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Histological Changes of Linear Scleroderma "en Coup de Sabre"

Introduction. Scleroderma is a chronic disease of unknown aetiology characterized by skin fibrosis and is divided into two clinical entities: localized scleroderma and systemic sclerosis [1]. But the localized scleroderma is not accompanied by Raynaud's phenomenon, acrosclerosis and internal organ involvement and the life prognosis of patients with localized scleroderma is good [1]. Scleroderma "en coup de sabre" (ECDS) is considered a linear localized form of scleroderma or morphoea. It usually involves, unilaterally, the frontoparietal area, but may extend downwards to the face. Most cases begin before 10 years of age [3]. The involved skin area is depressed, hard, hyperpigmented, shiny and devoid of hair. Facial asymmetry may result from underlying muscle and bone involvement [2, 4]. Early lesions of localized scleroderma are histologically characterized by perivascular lymphocytic infiltrate in the reticular dermis and swollen endothelial cells [1, 2]. However, there have been few information regarding histological features of localized scleroderma other than these findings.

The aim of our study was to investigate the histological characteristics and their clinical association in ECDS.

Materials and methods. The present study was carried out at the Department of Dermatology and Venereology in Tbilisi State Medical University. 11 patients (2 men and 9 women) with lesions clinically and histologically diagnosed as ECDS were retrospectively included. Patients who were treated with immunomodulating agents, including systemic corticosteroids and immunosuppressants before presentation, or patients complicated with Parry – Romberg syndrome were excluded from the study. All patients were subjected to:

1. History taking including: age, sex, duration of the disease, family history.
2. Clinical examination.
3. Skin biopsy – evaluated for epidermal atrophy, spongiosis, vacuolar degeneration of basal cell layer, satellite cell necrosis, basal pigmentation, melanin incontinence, perivascular infiltrate, perineural infiltrate, periappendageal infiltrate, vacuolar changes of follicular epithelium and dermal fibrosis.

The study protocol was approved by Ethical Committee of the University. **Results**. The age of the patients at the moment of presentation ranged from 11 to 60 years. The disease duration ranged from 2 months to10 years. The clinical features at the presentation were: 2 patients had erythema (Case1 and 7), 1 had hypopigmentation (Case 5), 2 – erythematous plaque with atrophy, depression and/or hair loss (Case 2 and 6), 3 –brownish and/or greyish plaque with atrophy, sclerosis, depression and/or hair loss (Case 3, 9 and 11), and hypopigmented plaque with atrophy, sclerosis, depression and/or hair loss (Case 4, 8 and 10). Regarding the central nervous system involvement, 2 patients (Case 3 and 8) had headaches, one had intracranial calcifications (Case 11) and 3 – abnormal electroencephalogram (Case 4, 9 and 10). The most prominent change in epidermis was interface dermatitis. Regardless of clinical presentation and disease duration, epidermal lymphocytic infiltrate accompanied with spongiosis, tagging of lymphocytes along the dermo-epidermal junction and vacuolar changes were found in all specimens. Furthermore, melanin incontinence was seen in 7 (63,7 %) patients.

Moreover, keratinocyte necrosis, which is frequently accompanied with moderate interface dermatitis was seen in 1 patient with early and active lesions, which are characterized by a hypopigmented plaque without sclerotic change and rapidly enlarging erythema respectively. These results suggest that interface dermatitis is a common histological feature of ECDS. Importantly, vacuolar changes accompanied with spongiosis in hair follicular epithelium were also seen in 6 (54,5 %) patients, but there was no correlation in the degree of these changes between epidermis and hair follicular epithelium. Regarding the histological features in the dermis, dermal fibrosis was found in all patients, but the degree of fibrosis did not correlate with disease duration. Perivascular and/or peri-appendageal lymphocytic infiltrate with scattered plasma cells was observed in all patients. Since sclerotic plaques spontaneously regress up to 3,8 years after disease onset in 50,0 % of ECDS patients, we divided the ECDS patients into two subgroups according to their disease duration, such as ECDS patients with disease duration of < 3 years

(early ECDS; 7 patients) and ECDS patients with disease duration of ≥ 6 years (late ECDS; 4 patients), and compared their histopathological features. Epidermal atrophy was more frequently seen in late ECDS patients than in early ECDS patients. On the other hand, 'perivascular and/or peri-appendageal infiltrate', 'vacuolar changes of follicular epithelium' and 'perineural infiltrate' were more prominent in early ECDS patients.

Conclusion. Contrary to the previous report showing no evidence of interface dermatitis in patients with localized scleroderma [2, 5], all ECDS patients demonstrated epidermal lymphocytic infiltrate, tagging of lymphocytes along the dermo-epidermal junction and vacuolar changes, regardless of disease duration, clinical presentation and the intensity of perivascular lymphocytic infiltrate. Furthermore, when we defined patients with disease duration of < 3 years and of ≥ 6 years, respectively, the degrees of perivascular and/or peri-appendageal infiltrate and vacuolar changes of follicular epithelium were much greater, whereas epidermal atrophy was less frequently seen, in early ECDS patients than in late ECDS patients.

The intensity of interface dermatitis in epidermis was comparable between early and late ECDS lesions. Also it's important to mention, that in our study in early stage localized scleroderma the characteristic histological finding is not only perivascular lymphocytic infiltrate. Vacuolar changes in epidermis is also a common histological feature in the sites of damaged skin of ECDS patients and vacuolar changes in follicular epithelium and peri-appendageal infiltrate serve as a histological marker of early and active ECDS lesions in addition to perivascular infiltrate. Although the pathogenesis of localized scleroderma still remains unknown, the present observation and received results are useful to determine the activity of skin lesions in ECDS and provide us a new clue to further understand the pathogenesis of this disorder.

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Scleroderma is a chronic disease of unknown aetiology characterized by skin fibrosis and is divided into two clinical entities: localized scleroderma and systemic sclerosis. "En coup de sabre" (ECDS) is considered a linear localized form of scleroderma and we focused on this disease to evaluate its histopathological features. A total of 11 patients with ECDS were retrospectively evaluated on the basis of clinical and histological findings. Vacuolar degeneration was found in all cases regardless of clinical manifestations. In early ECDS patients (disease duration of < 3 years) moderate to severe perivascular and/or peri-appendageal lymphocytic infiltrate and vacuolar changes in follicular epithelium were more prominent, whereas epidermal atrophy was less frequently observed, than in late ECDS patients (disease duration of ≥ 6 years).The present observation and received results are useful to determine the activity of skin lesions in ECDS and provide us a new clue to further understand the pathogenesis of this disorder.

Keywords: localized scleroderma, "en coup de sabre", histological changes.

Гістологічні зміни у випадку лінійної склеродерми

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Склеродерма – хронічне шкірне захворювання нез'ясованої етіології з вираженим фіброзом шкіри, для якого характерні два клінічних різновиди: локалізована склеродерма і системний склероз. "En coup de sabre" (ECDS) – лінійна локальна форма склеродерми, гістопатологічні особливості якої вивчено й оцінено в нашій роботі. Ретроспективно на основі клінічних і гістологічних даних вивчено 11 випадків ECDS. У всіх випадках, незалежно від клінічної симптоматики, виявлено вакуольну дегенерацію. На ранніх стадіях ECDS (тривалість захворювання понад 3 роки) спостерігалися помірна або виражена периваскулярна лімфоїдна інфільтрація та/або інфільтрати навколошкірних придатків і виражені вакуольні зміни в епітелії фолікулів, тоді як епідермальну атрофію, порівняно з пізніми випадками ECDS (тривалість захворювання 6 років і більше) фіксували рідко. Наші спостереження та отримані результати дають змогу визначити активність шкірного процесу у випадку ECDS і знайти нові ключові принципи для розуміння патогенезу склеродерми.

Ключові слова: локалізована склеродерма, гістологічні зміни.