Journal of Psychosomatic Research 72 (2012) 282–287

Contents lists available at SciVerse ScienceDirect

Journal of Psychosomatic Research

Psychological stress as a risk factor for postoperative keloid recurrence

Fabianne Furtado, Bernardo Hochman *, Paulo Luiz Farber, Marisa Campio Muller, Lilian Fukusima Hayashi, Lydia Masako Ferreira

Postgraduate Program in Plastic Surgery, Universidade Federal de São Paulo, Brazil

ARTICLE INFO

Article history:
Received 5 June 2011
Received in revised form 21 December 2011
Accepted 22 December 2011

Keywords:
Galvanic skin response
Keloid
Prognosis
Psychological stress
Recurrence

ABSTRACT

Objective: To investigate psychological stress on the prognosis of the postoperative recurrence of keloids.
Methods: Patients with keloids (n = 25), candidates for surgical resection and postoperative radiotherapy, had their psychological stress evaluated on the day before the surgical procedure. The parameters evaluated were pain and itching (Visual Numerical Scale), quality of life (Questionnaire QualiFibro/Cirurgia Plástica-UNIFESP), perceived stress (Perceived Stress Scale), depression and anxiety (Hospital Depression and Anxiety Scale), salivary cortisol and minimum and maximum galvanic skin responses (GSR) at rest and under stress (i.e., while the questionnaires were being filled out). Patients were evaluated during the 3rd, 6th, 9th and 12th months of postoperative care. During each return visit, two experts classified the lesions as non-recurrent and recurrent.
Results: The recurrence group presented the greatest values in GSR during a stressful situation. The chance of recurrence increased by 34% at each increase of 1000 arbitrary units in maximum GSR during stress.
Conclusion: Psychological stress influenced the recurrence of keloids.

Introduction

Keloid pathogenesis has not been entirely clarified (Fig. 1). Previous studies have related its development to factors of pilosebaceous [1], hormonal [2], genetic [3], melanocytic [4,5], vascular [6], nutritional-metabolic [7], immunological [8] and infectious origins [9].

Recently, a nervous origin has also been investigated [10–17] because the skin has a nervous system that effectively participates in the scarring process [18,19].

Evidence of the relationship between cutaneous scarring and peripheral innervation corroborates studies developed in the 1990s [20–24]. Denervated skin presents delays at all stages of scarring [25,26]. Conversely, an increase in cutaneous sensory innervation has been verified in multiple inflammatory lesions (e.g., psoriasis, atopic dermatitis) [18], hypertrophic scars [10] and keloids [16].

In addition to its own nervous system, the skin has its own immune and endocrine systems that are homologous to the systemic systems. A functional synergy is established between the "peripheral and central" systems through the interaction of the neuro-immune-endocrine system (NIES). A two-way communication, which is detailed in the next paragraphs, provides a central response from exogenous peripheral stress (e.g., ultraviolet radiation) and peripheral stimulation from endogenous central stress (e.g., psychological stress) [27].

When the skin is subjected to environmental stress, it transmits this stimulus to the central nervous system through orthodromic peripheral signaling. In this situation, the production of corticotropin-releasing hormone (CRH) by epidermal and dermal cells (e.g., keratinocytes, melanocytes, fibroblasts, sebaceous and mast cells) is similar to the production of CRH by the hypothalamus [28,29]. This hormone joins the hypothalamic CRH via the endocrine system and acts in the hypophysis to stimulate the production of peptides that are derived from proopiomelanocortin, α-melanocyte stimulating hormone, adrenocorticotropic hormone and β-endorphin [30].

Synergistically, when the body is subjected to stress of central origin, parts of the limbic system, especially the amygdala and the hippocampus, activate the production of CRH by the paraventricular nuclei of the hypothalamus and noradrenaline in the locus coeruleus [31]. The stress response is transmitted to all of the organs via the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system, including the skin via the NIES [32,27].

Recently, it was observed that the perception of stress in the central nervous system is translated to the peripheral tissues not only by stress hormones but also by neurotrophins and neuropeptides [33,34]. Therefore, in addition to cortisol, itching and pain are used as parameters to evaluate stress because they are associated with the release of neuropeptides from nerve fibers [35]. In some immunoinflammatory psychodermatoses, the direct proportionality between itching and pain with the perception of stress and vice versa has already been established [36,37].

* Corresponding author at: Rua Napoleão de Barros, 715, 4º andar, Division of Plastic Surgery, CEP: 04.023-002, Vila Clementino, São Paulo-SP, Brazil. Tel.: +55 11 5576 4118; fax: +55 11 55716579.
E-mail addresses: bernardohochman@uol.com.br, bibifst@yahoo.com.br (B. Hochman).

0022-3999/$ – see front matter © 2012 Elsevier Inc. All rights reserved.
doi:10.1016/j.jpsychores.2011.12.010

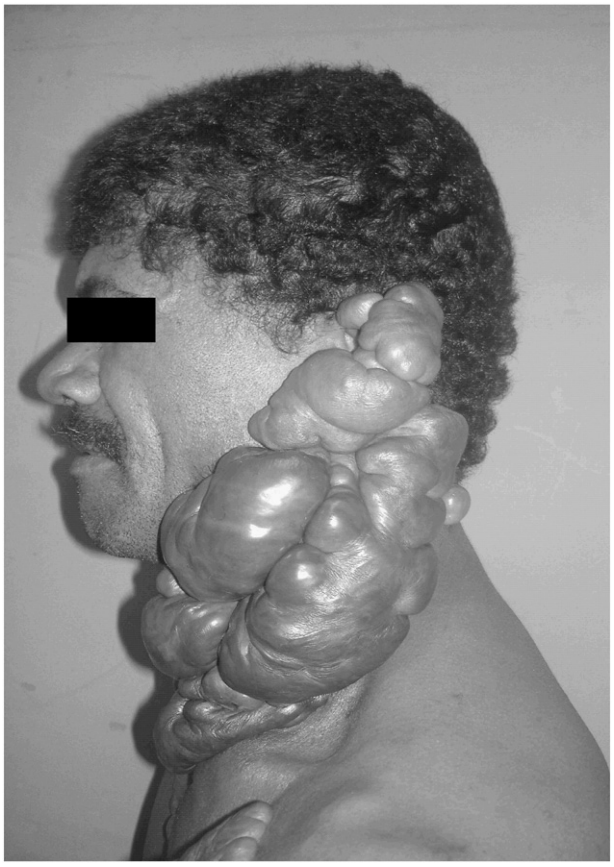

Fig. 1. Patient with extensive keloid in the auriculocervical region.

If stress is intense and sustained, it can trigger the onset of depressive and anxiety symptoms [38–40]. Any chronic disease alone increases the perception of stress [41].

The eccrine sweat glands, which are psychoreactive, also respond in stress situations to increase the amount of sweat that is released and, therefore, skin conductance [42–44].

The prognostic influence of psychological stress on the postoperative recurrence of keloid has not been studied. However, the identification of the prognostic factors is relevant not only to the selection of an appropriate therapy, but it is also for encouraging the individualization of treatment, which increases the understanding of the natural history of the disease.

Methods

Male and female patients with keloids who were over 18 years-old and were treated at the outpatient clinic of the Division of Plastic Surgery at the Universidade Federal de São Paulo were included in the study according to the following criteria: (1) a keloid located on the trunk of at least a 1-year evolution; (2) the keloid was resistant to previous treatment, such as intralesional corticosteroid injection, pressure therapy, excision or a combination of these therapies; and (3) a complete extralesional surgical excision in one session with primary closure of the defect without skin grafts or transposition was planned. Patients were excluded from the study if they met any of the following criteria: (1) had less than a basic education (5th grade); (2) failed to comply with the treatment protocol; (3) had a diagnosis of psychiatric disorder or cognitive impairment; (4) had physical disability that prevented the completion of the scale; or (5) were pregnant. All remaining individuals who understood the objective of the study were included and freely signed an informed consent form.

This study was divided into two stages. In the first stage, anamnesis and the collection of parameters indicative of psychological stress were performed on the day before the operation. In the second stage, the lesion recurrence was verified in the 3rd, 6th, 9th and 12th postoperative months.

1ª stage: collection of parameters indicative of psychological stress

Questionnaires

The following parameters were measured using self-applied questionnaires in a clear and quiet environment: quality of life, perceived stress, anxiety and depression, in that order.

Quality of life

This questionnaire was used with patients with keloids and hypertrophic scars [45]. The Brazilian version is called "Questionário QualiFibro/Cirurgia Plástica-UNIFESP" [46]. It is composed of questions that are divided into two scales after the scores are processed: one scale shows physical damage and the other scale analyzes the psychological damage. The scores vary from −5 (the best) to 5 (the worst) for each scale.

Perceived stress

For the stress analysis, the Perceived Stress Scale (PSS) was used [47]; the Portuguese version has been validated previously by Luft et al. [48]. The PSS measures the global level of perceived stress and adjusts the degree to which life situations are appraised as stressful as opposed to the presence of particular stressors. The PSS consists of 14 items, and the degree of stress for each item is rated on a 5-point Likert scale (range, 0–56). Higher scores on the PSS equate with more perceived stress.

Anxiety and depression

The Hospital Anxiety and Depression Scale (HADS) contains 14 items and two subscales: anxiety and depression. Each item is rated on a four-point scale, which yields maximum scores of 21 for anxiety and depression [49]. In Brazil, the HADS has been validated previously by Botega et al. [50].

Pruritus and pain

Itching and pain intensity were quantified using the Visual Numerical Scale from 0 (zero) to 10 (ten). Patients received instructions that 0 represented no itching and no pain and 10 indicated unbearable itching and pain. Patients indicated the degree of scar itch and pain by pointing to a number on the scale.

Salivary cortisol

The patient was advised not to eat food or drink 2 h prior to the collection of saliva. After a 20-minute rest and before the placement of a roll of cotton, the oral cavity was checked to verify the existence of gingival bleeding. The patient later rinsed their mouth with water. The patient was instructed to collect a saliva sample to be analyzed by Salivette® (Sarstedt, Rommelsdor, Germany). All samples were collected between 8 and 9 p.m., and centrifuged and stored in a freezer at −20 ° C until the assay was performed.

The free fraction of salivary cortisol was determined in duplicate using a radioimmunoassay technique without extraction with an anti-cortisol 3-oxime antibody conjugated to bovine serum albumin. The values for salivary cortisol concentrations are expressed in ng/dL.

Galvanic skin response (GSR)

The preparation that preceded the GSR analysis consisted of an acclimatization of the patient for 20 min in an environment with temperature and humidity that was controlled by a digital thermo hygrometer (Instrutherm HT-210 ®).