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Cutaneous Adverse Effects of Beta-Blockers: A Case of Psoriasis Induced by Nebivolol

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ABSTRACT

Nebivolol comes under the class of cardio selective Beta-blockers. Beta blockers are a very popular class of drugs used to treat both cardiovascular and non-cardiovascular diseases, including hypertension, ischaemic heart disease, arrhythmias, heart failure, hyperthyroidism, glaucoma, and anxiety disorders. Typically prescribed for high blood pressure, beta-blockers are among the drugs most commonly linked to psoriasis. Psoriasis is a complex, chronic, multifactorial, inflammatory disease that involves hyper-proliferation of the keratinocytes in the epidermis, with an increase in the epidermal cell turnover rate. This case report describes a 70 years old male with hypertrophic cardiomyopathy, Dyslipidemia, Coronary Artery Disease and systemic hypertension who developed psoriasis due to administration of nebivolol, a beta blocker used to manage HTN. The patient came with complaints of itchy erythematous scaly plaques with erosions over scalp, trunk and extremities for 1 month. Discontinuation of beta blockers such as nebivolol was advised. This case highlights our attention to the potential dermatologic adverse effects that may follow with a beta-blocker use, as well as proper reviewing of medical history for any allergic reactions and the optimization of drug therapy in order to avoid such drug-induced flares.

KEYWORDS: Nebivolol, Beta-blockers, Psoriasiform dermatitis, Adverse drug reaction, Hypertension

INTRODUCTION

Psoriasis is an autoimmune non-infectious, chronic, inflammatory skin disorder where altered keratinization of epidermal cell takes place with well-defined erythematous scaly plaques and white scales with a predilection for the extensor surface and scalp.[1]

The pathophysiological mechanism is complex and includes epidermal homeostasis disorders (affecting keratinocyte proliferation and differentiation), as well as abnormal activation of the immune system.[2] Etiology includes environmental and genetic factors. Erythematous, scaly skin lesions along with additional manifestations in nails and joints are commonly present. The most common form is plaque psoriasis. Pustular, guttate, inverse and erythrodermic psoriasis are the other forms.

Psoriasis and hypertension are found to be concomitantly related and most medications used in treating the co-morbidities are found to aggravate psoriasis. This co-occurrence is not random, it involves shared pathophysiological mechanisms, such as chronic inflammation, immune system dysregulation, oxidative stress, and metabolic syndrome. According to a 2010 review of studies in the Journal of Clinical and Aesthetic Dermatology, beta-blockers were considered a major factor in triggering severe psoriasis in people hospitalized for the disease. Several theories explain the pathogenesis of beta blocker-induced psoriasis, including delayed-type hypersensitivity reactions, immunological mechanisms such as impaired

lymphocyte transformation, and disruptions in the cyclic adenosine mono-phosphate (cAMP) pathway. cAMP, an intracellular messenger, regulates protein stimulation for cellular differentiation and inhibits proliferation. The most widely accepted theory suggests that beta-blockade of epidermal ß2 receptors reduces intra-epidermal cAMP levels, leading to keratinocyte hyper-proliferation. These drugs can also provoke new outbreaks in people previously undiagnosed with psoriasis. [3][4]

Drug-induced psoriasis is found to act in two ways. One is where the psoriasis is due to an adverse effect of the drug and which subsides on the gradual withdrawal of the drug. Second is an aggravation of the persisting psoriatic condition where withdrawal of drug has no much effect. Latency period from ingestion of β blockers to psoriatic flares varies from several days to 12 months in patients with psoriasis.[5]

CASE REPORT

A 71 year old male patient came to the dermatology department on 13th November 2024 with complaints of itchy erythematous scaly plaques with erosions over scalp, trunk and extremities for 1 month. He was diagnosed with systemic HTN and started the therapy with Tab. Nebivolol, 5mg once a day. He is a known case of hypertrophic cardiomyopathy, DLP, CAD and systemic HTN. On examination he was found to have generalised dryness of skin and mild erythema, erythematous plaque over upper limbs and erythematous scaly plaques with erosions over scalp, trunk and extremities . Skin biopsy was taken and is as follows-Epidermis shows confluent parakeratosis with focal neutrophilic aggregates in the stratum corneum and collections of plasma, diminished to absent granular layer, prominent spongiosis, areas of focal atrophy to focal mild acanthosis, lymphocytic and focal neutrophilic exocytosis. Few keratinocytes with reactive atypia noted. Papillary dermis shows edema, extravasated RBCs and mild perivascular infiltrates of lymphocytes, histiocytes and eosinophils. Deep dermis and subcutis are unremarkable and were diagnosed as Spongiotic dermatitis and psoriasiform dermatitis. General Medicine consultation was given to change Tab Nebivolol as it can aggravate psoriasis. He was advised to stop Tab. Nebivolol and changed to Tab. Cilnidipine 10 mg once a day to control hypertension. He was prescribed tablet Ciprofloxacin 500 mg BD for 7 days and cyclosporin 50 mg OD for 7 days. On follow up it is found that the patient is symptomatically better.

DISCUSSION

Nebivolol, a beta blocker, is mainly used in the management of HTN. One of the rare side effects of β blockers is psoriasiform drug eruptions. Psoriasis has several triggers and skin lesions often have an unpredictable outcome, thus the causal relation between psoriasis occurrence and drug exposure is often difficult to prove. [6]The cAMP-centric hypothesis is currently the most frequently supported explanation for beta-blocker–induced psoriasis pathogenesis in the literature. Keratinocytes and granulocytes express β2-adrenergic receptors (β2-ARs), which normally stimulate adenyl cyclase to produce cAMP inside the cells. When beta blockers (BB) are used, these β2-ARs are blocked, leading to reduced adenyl cyclase activity and a subsequent decrease in intracellular cAMP levels. As the intracellular levels of cAMP decreases, there is a drop in intracellular calcium levels, disrupting the epidermal calcium gradient with consequences including impaired kerationocyte differentiation, enhanced kerationocyte proliferation and increased release of pro-inflammatory cytokines, aggravating the inflammation typical in psoriasis.[6][7] Psoriatic skin shows increased synthesis and hydrolysis of cGMP, leading to elevated steady-state cGMP levels in affected epidermis. cGMP regulates calcium influx via cGMP-gated calcium channels, crucial for epidermal calcium homeostasis necessary for keratinocyte differentiation and function. Dysregulation

of both cAMP and cGMP pathways disrupts epidermal calcium gradients, keratinocyte proliferation/differentiation, and immune responses, collectively contributing to psoriasis pathogenesis. Abnormalities in cGMP metabolism or channel function disrupt epidermal calcium gradients, contributing to defective differentiation and hyperproliferation of keratinocytes seen in psoriasis. Therapeutically, targeting these pathways—like using PDE4 inhibitors to elevate cAMP or modulating cGMP-related signaling—offers routes to ameliorate psoriasis inflammation and keratinocyte dysfunction.[8][9]

Nebivolol induced psoriasis is classified as a Type B adverse drug reaction (ADR). Since it is dose dependent, unpredictable, immune mediated or hypersensitivity reaction, it falls under type B ADR. Drug induced psoriasis typically resolves once the offending medication is stopped, although the time to resolution can vary.

CONCLUSION

This case report highlights aggravation or exacerbation of drug-induced psoriasis could be reduced by discontinuing the intake of the particular drug. Health-care professionals should be vigilant in monitoring such drug induced psoriasis in patients receiving beta blockers and promptly identify and manage adverse events to ensure optimal patient care. Further research is warranted to better understand the mechanisms and risk factors associated with nebivolol induced psoriasis.

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