Post-inflammatory hyperpigmentation of the skin.

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Abstract

Post-inflammatory hyperpigmentation is the most benign cause of brownish discolorations of the skin. For this reason it has been little researched. In times of increasing treatments in the field of cosmetic medicine and simultaneous increased attention to the issue of skin cancer, a lack of knowledge may lead to over-treatment of post-inflammatory skin lesions.

Basic facts

Inflammation as an adaptive response to tissue infection or injury triggers the recruitment of leukocytes and plasma proteins from the microcirculation to extravascular tissues. Inflammatory responses in the skin are driven by interactions of numerous immunocompetent cells and soluble inflammatory mediators in the epidermis and dermis. The dermis contains most of the lymphocytes in the skin, as well as additional leukocytes that have migrated from the blood vessels, such as tissue macrophages and mast cells. Lymphocytes in the skin and components of the acquired immune system include T- and B-cells. They are mobile cells that originate from the bone marrow and only then split into the groups of T-and B-cells. They react directly with antigens, secrete specific mediators and store information about antigens. T-lymphocytes mature in the thymus and carry a T-cell receptor on their surface that recognizes a specific antigen. The B-lymphocytes are stimulated by the T-cells and subsequently differentiate into antibody-producing plasma cells or memory cells of the immune system. The latter ensure a rapid and strong immune response after the antigens re-enter the body. Dendritic cells, also called dermal dendrocytes, assume a central role in the wound healing process. Depending on the type, they develop from monocytes or precursors of T-cells. As a heterogeneous group of antigen-presenting leukocytes, they are important for innate and acquired immunity. Dendritic cells are defined as those cells that have the ability to take up and process antigens, transport the antigens to secondary lymphoid organs such as lymph nodes, and stimulate T-cells.[1,2]

Their dendritic shape enables them to perform these functions. They are specifically localized in the stratum papillare, often together with mast cells, near blood vessels. In non-inflamed skin, there are basically two cell populations: dermal myeloid and dermal plasmacytoid dendrocytes. In case of inflammatory reaction, an additional population of myeloid dendrocytes appears. Granulocytes represent a major portion of leukocytes as components of the innate immune system. Neutrophil granulocytes, also known as neutrophils, account for 50% of circulating leukocytes and are capable of phagocytosing microorganisms during acute inflammatory reactions and destroying them with the help of enzymes and their lysosomes. Eosinophil granulocytes play an important role in allergies and parasite defense. Circulating monocytes of the blood differentiate after tissue infiltration into macrophages, which are also called histiocytes. They possess phagocytic capabilities and can therefore eliminate bacterial pathogens and dead cells. Macrophages belong to the antigen-presenting immune cells because they cannot always fight the pathogens themselves. During tissue injury, neutrophils and macrophages infiltrate the wound.[3,5]

As the wound healing process progresses, the number of neutrophils reduces as they are cleared by macrophages. These become the dominant, inflammatory cell type as the wound progresses. In the early phase of inflammation, macrophages exert proinflammatory functions such as antigen presentation, phagocytosis, and production of inflammatory cytokines and growth factors. In the proliferative phase, macrophages stimulate tissue renewal in direct and indirect ways. The latter involves neovascularization, which occurs by stimulating fibroblasts and endothelial cells. At the end of the inflammatory response, macrophages die or migrate from the site of inflammation to draining lymph nodes.[1-4]

Mast cells are immune cells that can also be activated by non-immune processes such as acute stress and are involved in a variety of inflammatory diseases of the nervous system, skin, joints, and also the digestive and cardiopulmonary systems. Mast cells are specialized secretory cells produced by a pluripotent hematopoietic stem cell line in the bone marrow and occur ubiquitously in the connective tissues and mucous membranes of the body. They are most prevalent in regions exposed to the environment, such as the skin, respiratory tract, and digestive tract. In the skin, mast cells are found primarily in the stratum papillare of the dermis and are particularly localized around vessels, nerves, and skin appendages. Their percentage in dermal cells is 2-5%. They are immobile, long-lived, contain cytoplasmic granules and infiltrate the skin through the bloodstream.[4-6]

Their maturation takes place under the influence of mediators of neighboring cell types such as the fibroblasts and the keratinocytes. Examples of such mediators are stem cell factor ("SCF") and the cytokine interleukin-3. Mast cells contain in their granules a variety of preformed mediators such as histamine, tryptase, chymase, carboxypeptidase and heparin. Inflammatory mediators can also be formed de novo such as lipid mediators (e.g., prostaglandin D2), sulfide leukotrienes from the cell membrane, and cytokines. Cytokines, as glycoproteins, perform critical functions in the development, differentiation, and regulation of immune cells. On the cell membrane of mast cells there are high-affinity IgE receptors, which are activated by binding of proper antigens and cause release of mediators from granules. This so-called degranulation is one of the main functions of mast cells and can be triggered not only by IgE-dependent immune mechanisms but also by nonspecific stimuli such as mechanical stimuli, heat, bacterial and nonbacterial toxins, and by various endogenous mediators. Increased mast cell number and tryptase expression in heat-stimulated or UV light irradiated skin could be demonstrated, thus showing the influence of mediators of activated mast cells on a chronic inflammatory response. During degranulation, the granules fuse with the cell membrane and release their contents into the intercellular space. The release of mediators has regulatory functions in allergic and inflammatory diseases. It influences both angiogenesis by increasing vascular permeability and smooth muscle fiber contraction and wound healing and melanogenesis by attracting further immune cells.[1,3,4,5,6]

Post-inflammatory hyperpigmentation

Post-inflammatory hyperpigmentation is one of the most common causes of a change in normal skin color, called dyspigmentation. Other common hyperpigmentations that are also acquired include melasma, a pigmentation disorder that occurs during pregnancy and when taking oral hormone supplements, and age spot (lentigo senilis).Post-inflammatory hyperpigmentation can occur as a result of skin inflammations such as inflammatory dermatoses, infections, acne, allergies, and reactions to certain drugs and chemical peels, or as a result of mechanical injuries such as burns. Excess pigment can be defined or diffuse in the form of patches and can be either confined to small regions or have a widespread appearance. It is believed that depending on the cause and severity of the inflammation, the extent of hyperpigmentation varies. The color of any post-inflammatory hyperpigmentation

depends on the location of the excess melanin. Therefore, a general distinction is made between epidermal hypermelanosis and associated dark brown mottling and dermal hypermelanosis with the characteristic clinical appearance of gray-blue discoloration. Post-inflammatory hyperpigmentation occurs in all age groups, regardless of gender, and in all skin types, but is predominantly found in more pigmented individuals with Fitzpatrick phototype IV to VI. This specifically affects Asians, Africans, South Americans, and Native Americans. Post-inflammatory hyperpigmentation may persist for months or years and then fade, although the course in this regard is quite variable.[7,10,11]

At the cellular level, post-inflammatory hyperpigmentation is manifested by an increase in melanin production and/or abnormal melanin distribution. It is not known to what extent changes in melanocytes are relevant. These have been studied so far specifically in exogenously induced post-inflammatory hyperpigmentation. For example, it is known that in allergic contact dermatitis, a possible trigger of post-inflammatory hyperpigmentation, the number of active epidermal melanocytes increases. Similarly, the cell body size of melanocytes and the length of their dendrites increase. Furthermore, epidermal hyperpigmentation with increased melanocyte number could be detected after histological examination of scars caused by freezing injuries on an animal model. For this reason, previous research indicated that the small number of previous studies evaluating quantitative changes in melanocyte density in inflammatory skin processes should be expanded. In general, epidermal post-inflammatory hyperpigmentation is known to involve an increase in melanin synthesis and transfer to surrounding keratinocytes. This is triggered by the inflammatory response in the epidermis, in which arachidonic acid plays a crucial role, especially after its oxidation to prostaglandins and leukotrienes.[5,7,11]

In vitro, these mediators have been shown to stimulate human epidermal melanocytes, leading them to dendritic proliferation and size growth. The cellular mechanism leading to dermal post-inflammatory hyperpigmentation has been poorly described, leading to various theories regarding immigration of melanin into the dermis. On the one hand, destruction of the epidermal basal cell layer could occur, causing the degenerated basal keratinocytes and melanocytes to enter the dermis with their melanin and be phagocytosed by macrophages. On the other hand, melanosomes could be introduced directly into the dermis through the dendrites of melanocytes. Another theory is that macrophages migrate to the epidermis, where they phagocytose melanosomes, and then return to the dermis.[13,14]

Treatment methods are primarily healing the underlying inflammation and preventing further hyperpigmentation, for example, by applying high SPF sunscreens. Topical lightening agents are used for treatment, such as hydroquinones, azelaic acid, kojic acid, licorice extracts and retinoids. Chemical peels and laser therapy are also among the treatment options. Although some therapeutic alternatives are available for epidermal post-inflammatory hyperpigmentation, it often takes months to years to achieve successful depigmentation. In addition, inhibition of pigmentation is rarely reversible Alternative treatments that guarantee better and long-lasting success are the target of cosmetic research.[10-14]

Conclusion

Post-inflammatory hyperpigmentation is the most benign pigmented lesion we know about. In clinical practice, post-inflammatory hyperpigmentation poses a certain problem insofar as its appearance resembles that of a melanocytic tumor and, as a consequence, (not particularly serious) over-treatment by excision is performed. This usually happens when the patient does not remember the triggering injury or inflammation if it was a trivial case.

Conflicts of interest

None.

Ethical standards and patient's rights

This article is about scientific facts based on research literature. It is not reporting on a clinical trial, especially not a prospective one. Our research work is always conducted in accordance with the Declaration of Helsinki.

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