

COMMON MISTAKES IN CAPILLAROSCOPY

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Abstract. Nail fold capillaroscopy (NFC) is a non-invasive examination and the „gold standard“ in rheumatology practice to evaluate the microcirculation and distinguish primary from secondary Raynaud's phenomenon (RP). Alternatives to videocapillaroscopy are USB microscopy, dermatoscopy and ophthalmoscopy. Before the capillaroscopy examination, a detailed general history (including concomitant diseases) and occupational history (including a history of recent trauma to the fingers or onychophagia), a history regarding the patient's hobbies, practicing sports and physical activity, history of taking medications (beta-blockers, vasodilators, anticoagulants, antihypertensives), as well as the use of other vasoactive substances (tobacco, caffeine, cannabis, cocaine, amphetamines) should be taken. A detailed history regarding discoloration of the fingers is necessary to confirm the diagnosis of Raynaud's phenomenon (RP). Capillaroscopic examination should be carried out under certain conditions (not during an attack of RP, after acclimatization, in a certain position of the patient, without consumption of coffee and smoking before the examination, without manicure procedures in the last 15-30 days, examination of all 8 fingers, excluding those with recent trauma and/or infection). Correctly following all these steps will avoid technical errors that can change the interpretation of the result. It is necessary for the examiner to have a good knowledge of the normal capillaroscopic pattern, the variations of the norm in adults, the differences that might be found between children and adults, as well as the different pathological findings and specific patterns (‘‘scleroderma’’ and ‘‘scleroderma-like’’ type) in diseases occurring with secondary RP. While in rheumatology practice there are defined criteria for ‘‘scleroderma’’ and ‘‘scleroderma-like’’ capillaroscopic finding, the changes in some paraneoplastic, socially significant (AH and DM), occupational (VD) and infectious diseases (COVID-19) occurring with microangiopathy, which can lead to misinterpretation of the finding. The ‘‘scleroderma-like’’ pattern also differs in different rheumatic diseases and the findings can also be misleading. The results of the study must be carefully interpreted with a view to the correct assessment of the patients' condition.

Key words: capillaroscopy, capillaroscopy errors, norm variation, misinterpretation

INTRODUCTION

Nail-fold capillaroscopy (NFC) is a non-invasive in vivo imaging technique that, using an optical magnification instrument, allows examination of the microcirculation [1, 2, 3, 4, 5, 6, 7, 8, 9, 10]. The digital video capillaroscope allows dynamic assessment of microvascular abnormalities with optical magnification (200×) as well as computerized study of various capillary parameters [1]. Digital video capillaroscopy is currently the gold standard for morphological assessment of nail fold capillaries [6, 10, 11]. Although it can be performed in any of the anatomic sites in which terminal capillaries assume an orientation parallel to the skin (ocular conjunctiva, periareolar region, and labial mucosa), the capillaries of the nail fold of the hands are those that which, due to their availability, are routinely examined [1, 6, 9]. It is also possible to perform a capillaroscopy of the nail fold of the feet, but the informativeness of the study is significantly lower, therefore it is applied only in cas-

es of predominant appearance of the symptoms of the lower limbs, a recent manicure of the hands or in the presence of severe contractures in systemic sclerosis (SSc), which more commonly affects the hands. In most cases, RP symptoms of the toes develop later in the course of the disease, which could explain the lower incidence of capillaroscopic changes in Raynaud's phenomenon affecting the lower extremities [12]. Quantitative and morphological assessment of capillaries is the ‘‘gold standard’’ in rheumatology practice, allowing to distinguish primary Raynaud's phenomenon (RP) from secondary and to determine the presence of microvascular changes characteristic of various diseases [1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 13]. In addition, in some cases, capillaroscopy is extremely useful in monitoring the therapeutic response in patients with autoimmune diseases [3, 7, 9].

An alternative to the video capillaroscope is the USB microscope – a compact portable device con-

nected via a USB cable to a computer [3, 11]. USB microscopes also have different magnifications. [3] Unlike the specialized software of videocapillaroscopes, in the software of USB microscopes (which is not specialized) the stored images are not arranged in folders of the corresponding fingers on which they were taken and there is no possibility to automatically place a frame for measuring capillary density (it is necessary to manually mark a field 1 mm long). Despite these limitations, USB microscopes offer good capabilities for diagnostic purposes in terms of image quality and quantitative analysis, at a significantly lower cost [3].

Other possible alternatives to videocapillaroscopy are dermatoscopy and ophthalmoscopy [3, 6]. However, it should be noted that the dermatoscope has a lower magnification, which allows visualization of larger areas of the nail fold [3]. This feature is associated with lower sensitivity (60.2% vs. 81.6%) and higher specificity (92.5% vs. 84.6%) of the method compared to standard videocapillaroscopy [3].

Videocapillaroscopy with optical contact probes appears to be the most appropriate method to minimize technical failures [14].

EXAMINATION TECHNIQUE

It is necessary to take a detailed history regarding the patient's work and hobbies (practicing sports and physical activity). Patients should be asked which is their dominant hand. Medications that the patient is taking (beta-blockers, vasodilators, anticoagulants, antihypertensive medications), as well as use of other vasoactive substances (cannabis, cocaine, amphetamines) should be discussed during the examination (Fig. 1) [5]. A history of the patient's comorbidities, recent trauma to the fingers, as well as a habit of nail biting (onychophagia) and/or cuticle injury is required. The clinical manifestation of discoloration of the fingers is one of the symptoms necessary to confirm the diagnosis of Raynaud's phenomenon (RP). In cases where capillaroscopy is performed during an attack of RP, this should be reflected, and it is not recommended that capillaroscopy be performed during an attack. It is necessary to reflect the age of the patients. Patients should be specifically questioned for the presence of digital ulcerations. [5]

NFC should be carried out in a room with a temperature between 20-25°C [1, 2, 4, 6, 9, 10, 14] (22-24°C according to the national consensus for capillaroscopy [5]) in order to avoid changes

in capillary blood flow due to low skin temperature of the fingers; the patient should be at rest for at least 15-20 minutes [1, 2, 4, 5, 6, 9, 10], without exposure to extreme temperatures to avoid the appearance of vascular areas of vasoconstriction due to cold, a factor that can generate false positive results [1, 2, 4] such as spastic capillaries or slowed blood flow [9]. Patients should not consume coffee or smoke for at least four hours before the examination. (Fig. 1) [2, 9, 14]. In addition, manicure procedures should be avoided between 15 days and one month before the examination [1, 6, 9], as cuticular trauma can generate hemorrhages or capillary distortion when the cuticles are pushed [1]. To ensure optimal visibility of the capillaries in the area of the eponychium, the nail polish must be removed. [5] The patient should be seated, and the examined hand should be at the level of the heart, without pressure over the examined area [1, 4, 6]. In order to improve the visibility of the capillaries, immersion oil (cedar oil, liquid paraffin) is applied [1, 5, 6]. Examination should be done on all fingers except the thumb (ie, 8 fingers as standard) and on those fingers with active infections or recent trauma to the nail bed, as the normal pattern may be altered [1, 3, 4, 5, 6, 9]. From an international point of view, it is accepted to start with the fifth finger of the right hand, ending with the fifth finger of the left hand, to avoid errors when comparing results [1]. Image quality (focus and light intensity) and examiner's level of competence (capillaroscopy training, adherence to general and local recommendations, clinical experience) are also relevant [15]. Correctly following all these steps will avoid technical errors that can change the interpretation of the result [1]. Regarding the differences found with the different magnifications, those lower than 100× allow a panoramic view, observing the entire capillary pattern of the nail bed, while higher magnifications allow the morphological features of each capillary to be assessed [1]. Currently, the most commonly used magnification is 200×. Higher magnifications (up to 1000×) even allow observation of the individual passage of erythrocytes through the capillary loop; however, these lenses are mainly used in research and are not commonly seen in everyday practice [1]. In comparison, the dermatoscope, which has a low magnification, does not allow the morphology of the capillaries to be assessed, nor their individual measurements [1].

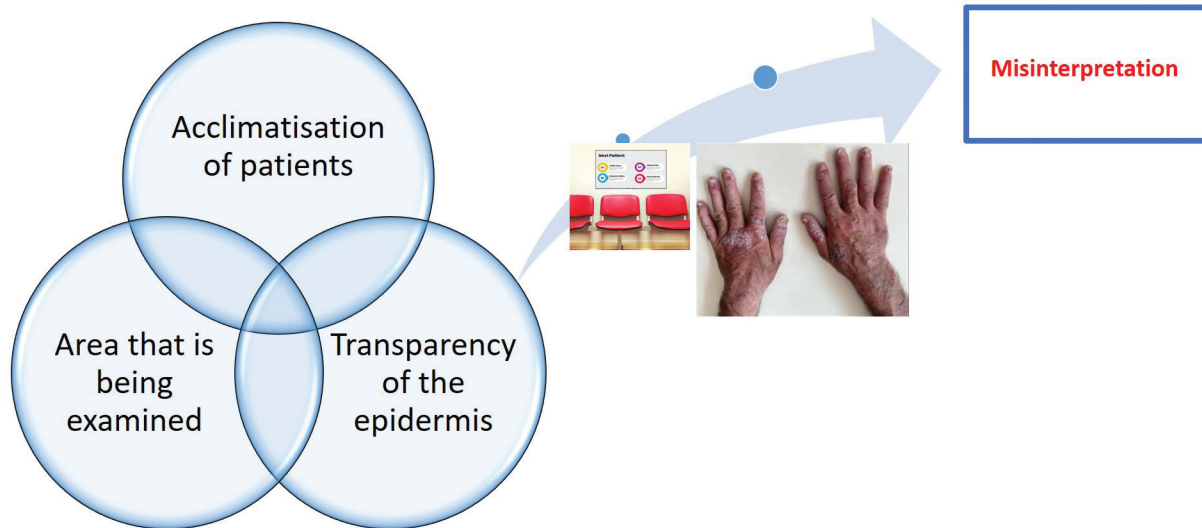


Fig. 1. Main factors responsible for the interpretation of the capillaroscopy finding

EVALUATION CRITERIA

Capillary diameters (arterial, venous arm and apical loop) are measured [3, 4, 5, 9, 10, 11], as well as number of capillaries per visual field [2, 3, 5, 9, 10, 11] (defined as mean number of capillaries in 1 mm) [2], capillary length (with a length over 300 μm the capillaries are elongated) [3, 5, 9, 10, 11, 16]. Possible presence of dilated capillaries ($\geq 20 \mu\text{m}$), giant capillaries ($\geq 50 \mu\text{m}$), morphological abnormalities, microhemorrhages (extracapillary findings, the color of which can vary from red-violet to brownish depending on the time of their formation and are clearly associated with the capillary from which they originate [11]), neoangiogenesis (the presence of capillary branches and dense capillaries as a result of a failed attempt at vascular repair in the context of tissue hypoxia [11]), avascular areas, pericapillary edema and changes in blood flow (velocity and erythrocyte stasis) [2, 3, 5, 9, 10, 11, 16].

NORMAL CAPILLAROSCOPY FINDING

Normal capillary density varies between 7 and 16 capillaries per mm. [3, 5, 9, 10, 11, 13, 17]. Capillaries are arranged in a comb-like shape and their number and morphology tend to remain stable over time [1, 18]. When observed individually, these capillaries are hairpin or inverted U shaped, between 200 and 250 μm in length, having arteriolar (6–19 μm , 15 μm by national consensus) and venous (8–20 μm) arm in a ratio of 1:2 [1, 5, 9, 11, 13, 17, 18]. Subcapillary plexus is visible in 30% [5, 10, 11] up to 60% of the normal population [1].

DIFFERENCES IN CHILDREN AND ADULTS

The normal comb-like capillaroscopic pattern can be detected from two years of age. The main differences between the capillaroscopic patterns in children and adults are: lower capillary density, greater heterogeneity, especially in capillaries with unusual shapes (36%), and greater visibility of the subcapillary venous plexus. In the elderly, it is difficult to define a normal capillaroscopic pattern, in part because of the difficulty of finding a healthy control population; however, it is clear that capillary elongation and increased tortuosity as well as secondary apical dilatation may be observed in this age group, possibly due to a longer history of microtrauma, as well as reduced cardiac output with increased peripheral vascular resistance. Finally, the subcapillary venous plexus may also be seen more easily, in part because of thinning of the skin and congestion of venules and capillaries associated with increased opening of arteriovenous anastomoses secondary to senile microangiopathic changes [1].

VARIATION OF THE NORM

Variations in the shape of capillaries are a common finding even in healthy individuals. [5, 9]. There are many unusual forms of capillaries that in themselves are not indicative of disease: crossed, curved, elongated capillaries, capillary disorganization, isolated microhemorrhages, as well as the presence of capillary edema [1]. According to the National Capillaroscopy Consensus, capillaries with folded arms

that do not cross each other or capillaries whose arms cross in one or two places, but the apical loop has a convex outward curve are considered normal [5]. In a study of 53 patients with Raynaud's phenomenon (12 cases with primary and 41 with secondary RP), nonspecific changes (dilated capillaries with arterial diameter > 0.015 mm, venous > 0.020 mm; hemorrhages; presence of elongated or increased number of tortuous capillaries) were found in 10 patients, without evidence of microangiopathy [3]. Hemorrhages are an extracapillary finding and originate from the breakdown of the hemoglobin of the erythrocytes. Hemorrhages can also be observed in healthy individuals as an expression of local trauma to the periungual tissues, and in these cases they are not associated with giant capillary loops. [5, 11]. In healthy subjects, single newly formed, atypical vessels/neoangiogenesis may be observed as a result of attempted vascular repair after local tissue trauma [5, 11]. In these cases, atypically shaped capillaries are an isolated finding, and capillary density and capillary arrangement in adjacent sections are unchanged (ie, no avascular zones and capillary disorder are observed) [5, 11].

COMPARISON OF CAPILLAROSCOPY FINDINGS OF UPPER AND LOWER EXTREMITY FINGERS

Poor visibility of the eponychium capillaries, mild capillary disruption, short capillary loops, and crossing capillaries are significantly more common capillaroscopic findings on examination of the toes. The changes are probably related to greater epidermal thickness and higher capillary pressure as an effect of Earth's gravity. Quantitative capillaroscopy reference values (capillary diameters and average capillary density) can be used for capillaroscopy of both fingers and toes. Various authors have observed a lower incidence of microangiopathy (megacapillaries, hemorrhages, and capillary loss with avascular areas) in the toes, which is probably related to the later onset of RP in the lower extremities [11].

PATHOLOGY

Devascularization is present when the number of capillaries is below 7 per mm [3].

There are changes that should never be considered normal. Certain signs of microangiopathy are giant capillaries, neoangiogenesis in combination with low capillary density, and avascular areas secondary to capillary loss that give the appearance of „ravaged areas“ either by the absence of 2 cap-

illaries in each dermal papilla or by the presence of an area of 500 μ m, devoid of them. [1, 5, 13]. The generalized loss of capillaries is different, where a homogeneous decrease in their number is observed by applying excessive pressure to the nail bed when performing capillaroscopy, and a sharp transition from a vascularized area to a completely avascular area can be observed, which is dynamic, since the position of video capillaroscope varies [1]. Another pathological finding is neovascularization - an attempt to restore tissue perfusion and normal architecture, which leads to great heterogeneity of shapes and sometimes to such intense revascularization that it gives the shape of a tree or a bushy capillary [1]. Giant capillaries (with a loop diameter greater than 50 μ m) are typical markers of microvascular damage in systemic sclerosis (SSc) [1, 3, 5, 13] and do not occur in healthy individuals [11]. Capillaries with an arterial diameter > 0.015 mm (15 μ m) and venous > 0.020 mm (20 μ m) but less than 50 μ m are defined as dilated [3, 13]. Capillary segmental dilatation or dilatation of only one loop are findings that are often observed in arterial hypertension and diabetes mellitus [1].

It has been estimated that only 40% of the healthy population have completely normal capillaries, 50% have minor abnormalities, and only 5% have any abnormality of significant clinical significance [1]. Studies in the healthy population have found at least 3 patterns of normality: a “perfectly normal” pattern in which all capillaries have adequate shape and configuration; a “normal” pattern in which up to 2 tortuous capillary loops are allowed, and an “abnormal normal” pattern in which at least one arborescent capillary, one microhemorrhage, or more than 4 tortuous capillaries can be found [1].

CAPILLAROSCOPY IN RAYNAUD'S PHENOMENON

The main indication for capillaroscopic examination in rheumatology is the presence of Raynaud's phenomenon (RF) which is a clinical manifestation of reversible vasospasm of small arteries and arterioles provoked by cold exposure and emotional stress [2, 4, 5, 7, 9, 10, 11, 13, 14, 18]. The condition is characterized by initial whiteness of the fingers, most often with cold exposure, followed by cyanosis, pain, and numbness and redness in the reperfusion phase [2, 4, 7, 9, 10, 18]. RP has a prevalence of 3 to 21% worldwide, more commonly affecting young women. [2] It can be primary (idiopathic) or secondary (as a manifestation of another disease) [4, 5, 7, 9, 10, 18].

The abnormal capillaroscopic finding has a positive prognostic value in about 47% of the analyzed patients. [9] In primary RP, the capillaroscopic picture is not specific – capillaries unchanged in number and shape, the diameter of the capillaries may be slightly increased, but the finding must be interpreted in conjunction with the clinical picture and the results of laboratory tests [4, 5, 18]. Usually, in primary RP, a pale background of the capillaroscopic field and various functional disorders (but not structural ones) are observed, while in secondary RP a cyanotic background of the capillaroscopic field, structural disorders and functional changes in the capillaries, hemorrhages, thrombosis, avascular zones and neoangiogenesis are characteristic [7, 9, 13]. Dilated capillaries are associated with tissue ischemia, and giant capillaries should be considered an indicator of future development of systemic connective tissue disease (SCTD), and these patients should be followed up [4, 5].

There is also an increasing number of scientific reports reporting Raynaud's phenomenon following recurrent infection with SARS-CoV-2 and following vaccination [19, 20]. Due to the long waiting period for an examination by a rheumatologist in most countries of Central and Western Europe, as well as the small number of qualified specialists who can perform and evaluate the examination [21], clinical and capillaroscopic changes in these patients remain undiagnosed for a long time [22]. This is one of the factors forcing patients to seek qualified medical care outside the borders of their own country and favors the development of medical tourism after the COVID-19 pandemic [23]. However, there is a lack of sufficient data on the incidence and prevalence of Raynaud's phenomenon after recurrent COVID-19 infection. Taking a detailed history and correct interpretation of clinical symp-

toms and capillaroscopic findings is necessary to avoid misinterpretation [22, 24].

MISINTAKES IN CAPILLAROSCOPY:

1. Technical mistakes

➤ Magnification other than 200×, poor image quality (lack of focus and greater or lesser light intensity) [15].

➤ Applying even minimal pressure to the eponychium can result in interruption of blood flow, misinterpretation of the density of capillary loops, or the presence of an avascular zone (Fig. 2).



Fig. 2. Pressure applied to the eponychium

➤ Occurrence of reflection (Fig. 3 and Fig. 4) or illumination (Fig. 5).

➤ Reduced visibility due to presence of nail polish or other factors (Fig. 6).

2. Misinterpretation of the results

Microtraumas resulting from manicure procedures (Fig. 7) or finger trauma (Fig. 8 and Fig. 9) in healthy individuals may be mistaken for a pathological capillaroscopic finding.

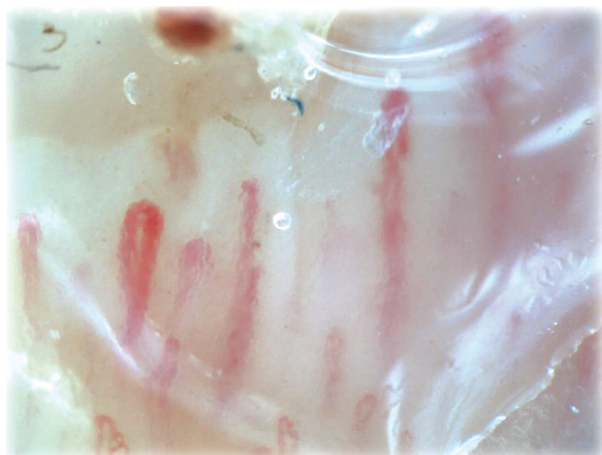


Fig. 3. Reflection

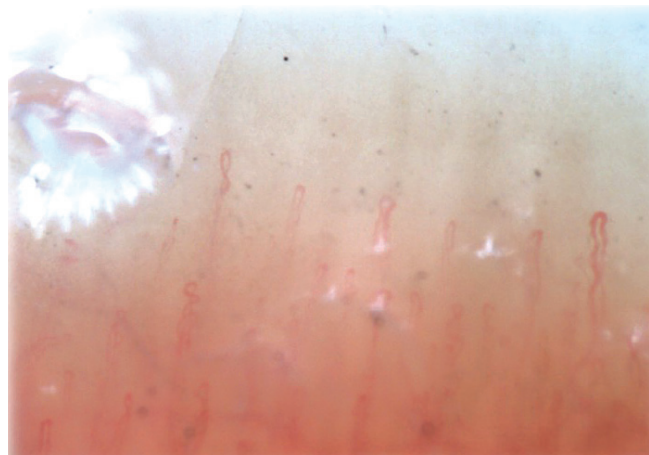


Fig. 4. Reflection

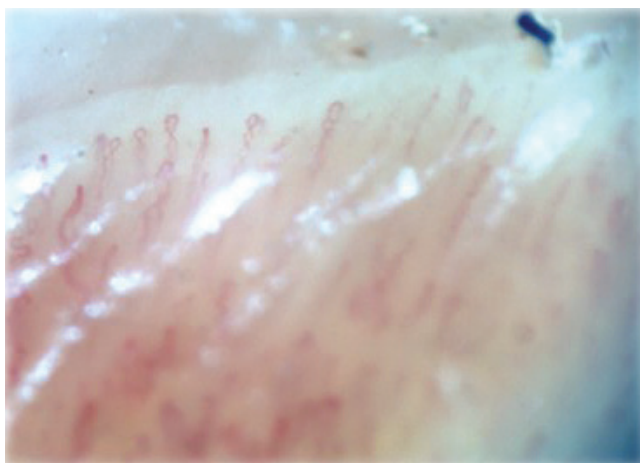


Fig. 5. Illumination



Fig. 6. Poor visibility of capillaries due to presence of nail polish and hyperkeratosis

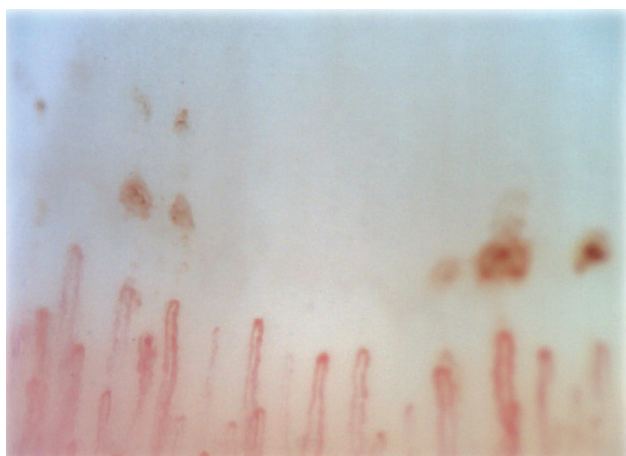


Fig. 7. Traumatic hemorrhages as a result of a manicure procedure

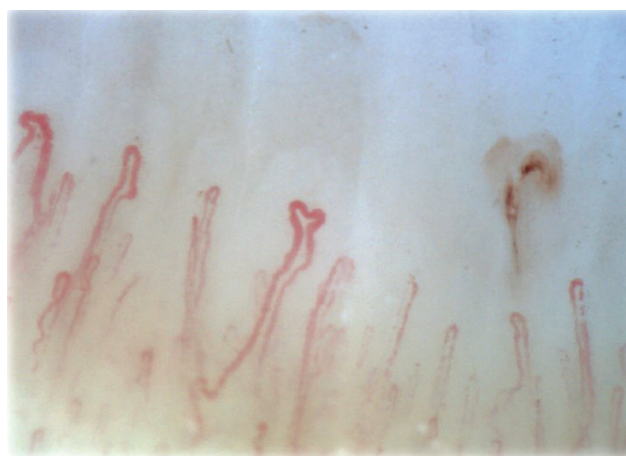


Fig. 8. Traumatic hemorrhages

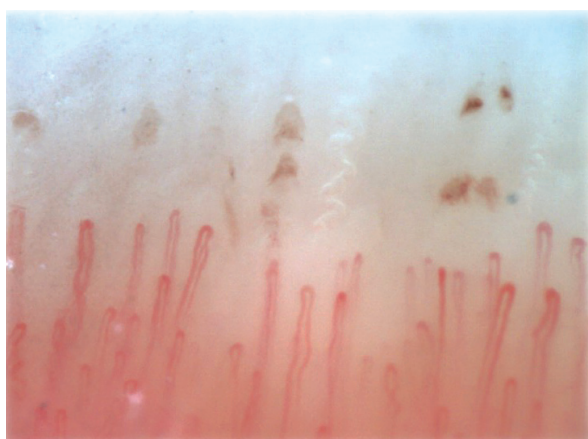


Fig. 9. Traumatic hemorrhages

CONCLUSION

Video capillaroscopy of the eponychium is a fast, non-invasive and extremely informative method for evaluating skin microcirculation. The results of the study should be carefully interpreted with a view to the correct assessment of the patients' condition and the differenti-

ation of the various diseases associated with microangiopathy and Raynaud's phenomenon. In view of this, it is extremely important that capillaroscopy is correctly interpreted in combination with a thorough general and occupational history taken, as well as in combination with the results of specific tests. It is necessary to comply with all the requirements for conducting the study, to distinguish the variation of the norm from the pathological finding and to take into account the general and professional risk factors leading to microangiopathy.

In conclusion, it can be said that the most frequently made mistakes during capillaroscopic capillaroscopy examination are due to non-observance of the rules for performing capillaroscopy, insufficient knowledge of the different capillaroscopy patterns and findings and/or the lack of sufficient clinical experience and practice.

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