possible prediction role of NFC in these patients. Third, the microangiopathy in vasculitis is different with respect to the evident changes present in the scleroderma pattern, showing mainly nonspecific alterations. To date, a wide range of capillaroscopy alterations are globally described as "nonspecific," in different disease and conditions, as diabetes [24] or systemic lupus erythematosus (SLE) [25]. It is possible that clusters of nonspecific alterations characterize a single vasculitis, as some authors reported for IAV, BD, and MC [11, 13, 15, 17, 19, 20, 22, 23]. This aspect must be evaluated in further, larger studies, addressed to explain if some alterations or clusters of alterations may represent "specific" capillaroscopy pattern for vasculitis. Fourth, we note also, that in the older, the methodology and the definitions of abnormalities were heterogeneous and sometimes difficult to interpret, and this fact underlines once again the necessity of standardization in capillaroscopy [26, 27]. Finally, to date, we found no data, regarding NFC in the other vasculitides comprised in Chapel-Hill definitions. In particular, no papers addressed specifically on SLE vasculitis were found.

We are aware that the review presents some weaknesses. First, it put together diseases of young and adult age. The cause of this decision was the fact that some vasculitides of children may also be present in adult age. Second, the majorities of the revised studies involved a low number of patients; this is due to the fact that vasculitides are rare diseases and studies on larger cohorts need multicenter enrollment. Third, the large time observed. This is due to the fact that there is no precedent review in this topic. This point also reflects in the fact that some papers were not available in the online archives of the journals.

Conclusions

In conclusion, in spite of a wide range of NFC changes reported in vasculitis, the evidence for the clinical impact is still poor, applications of NFC in vasculitis are still being developed, and further opportunities with ongoing research strategies are likely to arise, especially to test specificity of NFC changes and its criterion and concurrent validity and reliability in multicenter studies.

The overview confirms that NFC is a safe and non-invasive tool able to help the clinician in the assessment of vasculitis, and in some cases, may aid in define the disease status and suggest possible complications. However, there is still a deal of work to make to confirm the findings and elucidate the clinical impact of NFC in vasculitis.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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