ISSN 2473-4799

DERMATOLOGY
Open Journal

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Case Report

Photodistributed Hyperpigmentation Induced by Lercanidipine

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Article information
Received: December 28th, 2017; **Accepted:** January 5th, 2018; **Published:** January 5th, 2018

Cite this article
Gimenez-García R. Photodistributed hyperpigmentation induced by lercanidipine. *Dermatol Open J*. 2018; 3(1): 1-3. doi: 10.17140/DRMTOJ-3-128

INTRODUCTION

Hypertension (systolic blood pressure of 140 mmHg or above and/or diastolic blood pressure of 90 mmHg or above), is the most common chronic condition dealt with by primary care physicians and other health practitioners.[1] Calcium channel blockers (CCBs), introduced into clinical medicine in the 1960s, are a group of compounds with distinctive structures and pharmacologic effects, are first-line treatment option for hypertension.[2] In spite of their widespread use, little data have been published about the spectrum of cutaneous adverse reactions by CCBs.[3-6] Cutaneous adverse reactions induced by lercanidipine, a third-generation o dihydropyridine CCBs, are uncommon.[7-9] We present to our knowledge the first case of reticulated photodistributed hyperpigmentation induced by this drug.

CASE REPORT

A 68-year-old woman with a past medical history of hypertension and frontal fibrosing alopecia, presented with a 3 months history of hyperpigmentation on her face that started in summer after sun exposure. She had been taken lercanidipine approximately 2 years before. Concomitant medications included simvastatin that she had started many years ago. Physical examination showed reticulated, slate-gray to brown, pigmentation without infiltration on the cheek, temple, nose and eyelids regions (Figure 1). Histological examination revealed epidermal atrophy with flattening of the rete ridges, vacuolar alteration of the basal layer and prominent pigmentary incontinence (Figure 2). Laboratory testing included liver function test, complete blood cell count, serum urea and creatinine, serologic test for antinuclear antibodies were normal. Photodistributed hyperpigmentation due to lercanidipine was suspected therefore management of the hyperpigmentation consisted of the replacement of lercanidipine with telmisartan plus hydrochlorothiazide and photoprotection. She has improved very slowly after discontinuation of lercanidipine.

Figure 1. Reticulated Slate-gray to Brow Hyperpigmmented Macules on the Cheek and Eyelid

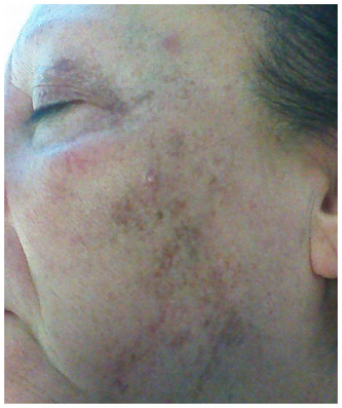
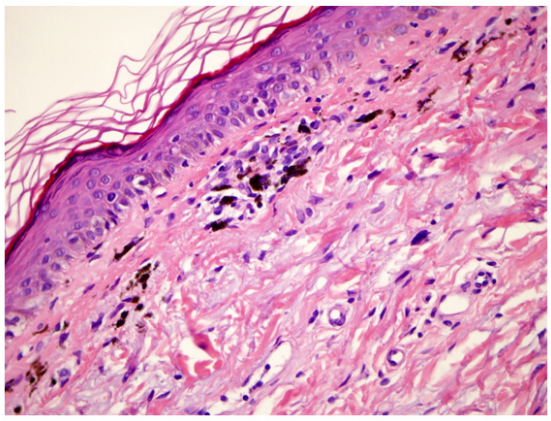


Figure 2. Epidermal Atrophy with Flattening of the Rete Ridges, Vacuolar Alteration of the Basal Layer and Prominent Pigmentary Incontinence



DISCUSSION

Drug-induced skin pigmentation is estimated to account for 10% to 20% of all cases of acquired hyperpigmentation. Drug-induced hyperpigmentation frequently occurs as post-inflammatory changes of a resolving drug-induced rash, but also directly promote through stimulation of melanin production , deposition of iron following vessels damage and/or deposition of drug (or drug metabolite) within the skin.[10-12] Drugs of several classes are associated with skin or mucous membrane pigmentation and include nonsteroidal anti-inflamatory drugs, antimalarials, amiodarone, antineoplasic agents, tetracyclines, heavy metals, clofazimine, oral contraceptives, psycotropic drugs. Anticonvulsants such as hydantoin, phenytoin and barbiturates.[10-16] other drugs reported to induce skin hyperpigmentation are amiodarone and some antihypertensives such as diltiazem, telmisartan and amlodipine.[17-25]

Calcium channel antagonists block the inward movement of calcium by binding to the L-type calcium voltage-gated channels located on the vascular smooth muscle, cardiac myocytes and cardiac nodal tissue causing vascular smooth muscle relaxation and vasodilation coronary arteries and peripheral arterioles, but not veins. They also decrease cardiac contractility (negative inotropic effect), automacity at the SA node and conduction at the AV node.

Published reports of CCBs reactions are infrequent. Range from non-serious reactions to serious and potentially fatal conditions, including erythema multiforme, Steven-Johnson syndrome, toxic epidermal necrolysis (TEN) or exfoliative dermatitis. It appears that the frequency is low but occasionally severe reactions are associated with the use of CCBs. Most serious reactions occur within two weeks of initiating drug therapy.[3] Flushing, ankle or pedal edema and gingival hiperplasia are common side effects. Other adverse cutaneous reactions include photosensitivity reactions, photodistributed facial telangiectasia or on non photoexposed areas, lichenoid eruptions, psoriasiform eruptions (simultaneous intake of β blockers might have a synergist effect on the onset of psoriasis), acute generalized exanthematous pustulosis, subacute cutaneous lupus erythematous, pemphigus and pemphigoid and hypersensitivity syndrome.[5,6]

Lercaninipine is a vasoselective lipophilic dihydropyridine calcium antagonist which causes systemic vasodilatation by blocking the influx of calcium ions through L-type calcium channels in cell membranes. Once daily administration of lercanidipine 10 or 20 mg effectively reduce blood pressure. Has a slower onset and longer duration of action than a number of other CCBs. Antihypertensive effect comparable to that of amlodipine but a better tolerability profile. What distinguishes lercanidipine from other members of the DHP class is its lower incidence of adverse effects, particularly edema.[26-29] Drug reaction with eosinophilia, bullous eruption and systemic symptoms (DRESS) and macupapular rash induced by lercanidipine has been reported.[7-9]

Photodistributed hyperpigmentation (reticulated or homogenous) induced by dialtiazem and amlodipine has been reported in darker skin phototypes. A long interval between the initiation of antihipertensives therapy and the emergence of the hyperpigmentation (mean duration: 15 months), which was markedly longer than the intervals for other types of drug reactions. The face was affected in all cases, followed by neck and forearms. Cessation of the suspicious drug results in a gradual fading of the rash, although in some cases it never resolves.[18-24] No previous cases of hyperpigmentation have been reported following exposure to lercanidipine.

Adequate photoprotection and diet supplementation with antioxidants may be beneficial in increasing the minimun erytemal UV dose radiation.[30]

CONCLUSION

In conclusion**,** drugs-induced hyperpigmentation, must be considered in unexplained pigmented lesions. Photodistributed hyperpigmentation, with distinctive morphological appearance slate-gray to brown and reticulated must be a cutaneous drug reaction, in particular with antihyertensive medications.

ACKNOWLEDGEMENT

This case was presented in a communication in the Annual Congress & Medicare Expo on Primary Healthcare. April 25-27, 2016 Dubai, UAE.

CONSENT

The author have received oral informed consent from the patient whose photographs are involved in the manuscript.

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