SKIN

BRIEF ARTICLE

Identifying a Case of an Atenolol-induced Papulosquamous Eruption

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ABSTRACT

While beta-adrenergic blocking agents (beta blockers) are generally safe, their incidence of medication-induced cutaneous eruptions remain under-recognized in the primary care setting. The adverse dermatologic effects of these medications may arise in the days to years following drug initiation, contributing to its delayed diagnosis and management. Here we report a case of a papulosquamous drug eruption in an older adult due to atenolol. We also discuss pertinent morphologic findings, diagnostic methods, management, and how to distinguish this type of eruption from other papulosquamous disorders.

INTRODUCTION

Beta blockers are among the most frequently prescribed cardiovascular medications. Cardioselective agents such as atenolol are approved for use in treating hypertension, angina pectoris, heart failure, arrhythmias and acute myocardial infarctions.[1,2] Although beta blockers have a good overall safety profile, commonly reported adverse effects include depression, fatigue, and sexual dysfunction.[1] While some cutaneous eruptions have been reported in patients being treated with beta blockers, these remain under reported and often unidentified.

Reported cutaneous adverse drug reactions (ADR) in the setting of atenolol use include psoriasiform dermatoses, eczematous reactions, and lichen planus-like eruptions.[3–5] Diagnosis of suspected cutaneous ADRs requires comprehensive documentation of symptom onset and progression in relation to initiation of the patient's systemic medications. If an ADR is suspected, the potentially offending drug should be discontinued. Employing a monitored discontinuation followed by a controlled rechallenge remains the diagnostic gold standard to ascertain a medication's involvement in a cutaneous drug eruption.[6] For mild manifestations, topical corticosteroids may suffice, while severe presentations may necessitate systemic therapy and vigilant monitoring for complications. In this context, discontinuation of atenolol has been observed to lead to marked improvements in cutaneous eruptions within a span of days to weeks.[4,7]

CASE REPORT

A 68-year-old Eastern European male with a past medical history of hypertension and

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hypercholesterolemia presented with seven-year history of a non-pruritic, non-tender papular rash on the trunk and extremities. Previous treatments with multiple potent and superpotent topical corticosteroids, antifungal agents, minocycline, and methotrexate were unsuccessful and patch testing was negative. His other medications included atenolol, atorvastatin, and fenofibrate. The patient had no prior personal history of cutaneous disorders. Physical examination revealed multifocal scaly erythematous papules on the trunk and extremities (**Figures 1-A, 2-A, 3-A**). The main differential diagnoses at first visit included atopic dermatitis (AD), psoriasis, transient acantholytic dermatosis (Grover disease), and drug-induced papulosquamous eruption. Two punch biopsies of the superior and mid right back were performed. Hematoxylin and eosin (H&E) stain revealed hyperkeratosis, parakeratosis, spongiosis, exocytosis of lymphocytes, and a superficial perivascular lymphocytic infiltrate consistent with lichenified spongiotic dermatitis. Due to concern for a papulosquamous drug eruption (PSQDE), the atenolol was discontinued with approval and follow-up from the patient's primary care physician. Upon 2-week follow-up, the patient's rash had essentially cleared (**Figures 1-B, 2-B, 3-B**). Upon re-challenge 3 days later, the cutaneous eruption returned within 5 days.

DISCUSSION

The recurrence of this rash following discontinuation of atenolol with re-challenge supports the diagnosis of a PSQDE. Beta blockers have been infrequently reported to elicit both eczematous and psoriatic eruptions on the scalp, trunk, and extremities.[4,5] Lesions are most commonly psoriasiform in appearance, presenting as erythematous and scaly papules and plaques, sometimes annular or pustular in appearance.[4] Reports have noted variable associations including pruritus, hyperkeratotic involvement of palms and soles, and nail changes.[4] While PSQDEs were correlated with prolonged beta-blocker use, there was no association with a patient history of psoriasis.[4,5] Onset occurred from 2 days to 6 years following drug initiation.[4,5]

The proposed pathogenesis underlying cutaneous drug eruptions in response to beta-blockers is multifactorial and involves immunological and non-immunological mechanisms. It is attributed to the blockade of beta-adrenergic receptors located on keratinocytes involved in cell differentiation and immune activation. Beta blockade has been suggested to downregulate intracellular cyclic adenosine monophosphate (cAMP) levels, an intracellular messenger crucial for stimulation of cellular differentiation and inhibition of proliferation.[3] Impaired keratinocyte differentiation leads to a dysregulation of cytokines and growth factors eliciting excessive activation of lymphocytes, neutrophils, and macrophages.[8] Beta-blockers are also associated with Th17 differentiation and upregulation of IL-23, TNFa, and IL-6, which may account for their role in psoriatic drug eruptions.[9] Biopsies taken from cardioselective beta-blocker-induced eruptions such as atenolol have a characteristic excessive degranulation of neutrophils in the dermis.[3] Further research is still needed for definitive pathogenesis and mechanism of cutaneous drug eruptions in response to beta-blockers.

The primary differential diagnoses to rule out when suspecting a PSQDE are AD and psoriasis. AD is typically ill-defined, pruritic, lichenified, xerotic, and often accompanied by keratosis pilaris. AD commonly presents on flexures and palms of adolescents and

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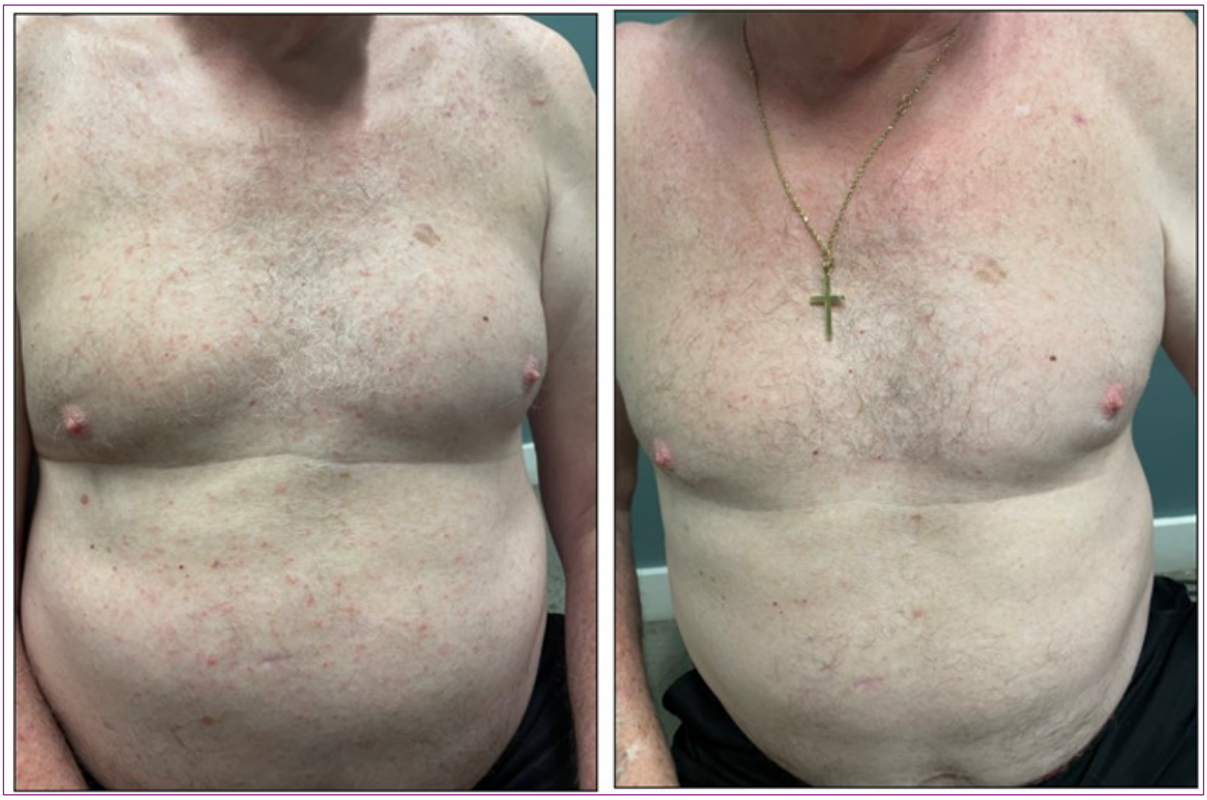

Figure 1. Erythematous scaly papules of the anterior trunk.
Figure 1-A. Initial visit (left); **Figure 1-B.** 2 weeks post atenolol discontinuation (right).

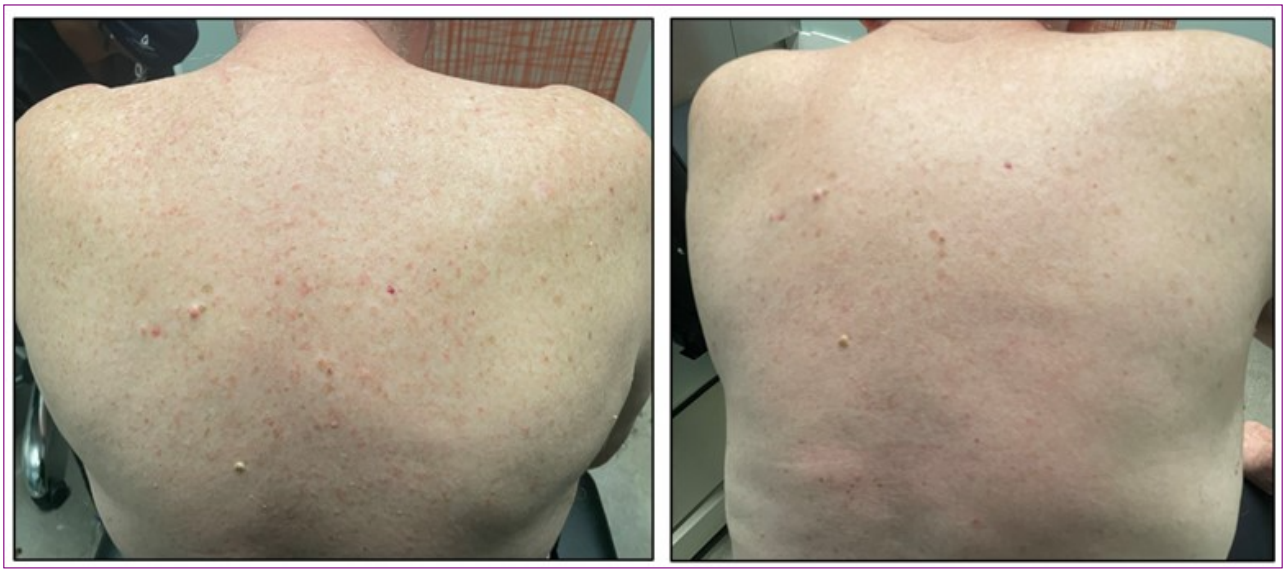

Figure 2. Erythematous scaly papules of the posterior trunk.
Figure 2-A. Initial visit (left); **Figure -B.** 2 weeks post atenolol discontinuation (right).

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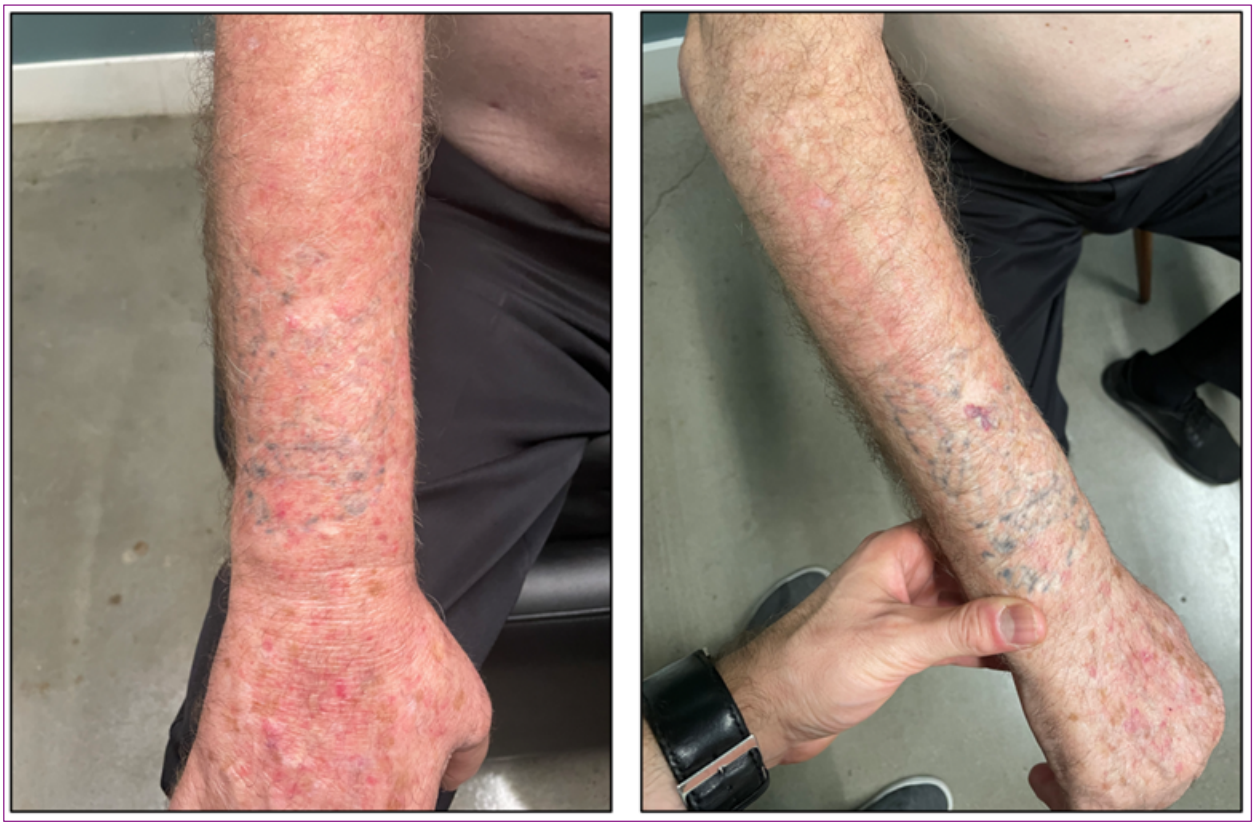

Figure 3. Erythematous scaly papules of the right upper extremity.
Figure 3-A. Initial visit (left); **Figure 3-B.** 2 weeks post atenolol discontinuation (right).

young adults with a family history. In contrast, PSQDEs present with a more papular or vesicular appearance, less frequent pruritus, and often occurs in older adults following initiation of new medications. Findings on H&E of PSQDE often include spongiosis, parakeratosis, keratinocyte necrosis, perivascular mononuclear infiltrate, and irregular acanthosis. These lesions lack the Munro microabscesses and neutrophils seen in psoriasis.[8] Patch testing may be used to confirm presence of delayed skin eruptions including drug hypersensitivity, allergic contact dermatitis, and PSQDE.[10]

The most important aspect in the evaluation of a patient with a suspected PSQDE is gathering an accurate timeline of initiation of any new medications in relation to the onset of cutaneous symptoms. Proper identification of a PSQDE is frequently challenging due to poor patient recollection of drug initiation and onset of cutaneous findings often convoluted by other multiple chronic medications particularly in elderly patients, inaccessible patient medical records from previous prescribing providers, inability to discontinue or substitute essential medications, difficulties in coordinating co-management with prescribing providers, and overall lack of awareness of PSQDEs. Eruptions precipitated by atenolol have demonstrated clear improvement within days to weeks following withdrawal of the culprit medication.[4,7] Concurrent treatment with topical corticosteroids, calcineurin inhibitors, and antihistamines may offer relief of pruritus but overall efficacy is limited.[4,7] Patients with long-standing PSQDEs can achieve great outcomes as long as the correct

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pharmacological culprit is identified and discontinued safely and appropriately.

Conflict of Interest Disclosures: None

Funding: None

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