Histopathological lesions in different types of skin aging

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ABSTRACT

Objective: Determination of histopathological changes in different types of skin aging.

Methods and Results: The study included a group of 60 women with various types of skin aging. Three groups were distinguished, each group containing 20 individuals. Group I consisted of women with menopausal skin aging, Group II with photoaging, and Group III with chronological aging. Biopsy specimens were taken from the preauricular region for morphological examination. Signs of elastosis, inflammatory infiltrations, and collagenization were assessed. Elastosis was most often observed in Group II (in 80% of cases). Inflammatory infiltrations were observed in Group II in 75%, in Group III in 60%, and in Group I in 55% of patients. The largest collagenization lesions were found in photoaging. This phenomenon was observed in 90% of the women. Collagenization occurred in 55% of women in Groups I and III.

Conclusions: The morphological picture of photoaging is typical and consists of collagenization occurrence in the corium, more pronounced elastosis, and the presence of inflammatory infiltrations. There are no characteristic morphological differences between chronological and menopausal aging, in which lesions occur to a considerably lesser degree.

KEY WORDS

skin aging, photoaging, elastosis, collagenization

Introduction

The process of skin aging involves the whole organism, including the skin. Because skin is directly exposed to the destructive action of external factors, skin undergoes more rapid aging than the other organs that can be easily observed during physical examination. Biological, biochemical, and molecular mechanisms influence the development of all types of skin aging. Some types of skin aging are distinguished: 1) endogenous aging, or that connected with age (chronological) and hormonal (menopausal), 2) exogenous aging (photoaging), which appears due to the influence of exogenous factors, those connected with excessive exposure to UV radiation (photoaging) and connected with cigarette smoking (smoker's skin), and 3) mimical aging (myo-aging; 1–5).

Histopathological examination can reveal the presence of lesions in all types of skin aging involving the epidermis, corium, and subcutaneous tissue. Some histopathological features are characteristic for en-

dogenous aging – both chronological and menopausal – and they also have an atrophic character. These lesions consist of epidermal hypertrophy in photoaging. Aging processes overlap and influence one another. They are present in different proportions and proceed individually in every person, and may or may not correlate with age (6–12).

The aim of this study was to determine the types of lesions in histopathological examination during the course of particular types of skin aging.

Materials and Methods

This study included a group of 60 healthy women, 26 to 62 years old, with various signs of skin aging. Three separate groups were distinguished, each group containing 20 individuals.

Group I consisted of women (with symptoms of menopausal skin aging) 45 to 62 years old, mean age 52.70 ± 4.73, non-smoking, not menstruating, not using hormonal replacement therapy, not using tanning beds or sunbathing, and using photoprotection.

Group II (photoaging) comprised 20 women 26 to 49 years old, mean age 38.3 ± 7.46. Eleven (55%) of the women in this group smoked cigarettes, from several to several dozen cigarettes a day. This group included menstruating women that do not use hormonal replacement therapy or hormonal contraception. These women often sunbathed, used tanning beds 2 to 12 times a month, and did not use photoprotection.

The third group was formed of women (with symptoms of chronological skin aging) between 49 and 62 years old, mean age 55 ± 3.78. All the women in this group were non-smokers, used hormonal replacement therapy during the study, did not use tanning beds, did not sunbathe, and used photoprotection daily.

Biopsy specimens for examinations were taken under regional anesthesia (after administration of 2% lignocaine solution without adrenaline) from the preauricular region, using a punch biopsy. Biopsy specimens were fixed in 10% buffered formalin. Specimens were routinely stained with hematoxylin and eosin (H-E). The presence of elastosis, lymphocytic inflammatory infiltrations, and collagenization were assessed in histopathological examination. A four-point scale was used to assess the degree of elastosis:

0 = No degeneration
1 = Focal lesions or a thin layer just under the epi dermis
2 = Lesions reaching skin appendages
3 = Extensive lesions in the whole corium
Inflammatory lymphocytic infiltration was assessed on a four-point scale:
0 = No infiltration
1 = Small: some to several cells together with single skin appendages
2 = Strong: a few hundred cells together with single skin appendages
3 = Extensive to infiltration together with nu merous skin appendages

Statistical analysis

Interpretation of the results obtained was based on standard statistical methods. Selection of the statistical test in the case of normal distribution depended on the result of variance comparison. If there was no basis for rejecting the hypothesis of variance equality, a traditional Student's *t*-test was used. The generalized Student's *t*-test (Cochran-Cox test) was used in cases that justified rejection of this hypothesis.

Results

The presence of lesions of varying severity and percentage of prevalence were observed in all groups. The most frequent and most severe symptoms occurred in Group II. Elastosis lesions were found in 12 women in Group I (60%) and they were most often symptoms graded as grade 1. This level occurred in seven (35%) of these individuals, but in five (25%) individuals elastosis reached the skin appendages (grade 2). Symptoms of elastosis were not observed in the remaining eight women (40%). In Group II, as many as 16 (80%) of the patients showed symptoms of elastosis, including 10 (50%) women with grade 2 lesions (they reached the shin appendages), but the remaining patients revealed focal lesions or lesions just under the epidermis. Symptoms of elastosis occurred in the corium in Group III in 10 (50%) individuals. These lesions were focal in nature or they occurred as thin layer just under the epidermis (grade 1) in five of the patients, and they also reached grade 2 in five women (Figure 1). In comparing the results of the presence and severity of elastosis among Groups I and II and also Groups I and III, no statistically significant differences were found. However, statistically significant differences occurred between Groups II and III ($p = 0.047$; Figure 2).

Lymphocytic infiltrations were observed most often in Group II. The presence of inflammatory infiltrations in Group I was observed in 11 (55%) individuals. Low-level infiltrations (grade 1) in the form of some or several lymphocytic cells together with single skin appendages were found in 10 (50%) individuals. The remaining nine (45%) individuals did not show the presence of inflammatory infiltrations. Lymphocytic inflammatory infiltrations were observed in Group II in 15 (75%) individuals. The level of infiltration varied; small amounts of infiltration (grade 1) occurred in

nine (45%) individuals, moderate amounts (grade 2) in four individuals, and two individuals showed infiltration of a few hundred cells together with numerous skin appendages. In Group III, 12 (60%) individuals showed the presence of infiltrations in low amounts (grade 1), but three individuals had moderate amounts (grade 2), and one case showed extensive infiltrations (grade 3; Figure 3). Differences in the occurrence and amount of inflammatory infiltrations were noticeable between groups, but they were not statistically significant (Figure 4).

The most significant collagenization lesions were found in the photoaging group. These changes were observed in 18 (90%) women. Symptoms of collagenization were observed in 11 (55%) women from Groups I and III (Figure 5). In comparing the occurrence of this phenomenon in all groups, a statistically significant difference was found between Groups I and II and also between Groups II and III, with $p = 0.013$ in both cases. A statistically significant difference was not found between Groups I and III (Figure 6).

Discussion

This study assessed the occurrence of lesions within collagen and elastic fibers and the presence of infiltrations from lymphocytic cells. Degenerative symptoms concerning collagen fibers were found in 55% of the women in Group I with symptoms of menopausal aging. The majority of researchers have similarly noted a decreased number of fibroblasts in the corium resulting from menopausal aging, as well as degenerative changes in the elastic and collagen fibers and disturbance of the collagen type I:III ratio. In 1941, Fuller Albright was the first to observe a decreased amount of type I and III collagen simultaneously with osteoporosis in postmenopausal women. Mark P. Brincat observed not only a decreased amount of collagen in postmenopausal women, but also many degenerative lesions and irregular locations of these lesions (8). Similar observations were also made by other researchers. Studies using immunohistochemical and computer photo analysis demonstrated that this decrease occurs predominantly during the postmenopausal period (2, 13–17). According to the literature, this decrease in the amount and quality change of collagen fibers also occurs in chronological aging. Most often the lesions involve collagen type III, but to a lesser extent they also involve collagen type I. Our study also revealed signs of collagenization in 11 women from Group III (55%). These data are in accordance with results of studies performed by other authors (1, 11, 18). Lesions in Groups I and III, and also the lack of statistically significant differences between them, prove that the collagenization process is similarly advanced within collagen fibers regardless of the type of endogenous aging.

Many studies have stated that hypertrophy of the horny layer of the epidermis occurs under the influence of UV radiation, while collagen fibers in the corium become thicker, deformed, and less numerous, but lesions in the corium have a form of elastotic degeneration (19–22). The results of our study are consistent with other researchers' results. The most significant collagenization lesions involving collagen fibers were observed in Group II (photoaging). This phenomenon was observed in as many as 90% of the women. Comparing the incidence of collagenization signs between Groups I and II and also Groups II and III (in which this phenomenon concerned 55% of women), this difference was statistically significant. UV radiation causes lesions within collagen and elastic fibers and also causes increases in reactive oxygen forms, activation of epidermal growth factor (EGF), interleukin 1(IL-1), tumor necrosis factor α (TNFα), transcription factor AP-1, ranks of kinases, and the matrix metalloproteinases MMP-1, MMP-3, and MMP-9 (7, 11, 23–25). It should be added that 55% of in the individuals in Group II smoked cigarettes. Other studies have demonstrated that smoking cigarettes and external environmental pollution additionally intensify these processes. Increased activity of MMP-1, MMP-3, RFT, and mRNA occurs under the influence of cigarette smoke, resulting in additional lesions within collagen and elastic fibers (26–28). It was found that cigarette smoking by women in amounts over five cigarettes daily causes menopause to start about 2 years earlier in relation to non-smoking women (29).

The most characteristic symptom of photoaging is elastosis, particularly in the upper layers of the corium. Our studies revealed that elastosis signs of various degrees of lesion severity most often occurred in Group II and concerned up to 80% of the women. This abnormal accumulation of elastin masses under the influence of UV rays is connected with degradation of protein netting elastin (fibrillin) on the dermal-epidermal border. Lesions within elastic fibers also occur in chronological and menopausal aging, but they are definitely less severe and they mainly consist of lower amounts of fibers and elasticity, and irregular fiber locations (18, 23, 30).

Our study also revealed signs of elastosis in the menopausal aging group (I) and chronological aging group (III), but to a lesser degree than in the photoaging group (II). A statistically significant difference concerning elastosis incidence between Groups II and III was demonstrated. Like other studies, our study showed that elastosis occurs in all types of skin aging. Women with photoaging showed significantly higher

grades of these changes, which could reflect the negative influence of the external environment.

Another feature characteristic of photoaging that occurs as a result of the chronic influence particularly of UVA in the corium is inflammatory infiltrations mainly consisting of lymphocytic cells (24, 31, 32). These lymphocytic infiltrations in the corium, called "sun dermatitis," were observed in our studies in all groups, with the greatest severity in Group II. Although the differences between the groups were not statistically significant, they probably indicate that inflammatory processes occur with greater intensity in photoaging than in endogenous aging.

Conclusions

Our study revealed that morphological lesions occur in all types of skin aging. The greatest severity appears in photoaging, which indicates the damaging activity of UV radiation and other external factors, including cigarette smoke. Morphological changes in photoaging are characteristic and consist of collagenization, pronounced elastosis, and inflammatory infiltrations in the corium. There were no characteristic differences in morphological changes between chronological and menopausal aging, in which lesions occur to a lesser degree than in photoaging.

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