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Skin aging in patients with acquired immunodeficiency syndrome

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ABSTRACT

To evaluate the histomorphometric skin changes over aging patients with autopsied acquired immunodeficiency syndrome (AIDS). In 29 skin fragments of autopsied elderly (older than 50 years) and nonelderly patients with AIDS, epidermal thickness, the number of layers, the diameter of cells, the percentage of collagen and elastic fibers in the dermis, and the number and morphology of Langerhans cells were assessed. Statistical analysis was performed by SigmaStat 2.03 program. The thickness of the epidermis (92.55 × 158.94 μm), the number of layers (7 × 9 layers), and the diameter of the cells (13.27 × 17.6 μm) were statistically lower among the elderly. The quantity of collagen fibers (9.68 × 14.11%) and elastic fibers (11.89 × 15.31%) was also significantly lower in the elderly. There was a decrease in total (10.61 × 12.38 cel/mm^2) and an increase in immature Langerhans cells (6.31 × 4.98 cel/mm^2) in elderly patients with AIDS. The aging of the skin of patients with AIDS is amended in different histomorphometric aspects, the epidermis constituents suffer less pronounced changes in normal aging, and the dermis has more intense changes in elastic fibers and collagen.

1. Introduction

Acquired immunodeficiency syndrome (AIDS) is considered one of the most serious diseases of the late twentieth century and a major challenge to the world health [1]. In Brazil, the number of AIDS cases being reported has increased from 2707 in 2000 to 5521 in 2010, which is a 103% increase rate. Men are more frequently affected by AIDS than women [2].

The spectrum of immune disorders seen in AIDS is induced by the human immunodeficiency virus (HIV) and the condition mimics the phenomena of immunosenescence. Reduction in the ability to mount sufficient T Helper Cell Type 1 (Th1) response and increase in the proportion of effector T cells relative to that of naive T cells are inherent disturbances occurring in the senescence process and in retrovirus infections. Such aggregated disorders can impair the reconstitution effectiveness of the immune system during therapeutic treatments in the elderly patients [3].

There is a high prevalence of skin diseases in patients with AIDS because the mucocutaneous manifestations present themselves from the onset of the disease and continue with the progression of immunodeficiency, with increased severity with advancing immunosuppression [4-11].

The involvement of skin in infected individuals encompasses malignancies, infections, and inflammatory disorders. With the deterioration of natural immune mechanisms, the susceptibility to viral, fungal, bacterial, and parasitic agents as well as the occurrence of noninfectious inflammatory diseases increases. It is important to study the skin health of patients with AIDS, considering the unusual manifestations of disease lesions, their potential atypical distributions, and the general concomitant pathological processes reported for biopsy specimens [12].

The objective of the present study was to evaluate the changes in skin with aging in autopsied patients with AIDS through histomorphometric analysis of the epidermis and dermis constituents.

2. Material and methods

This study was approved by the Triangulo Mineiro Federal University (UFTM) Research Ethics Committee, protocol number 1027. Autopsy protocols of carried out in this university clinic hospital between 1994 and 2014 were revised. Skin postmortem samples of 29 elderly (n = 13) and nonelderly (n = 16) patients with AIDS were recovered from an archive in the Division of General Pathology (UFTM), being collected from the thoracic region because of the lower solar incidence in this area. The AIDS scenario is considered in elderly individuals older than 50 years [13]. Patients were selected independent of the cause of death. All patients with AIDS observed in this study died after 1996 during the post–highly active antiretroviral therapy era [14].

Data concerning age, body mass index, cause of death, and macroscopic alterations of the skin were collected from the autopsy reports. Cases with an incomplete autopsy report or infectious diseases that might influence the findings were excluded.

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The fragments were submitted to histological processing and later, serially sliced at 4 μm in thickness for histochemistry and immunohistochemistry. Patients were selected regardless of the cause of death or underlying disease. Hematoxylin-eosin (HE) staining was carried out for the morphometric analysis of skin thickness, picrosirius for the quantitative analysis of collagen fibers, and Verhoeff staining for the measurement of the elastic tissue.

Images of the histological fields for the morphometric analysis were captured by a video camera connected to a conventional light microscope. Image J (National Institutes of Health, Bethesda, Maryland) program, an interactive analysis system, was used to measure epidermal thickness, which was measured by tracing 5 straight lines on different parts of each field to be analyzed. Along each line, the number of keratinocyte nuclei was counted to determine the number of cell layers in the epidermis. The average cell diameter was obtained by dividing the epidermal thickness by the number of keratinocyte nuclei in each measure [15].

To investigate the amount of collagen fibers in the dermis, picrosirius-stained fragments were examined under polarized light and quantified by KS-300 (Kontron Elektronic, Carl-Zeiss, Germany) software. To analyze elastic fibers, skin samples stained with Verhoeff stain were examined under a conventional light microscope and quantified by an image analysis system KS-300 using a ×40 objective.

To evaluate the number of Langerhans cells (LCs), antibody Anti-S100 (Dako®, Inc., Glostrup, Copenhagen, Denmark) was used at a concentration of 1 of 400. For antigen retrieval, heating in sodium citrate buffer and for blocking of nonspecific staining, bovine serum albumin was used. The primary antibodies were incubated for 2 hours and with secondary antibody Novolink™ Max Polymer Detection System (Leica Microsystem, Inc., Wetzlar, Hessen, Germany) for 30 minutes; diaminobenzidine (DAB) was used as substrate-chromogen.

The LCs positively stained by immunohistochemistry were counted in the whole extension of the epidermis and were expressed as number of cells per area (mm^2). The total number of LCs was determined in each field. The mature LCs presented apparent irregularly shaped dendrons. The immature LCs or LCs with altered morphology exhibited as round shapes and showed are duction in the number and size of dendritic processes [16,17].

Statistical analysis was carried out through SigmaStat 2.03 software (SPSS, Chicago, USA) program. As the variables presented nonnormal distribution, they were analyzed through Mann-Whitney (T) test to compare 2 groups and Kruskal-Wallis (H) to compare more than 2 groups, followed by Dunn test when necessary. Correlation between both variables with normal and nonnormal distribution was determined through Pearson (r) and Spearman (rS) tests, respectively. Differences in which "P" was lower than 5% ($P < .05$) were considered statistically significant.

3. Results

The average age of the 13 elderly patients with AIDS was 57.08 ± 5.28 years and of the 16 nonelderly patients with AIDS was 37.31 ± 7.48 years. Most elderly belongs to the male (10; 75%), whereas in the nonelderly group, female prevailed (10; 56.25%). Regarding color, 9 (75%) were classified as Caucasian in the elderly and 13 (81.25%) among nonelderly. The average body mass index in the elderly group was 19.70 ± 11.76 kg/m^2 and in the nonelderly group was 19.99 ± 5.42 kg/m^2.

Of the 29 patients, 7 (43.75%) nonelderly and 4 (30.76%) elderly presented some type of change in the skin, such as inflammatory lesions, scaly, and mycosis at the time of autopsy.

The epidermal thickness was significantly lower in the elderly group (Figure, Table). There was a negative and significant correlation between the thickness of the epidermis and the age of patients ($r = -0.566$; $P = .001$).

The number of layers and the diameter of keratinocytes were statistically lower in the elderly group compared with the group of nonelderly (Table). Regarding the thickness and the diameter of keratinocytes, the correlation was positive and significant ($r = 0.862$; $P = .000$). However, there was a negative and significant correlation between age and number of cell layers ($rS = -0.750$; $P = .000$).

The amount of immature LCs was significantly higher in the group of elderly patients with AIDS ($T = 111\,548.000$; $P < .001$). In analysis of the total LCs density and number of layers, the correlation was positive and significant ($rS = 0.443$; $P = .0185$). The correlation between immature LCs and the thickness of the epidermis was negative and significant ($rS = -0.387$; $P = .041$).

The percentage of collagen fibers was significantly lower in the elderly group (Table). There was a negative and significant correlation between percentage of collagen fibers and age ($r = -0.699$; $P = .000$). In the analysis of percentage of collagen fibers and number of cell layers, the correlation was positive and significant ($rS = 0.567$; $P = .001$). Relative to the thickness and the percentage of collagen fibers, the correlation was positive and significant ($r = 0.535$; $P = .002$).

It was observed that the percentage of elastic fibers was statistically lower in the elderly group (Table). There was a positive and significant correlation between percentage of elastic fibers and collagen fibers ($r = 0.576$; $P = .001$).

4. Discussion

Examination of morphological and morphometric changes was performed in the aged skin of autopsied patients with AIDS. Signs of malnutrition were observed in the elderly patients with AIDS; this factor possibly contributes to the thinning of the epidermis, as the shortage of primary nutrients can impair energy synthesis and, consequently, the cellular functions [18].

In addition to reduced energy expenditure with aging, along with the decrease in food intake, the nutritional status of infected individuals was characterized by catabolic hypermetabolism, which worsens in the elderly population as the energy and nutrient requirements increase [19]. These data corroborate with those published previously, mainly because HIV patients aged 50 years tend to present with the effect of exacerbated and accelerated immunosuppression along because of this disease and other common age-related ailments [20].

The most commonly reported types of skin lesions in patients with AIDS are scaly, inflammatory, and mycotic. These findings corroborate the ones published previously, with papulosquamous, infectious, and photosensitive lesions being commonly reported in patients with AIDS [21,22]. Other researchers have suggested oral candidiasis as the most frequent dermatological disease affecting HIV individuals [23], it occurs up to 50% of the cases over the course of the disease [11]. This fact relates to the senescence and retrovirus infection as the thickness of different epithelia decreases in AIDS.

A significant reduction in epidermal thickness in elderly patients, associated with a decrease in the number of layers and diameter of keratinocytes was observed in this group. This fact is related to senescence and itself with the retrovirus infection, because AIDS causes a decrease in thickness of different epithelia. In a study by Oriya et al, a reduction of the epidermal thickness was noted in elderly (59 ± 6 μm) as compared with that in nonelderly patients (94 ± 3 μm) [24]. The fact that HIV indirectly induces increased apoptosis of keratinocytes and is involved in the reduction of the synthesis of intracellular components [18,25,26] justifies the findings of the present study. Furthermore, with increasing age, the skin tends to become thin and limp because of the decrease in the size of keratinocytes, decreased cell proliferation, and, thereby, reduced cell layers [27].

The number of altered LCs was high in the elderly group. Langerhans cells are a type of dendritic cell having functions that involve antigen presentation and the induction of T-dependent response [28]. Their morphology is analyzed according to their state of maturity. The mature