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Evaluation of the Relationship between Capillaroscopic Symptoms and the Severity of Systemic Lupus Erythematous

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Abstract

Objectives: Use of imaging tools can detect some specific pathological changes associated with systemic lupus erythematous (SLE). This study aimed to investigate the relationship between capillaroscopic symptoms and the severity of SLE.

Methods: This was a cross-sectional study carried out on 56 patients with SLE undergoing capillaroscopy referred to Rasool-e Akram hospital in Tehran in 2018. Capillaroscopy findings were assessed according to demographic characteristics and duration of disease.

Results: All patients had at least one positive finding related to capillaroscopy. Regarding capillaroscopic findings, abnormal microvascular structure in 37.5%, decreased vascular density in 78.6%, enlarged cap loop in 32.1%, microhemorrhage in 16.1% and neoangiogenesis in 25.0% were observed. The results revealed higher vascular density loss in women and higher neoangiogenesis in affected men and higher rate of abnormal microvascular structure at older ages and microhemorrhage at younger ages. Direct relationship was also found between duration of disease and microhemorrhage.

Conclusion: Almost all patients with SLE undergoing capillaroscopy had at least one pathophysiological change in the capillary bed. The most common pathophysiological change was decreased vascular density, abnormal microvascular structure and capillary loop enlargement.

Keywords: Systemic lupus erythematous, Pathophysiology, Capillaroscopy

Introduction

Systemic lupus erythematous (SLE) is one of the most common rheumatic diseases with a global incidence of 50 to 70 cases per million people and the prevalence of 500 cases per one million people resulted in significant functional disabilities in 6.2% of cases [1]. SLE involves most of the body systems and thus is identified as a multisystem disease [2]. The most frequent sequels of SLE include involvement of the cardiovascular, nervous, homologous, renal, musculoskeletal, and skin-mucosal systems [3], and the most common symptoms are musculoskeletal, cutaneous, and renal manifestations seen in 83.2%, 81.1% and 65.4% of patients, respectively [4]. SLE and its complications can cause a significant reduction in the quality of life of patients, which is affected by various factors, especially the severity of the disease and its duration [5,6]. Although, SLE is more common in people aged 20 and 40 years but it can affect other age groups and even children [7], and the prognosis improves in advanced ages [8]. Five-year survival rate in patients with SLE is reported to be 57% and 72%, and the most common causes of death in these patients are infections and kidney failure [9]. The earlier diagnosis of SLE increases the likelihood of quality of life and therapeutic response, so it is important to use diagnostic methods that can diagnose SLE or its complications earlier [10]. This issue is especially evident in developing countries and therefore faster diagnosis and proper care during the course of treatment and evaluation of treatment complications are of particular importance [11].

One of the issues raised in this regard is the capillaroscopy symptoms of patients, which in fact indicate vasculopathy

and are important findings in rheumatic diseases such as SLE [12]. Capillaroscopy is a completely non-invasive technique based on the evaluation of small microcirculation vessels [13]. In systemic diseases with vascular damage, morphological changes in the capillaries are predictable, and these changes occur even before the onset of clinical symptoms [14]. Such vascular changes can be commonly seen in patients with SLE and thus the pointed technique can be very valuable to assess the severity of SLE [15]. We decided to investigate the relationship between capillaroscopy symptoms and the severity of SLE.

Materials and Methods

This descriptive-analytical cross-sectional study carried out on 56 patients with SLE undergoing capillaroscopy referred to Rasool-e Akram hospital in Tehran in 2018. Inclusion criteria included not having concomitant rheumatic diseases. Exclusion criteria were anatomical problems of the hands and nails and various types of vasculopathy. Regarding capillaroscopy findings, the abnormal microvascular structure of the enlarged cap loop density was examined in neoangiogenesis microhemorrhage. In this regard, the pointed measured value was nail fold capillaroscopy (NFC) [16]. In our study, the severity of the disease was determined based on the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). It consists of 24 weighted clinical and laboratory variables of nine organ systems. This instrument was derived by consensus among experts in rheumatology followed by application of regression models to assign relative weights to each parameter. SLEDAI was modeled on the basis of clinician global judgment. The scores of the descriptors range from 1 to 8, and the total possible score for all 24 descriptors is 105 [17]. Ethically, the whole interventions were performed with the personal consent of the patients and all the details of the study were explained to the patients so that they have enough information about their treatment process. All therapeutic interventions were performed with the knowledge and consent of the patient or his/her legal guardian and the results were used to improve the quality of life of these patients. Patients were treated free of charge by the facilitator in case of complications due to diagnostic and therapeutic evaluation. The research stages were methodologically and ethically approved by the Research and Ethics Committee of Iran University of Medical Sciences.

Ethical issue

The research followed the tents of the Declaration of Helsinki. The Ethics Committee of Iran University of Medical Sciences approved this study. The institutional ethical committee at Iran University of Medical Sciences approved all study protocols (IR.IUMS.FMD.REC.1399.884).

Statistical analysis

For statistical analysis, results were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by frequency (percentage) for categorical variables. Continuous variables were compared using t test. Categorical variables were compared using chi-square test. For the statistical analysis, the statistical software SPSS version 23.0 for windows (IBM, Armonk, New York) was used.

Results

The mean age of the patients was 39.24 ± 9.65 year ranging from 18 to 61 years and 51 cases (91.1%) were female. The mean duration of the disease was a 10.15 ± 7.02 year ranging from 1 to 28 years. The mean anti-dsDNA antibody titer at the time of the study was 28.28 ± 7.31 units per ml. In respect of disease severity based on disease activity index (DAI), 22 cases (39.3%) were mild, 28 cases (50.0%) were moderate and 6 cases (10.7%) were severe. All patients had at least one positive finding related to capillaroscopy. Regarding capillaroscopic findings, abnormal microvascular structure in 37.5%, decreased vascular density in 78.6%, enlarged cap loop in 32.1%, microhemorrhage in 16.1% and neoangiogenesis in 25.0% were observed. Normal NFC score in 48.2%, nonspecific morphological disorder or NSMA in 30.4% and scleroderma pattern in 21.4% were observed. In 12 patients who had scleroderma pattern, 7 cases (58.3%) had early pattern, 4 cases (33.4%) had active pattern and 1 case (8.3%) had delayed pattern. As shown in **Table 1**, there was no significant relationship between disease severity and any of the capillaroscopy findings. The assessment of relationship between capillaroscopy findings and patients' gender showed greater prevalence of decreased vascular density in women and greater prevalence of neoangiogenesis in men (**Table 2**). Also, as indicated in **Table 3**, the greater prevalence of abnormal microvascular structure was observed at older ages

Table 1: The relationship between disease severity and any of the capillaroscopy findings.

Capillaroscopy findings	Mild	Moderate	Severe	P value
Abnormal microvascular structure	27.3%	16.7%	33.3%	0.799
Decreased vascular density	68.2%	100%	83.3%	0.241
Capillary loop enlargement	31.8%	16.7%	16.7%	0.633
Microhemorrhage	9.1%	0.0%	0.0%	0.560
Neoangiogenesis	36.4%	0.0%	16.7%	0.168

Table 2: Capillaroscopy findings according to gender.

Capillaroscopy findings	Male	Female	P value
Abnormal microvascular structure	40.0%	37.3%	0.904
Decreased vascular density	40.0%	82.4%	0.028
Capillary loop enlargement	40.0%	31.4%	0.693
Microhemorrhage	40.0%	13.7%	0.178
Neoangiogenesis	60.0%	21.6%	0.048

Table 3: Capillaroscopy findings according to age.

Capillaroscopy findings		Mean age, year	P value
Microvascular structure	Abnormal	42.48 ± 8.43	0.042
	Normal	37.24 ± 9.93	
Vascular density	Decreased	40.28 ± 9.35	0.131
	Normal	35.50 ± 10.24	
Capillary loop	Enlarged	37.24 ± 9.55	0.308
	Normal	40.13 ± 9.69	
Microhemorrhage	Present	33.89 ± 7.15	0.037
	Absent	40.28 ± 9.79	
Neoangiogenesis	Present	35.38 ± 9.77	0.100
	Absent	40.43 ± 9.41	

and microhemorrhage at younger ages. There was a direct relationship between the SLE duration and the occurrence of microhemorrhage (**Table 4**). Moreover, we also found no significant association between capillaroscopy findings and the level of Anti-dsDNA antibody (**Table 5**).

Discussion

Nowadays, diagnosis and the severity of SLE due to its etiological and pathophysiological complexity remains an important challenge among physicians. However, some tools have recently been used to enable early detection of disease manifestations and consequences, as well as disease classification. Given the evidence of changes in the vascular bed, especially the small vascular bed and capillaries, it seems that the use of imaging tools of this vascular bed can detect some specific pathological changes associated with SLE. Thus, the use of capillaroscopy in the diagnosis and exacerbation of

Table 4: Capillaroscopy findings according to disease duration.

Capillaroscopy findings		Mean age, year	P value
Microvascular structure	Abnormal	10.84 ± 6.91	0.654
	Normal	9.07 ± 7.24	
Vascular density	Decreased	10.61 ± 7.34	0.378
	Normal	7.60 ± 4.34	
Capillary loop	Enlarged	11.85 ± 7.94	0.478
	Normal	9.69 ± 6.85	
Microhemorrhage	Present	16.75 ± 7.27	0.043
	Absent	9.24 ± 6.60	
Neoangiogenesis	Present	8.00 ± 5.14	0.466
	Absent	10.54 ± 7.32	

Table 5: Capillaroscopy findings according to Anti-dsDNA antibody level.

Capillaroscopy findings		Mean age, year	P value
Microvascular structure	Abnormal	19.82 ± 17.06	0.564
	Normal	30.75 ± 8.61	
Vascular density	Decreased	23.38 ± 8.88	0.277
	Normal	42.51 ± 14.04	
Capillary loop	Enlarged	43.37 ± 14.24	0.197
	Normal	21.81 ± 8.71	
Microhemorrhage	Present	47.40 ± 7.27	0.282
	Absent	26.60 ± 7.70	
Neoangiogenesis	Present	49.02 ± 13.52	0.090
	Absent	19.34 ± 8.42	

patients with SLE has received much attention; however, there are still conflicting findings of this tool among patients with SLE in different communities, possibly due to the close link between genetic predisposition and the condition in the capillary bed. Considering that no study on capillaroscopy findings in SLE patients in the Iranian community has been published so far, we decided to evaluate these findings in a selected sample of patients in Iran. In our study, the most important findings of the present study were: 1) First, all patients had at least one of the positive findings related to capillaroscopy and therefore the prevalence of these findings in our patients was equal to 100%. Also, the most common changes in capillary bed based on capillaroscopy in these patients included decrease in vascular density in 78.6%, abnormal microvascular structure in 35.5% and enlargement of capillary loop in 32.1% and other findings such as microhemorrhage and neoangiogenesis was seen in 16.1% and 25% of patients, respectively. Also, the pattern of scleroderma was visible only in 21.4% of the patients. This finding was significantly different from the findings of other studies. In a systematic review by Cutolo et al. in 2018, the most common findings included capillaries complexity, abnormal morphology, and capillary hemorrhage [18]. In a study by Schonenberg-Meinema et al. in 2020 on children, changes in capillary diameter, capillary morphology, and hemorrhage were not observed in patients with SLE, and the occurrence of scleroderma pattern was very rare [19]. In a study by Kuryliszyn-Moskal et al., the prevalence of positive capillaroscopy findings was equal to 92.5% in patients with SLE, which was close to our study [20], whereas in a study by Riccieri et al. in Italy, only 20% had positive symptoms [21]. Also, in a study by Shenavandeh et al., 94.4% had capillaroscopic symptoms, which was close to our study [22], however, in another study by Kuryliszyn-Moskal et al. in Poland, positive capillaroscopic findings were observed in 52.9% of the patients [23]. Therefore, it can be concluded that, firstly, a wide range (including 20 to 100%) of the patients with SLE may have a positive capillary finding of pathological changes in the capillary bed. Second, no specific tissue associated with the disease can be found on capillaroscopy that definitively leads to the diagnosis or even the severity of the disease. Third, the prevalence of pathological changes in SLE-related capillaroscopy is very different in different societies, and therefore the theory of the influence of genomic factors on the occurrence of such changes is strengthened.

Another important point in our study, which was inconsistent with many studies, was the lack of association between disease severity and capillary manifestations in capillaroscopy. Of course, the absence of such a relationship may be due to the small sample size of the study or it may not really exist in our society and therefore capillaroscopy findings do not have a prognostic feature to determine the severity of the disease in our society. In a systematic review by Cutolo et al., the capillaroscopic score of the nail bed in patients with SLE was much higher than in healthy individuals and the severity and activity of the disease were directly correlated with the NFC score [18]. In a study by Kuryliszyn-Moskal et al., the capillaroscopic findings in the patients with the SLEDAI, which indicates the severity of lupus, showed a significant relationship [20]. In a study by Ciołkiewicz et al., there was a significant direct linear relationship based on the correlation test between capillaroscopic symptoms and SLEDAI in the studied patients [24]. In a study by Riccieri et al. in Italy, positive capillaroscopic symptoms showed a significant relationship with disease activity and the positivity of some markers such as Anti-ds-DNA [21], which again was inconsistent with our study. In a study by Shenavandeh et al., there was a significant relationship between these symptoms and the severity of lupus, especially in the case of skin findings [22]. Also, in a study by Kuryliszyn-Moskal et al., positive capillaroscopic findings were observed in 52.9% of patients with severe disease with organ involvement and 21.4% of patients with mild disease without organ involvement [23].

Regarding the indicators related to capillaroscopic findings, we showed that the existence of some findings is related to the gender, age of patients and the duration of the disease in which the higher vascular density loss in women, higher neoangiogenesis in affected men, higher rate of abnormal microvascular structure at older ages and microhemorrhage at younger ages, as well as the direct relationship between duration of disease and microhemorrhage were all expected. Therefore, depending on gender (probably due to hormonal differences and different environmental and physical conditions of the two sexes), age (degenerative changes with age) as well as the duration of the disease (pathological changes with later stages of the disease and possibly the severity of the disease), the manifestations found on capillaroscopy can vary.

Conclusion

At first, almost all patients with SLE will undergo capillaroscopy with at least one pathophysiological change in the capillary bed. The most common of these changes in patients in Iranian society include decreased vascular density, abnormal microvascular structure, and capillary loop enlargement. Changes such as abnormal microvascular structure and the occurrence of microhemorrhage are affected by age. Also, microhemorrhage is associated with the duration of the disease.

Conflict of Interest

None.

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