COMMON PHYSIOPATHOLOGICAL PATTERNS BETWEEN PSORIASIS AND VITILIGO

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Summary

Psoriasis and vitiligo are two autoimmune, multi-factorial, chronic diseases with an increased prevalence worldwide. Although the clinical characteristics are different, multiple associations are observed between the two conditions. The literature describes numerous directions regarding management focused on either psoriasis or vitiligo, seen as two separate entities. For this reason, current studies related to this association are converging towards new horizons that allow the use of a single therapy, personalized and equally focused on both conditions.

The aim of this paper is to formulate an overview of the current knowledge regarding psoriasis and vitiligo and to determine a possible relation between them.

***Key words**: psoriasis, vitiligo, biological therapies, phototherapy, JAK inhibitors.*

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Introduction

Vitiligo and psoriasis are two relatively common, multifactorial skin diseases characterized by a genetic predisposition and environmental factors that trigger various immune pathways. While the association between the two diseases could simply be coincidental, it has been hypothesized that patients with an immune-mediated inflammatory disorder are more likely to have another inflammatory disorder, increasing the possibility of a common etiology [1].

The purpose of this paper is to formulate a review of the existing literature focused on the coexistence of the two conditions mentioned above and to determine a possible relation between them.

Etiopathogenesis

One explanation for the association between psoriasis and vitiligo is the shared genetic basis for autoimmunity and inflammation. Genome-wide association studies have found increasing evidence of genetic predisposition to autoimmune diseases. Inflammasomes, multiprotein complexes in the cytoplasm that activate pro-inflammatory cytokines, may play an important role. Inflammasome-related gene sequence variants have been found to be associated with

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psoriasis in patients known to have generalized vitiligo. The skin inflammasome markers NLRP3 (nucleotide binding domain) and NLRP1 have been identified in both vitiligo and psoriasis [1]. In addition, psoriasis and vitiligo have unique nucleotide polymorphisms in classical human leukocyte antigens [2]. Several human leukocyte antigens (HLAs), including B13, B37, B46, B55, CW1, CW6, DR7, and DQ9, are associated with psoriasis, while HLA A2, DR4, DR7, and CW6 have been involved in the pathogenesis of vitiligo.

The second explanation is the shared importance of cellular immune pathways, including Th1 and Th17. Shared cell-mediated immune pathogenesis, including Th1 and Th17 pathways, may contribute to similar patterns of hyperactive cellular response in both diseases [3].

Also, an increased level of tumor necrosis factor (TNF)-α and the level of interferon-γ were detected in both diseases. In the pathogenesis of psoriasis, TNF-α is an important messenger substance for the activation of naïve T cells, being a pro-inflammatory marker. Among the other effects of TNF-α are the inhibition of melanocyte activation from stem cells and melanocyte function, as well as the destruction of melanocytes by the mechanism of apoptosis. On the other hand, TNF-α can induce the proliferation of regulatory T cells (Treg), so that the absolute number of Treg in the skin of patients with vitiligo, but also in those with psoriasis, is considerably increased. However, the ratio of Treg to CD3+ cells is increased in psoriasis patients compared to vitiligo patients.

Involved in the pathogenesis of these conditions, various genetic and environmental elements have been described, such as the Koebner phenomenon [4]. In vitiligo, studies have shown that patients with Koebner phenomenon have a longer duration of the disease, a larger affected body surface, but also a delayed, inadequate response to treatment [5]. Koebner can also provide an explanation for psoriatic lesions located strictly in the vitiligo-affected areas, but also for those psoriatic lesions with unusual sites [6].

Although the association of the two conditions has been a topic of interest over time, the relation between these pathologies has not been fully understood. Due to the increased prevalence among the world population, the presence of psoriatic lesions in a patient with vitiligo can be considered a coincidence, being located in different areas, but there can also be situations where these lesions appear at the level of vitiligo lesions.

The relation between the two conditions has been analyzed in literature and through the lens of response to biological therapies, but the results did not lead to a unanimous conclusion. There are reported cases in which biological therapies led to an improvement of vitiligo lesions among patients with psoriasis, as well as situations in which there was a worsening of them, as a result of the use of mainly anti-TNF alpha, but also anti-IL-12/23 and anti-IL-17.

Management

Psoriasis management is a difficult one, being influenced by multiple variables, such as the patient's profile and adherence to therapy, but also psychological aspects. The choice of therapy for psoriasis is determined by disease severity, comorbidities, and access to healthcare.

Current treatment options for vitiligo are considered to be suboptimal because they are not always effective and some therapies are limited to certain types of vitiligo. The two main categories of treatment, topical and oral immunosuppressive agents and phototherapy, can be used together to slow the progression of the condition, stabilize hypopigmented lesions and promote repigmentation. In addition, it is important to note that the effectiveness of a line of treatment can only be determined after a longer period of use, up to 2-3 months.[7]

Phototherapy

In vitiligo, phototherapy is the first-line treatment. Psoralen UV-A (PUVA) was the first therapy introduced in 1948, and it involves phototoxic effects and risk of skin malignancy [8]. Also, PUVA cannot be used for pregnant women and children [9]. Narrow-band UVB phototherapy (NB-UVB) has replaced PUVA therapy, due to its superior adverse reactions profile. This

is indicated by generalized or rapidly progressive vitiligo, where more than 5%-10% of the body surface is affected [10]. The efficiency of NB-UVB depends on the affected body area, with the most responsive areas to repigmentation being the face, neck, trunk and limbs, and the least responsive being the hands and feet [11]. In the case of localized vitiligo, with lesions affecting less than 10% of the body surface, excimer laser or excimer lamp is recommended [12].

Both PUVA and NB-UVB are recommended for the treatment of psoriasis, which work by increasing regulatory T cells and inhibiting the Th17 pathway [13]. Also, UVA acts by reducing the levels of pro-inflammatory cytokines, inducing T-cell apoptosis, but also inhibiting the activity of antigen-presenting cells [14]. Due to the higher risks associated with PUVA therapy, dermatologists prefer NB-UVB as the first line of treatment.

Jak inhibitors

In a phase 2 double-blind, randomized study, on a number of 12 patients with plaque psoriasis, a 10 mg dose of Tofacitinib was administered orally, two times a day, for 12 weeks. Results showed an improvement in PASI scores and a reduction in epidermal thickness, Ki67 levels, and KRT16 expression [15]. Another phase 3, randomized, double-blind trial in a cohort of patients with moderate-to-severe psoriasis vulgaris from multiple centers in China, Taiwan, and Korea who received Tofacitinib 5 mg twice daily and 10 mg twice daily showed showed its efficacy and good safety profile [16].

A study conducted by Mumford et al. demonstrated repigmentation of vitiligo lesions following the oral administration of Baricitinib 4mg/day for 8 months [17].

Anti IL17/IL23 Agents

Ustekinumab is a monoclonal antibody that blocks the p40 subunit of IL12 and anti IL23, and which has been approved for the treatment of moderate to severe plaque psoriasis vulgaris and psoriatic arthropathy, due to its efficacy and safety in the treatment of these pathologies [18, 19]. We note a singular case where Ustekinumab was administered to a patient who associated psoriasis vulgaris, vitiligo and alopecia areata, with satisfactory results on all 3 types of lesions [20]. Several other studies have demonstrated an aggravation of vitiligo lesions [21] or the novo appearance [22] of this pathology under treatment with Ustekinumab.

Secukinumab is a humanized anti-IL17A monoclonal antibody that showed its efficacy and safety in the treatment of plaque psoriasis through ERASURE and FIXTURE phase 3 trials [23]. Multiple studies have shown that Secukinumab causes the appearance or progression of vitiligo lesions [24,25].

Also, multiple studies have shown the good results in the management of psoriasis vulgaris of Ixekizumab. One notable side effect was the appearance of vitiligo lesions [26]. In the case of the association of the two pathologies, Ixekizumab was effective in the treatment of psoriasis lesions, but not of vitiligo lesions [27].

Conclusions

Both vitiligo and psoriasis are T-cell-mediated autoimmune diseases with overlapping pathogenic mechanisms that may contribute to similar hyperactive cellular response patterns in both diseases.

The cited studies suggest that the existence of psoriasis or vitiligo in one patient may be a predictor of the occurrence of the second disease in the same patient or his family. Further research is needed to explain the pathological mechanism underlying this epidemiological observation. The potential efficacy of Tofacitinib and narrowband ultraviolet B phototherapy in the management of both autoimmune diseases is currently being demonstrated. Avoidance of triggers, local therapy and phototherapy (narrow spectrum UVB), can be additional treatment steps in patients with psoriasis and vitiligo.

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Conflict of interest
NONE DECLARED

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