

Case Report

A case report on hydroquinone induced exogenous ochronosis

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ABSTRACT

Exogenous ochronosis is an infrequent skin disorder characterised by bluish-black or grayish brown pigmentation on dermis. It is the most common condition caused due to long term application of Hydroquinone skin preparations for melasma, skin brightening, cholasma, acne induced pigmentation etc. This report refers to a case of 39-year-old female patient who presented to the hospital with chief complaints of progressive formation of dark lesions over face, neck since one and half-year. She had history of usage of hydroquinone (4%) cream for skin brightening for a period of three months. Based on clinical findings and history she was diagnosed to have acquired exogenous ochronosis and was treated with microdermabrasion, cosmelan peel, yellow peel, glutathione tablets, topical sunscreen and kojic acid cream. Patient noted 50% improvement in her condition after 4 months of treatment. It is believed that application of high concentrations of hydroquinone for a prolonged period causes exogenous ochronosis. This case report suggests that exogenous ochronosis can occur after three months of application.

Keywords: Bluish-black pigmentation, Hydroquinone, Ochronosis, Skin brightening

INTRODUCTION

Hydroquinone (benzene 1, 4-diol or quinol) a phenol derivative, is a melanin synthesis inhibitor and an antioxidant. It is a major constituent in skin lightening creams almost since 50 years and is a standard depigmentation agent used in melasma, cholasma, solar lentigines, post inflammatory hyperpigmentation caused by acne vulgaris, eczematous dermatoses, contact dermatitis, psoriasis and burns.¹ Hydroquinone decreases pigmentation by affecting the non-follicular and follicular melanocyte system. It decreases formation of

melanosomes, alters their internal structure and degrades the membranous structures of melanosomes and eventually causes necrosis.²

Exogenous ochronosis is an infrequent disorder characterized by diffuse bluish -black or grayish -brown pigmentation due to deposition of ochre colored pigment in the dermis. It occurs secondary to long-term application of skin-brightening creams containing hydroquinone or due to topical contact with phenol, resorcinol and use of systemic anti-malarials such as quinine or prolonged sun-exposure.³ The most accepted

theory proposes that hydroquinone inhibits the local activity of the homogentisic acid oxidase enzyme, resulting in accumulation of homogentisic acid, which gets polymerize, forming the ochronotic pigment and get deposited in the dermis.⁴

It manifests as symmetrical hyperpigmentation at the zygomatic areas of the face, sides, and back of the neck and localizes to the area where the causating agent was applied. The affected areas are bright, smooth and inelastic. The incidence of exogenous ochronosis globally unknown but is relatively low in Asia and reports are increasing from India. Exogenous ochronosis is clinically and histologically similar to an inherited disorder alkaptonuria which exhibits systemic effects. It is very difficult to treat exogenous ochronosis as it is a cosmetically disfiguring and psychologically disturbing condition with unsatisfying treatment options.⁵

CASE REPORT

A 39 year old female patient visited Department of Dermatology with complaints of progressive formation of dark lesions on face and neck since one and half year. (Figure 1 provided below shows hyperpigmentation marks on face and neck of patient). On examination she had diffuse hyperpigmentation over face and neck. She gave history of using Hydroquinone 4% w/w cream over face and neck for skin whitening for three months. After using for three months she observed progressive formation of blue-black macules over the applied region and it evolved lately into bluish-black hyperpigmentation. She denied any other symptoms, no similar familial history or use of other oral or topical medications and there are no other comorbidities. Based on clinical findings she was diagnosed as having Acquired Exogenous ochronosis and was initially treated with microdermabrasion and cosmelan peel but there was no improvement. On causality assessment based on WHO probability scale the reaction is assessed to be probable. After one month she had 50% glycolic acid peel along with microdermabrasion and treated with Yellow peel, Glutathione tablets, topical sunscreen and kojic acid creams in the subsequent sessions. Patient noted 50% reduction in pigmentation after about 4 months of treatment.

DISCUSSION

The etiological factors behind exogenous ochronosis have been well studied and majorly include usage of skin lightening creams and unprotected sun exposure. Despite hydroquinone being an effective treatment for various skin pigmentation colour changes, its use is associated with the rare complication of exogenous ochronosis. The association between topical hydroquinone use and exogenous ochronosis is well studied in literature.⁶ The first case of exogenous ochronosis was reported from Maharashtra, India 2004 in a female farmer, who developed exogenous ochronosis after unsupervised

application of 4% Hydroquinone containing preparation for more than three months for melasma. Subsequently, a few more case reports from other parts of India also have been described by other authors. In all these reports, unsupervised usage of the skin-lightening agents was a common highlighting feature.⁷ On considering this data from India all the physicians who are prescribing should also look for the adverse outcomes on a biweekly basis atleast to prevent the complications associated with the use of the medications.



Figure 1: Patient with hyperpigmentation on face and neck.

Hydroquinone has been marketing since many years and this is most widely used by patients on prescription and over the counter. Many issues have been raised regarding its side effects and this almost led to banned from US market by the FDA in 2006.⁸ Many case reports suggested that exogenous ochronosis is largely refractory to topical agents, improvements have been reported after treating with physical modalities such as microdermabrasion, laser with CO₂ and Q-switched 75nm alexandrite laser irradiation, retinoic acid, azelaic acid, kojic acid, cryotherapy among others. In this case patient is treated with microdermabrasion and treated with Yellow peel, Glutathione tablets, topical sunscreen and kojic acid creams in the subsequent sessions and noted 50% reduction in pigmentation after about 4 months of treatment, but the condition remained difficult to treat in many cases.⁹ Patient history and clinical findings in our report demonstrated that exogenous ochronosis is a result of application of topical Hydroquinone. It mimics melasma so clinical diagnosis of exogenous ochronosis may be missed in early stages. Due to lack of skin biopsy findings the diagnosis may not be confirmed, so the incidence of this condition is more than that of reflected in the literature.¹⁰ Exogenous ochronosis is an uncommon

adverse reaction associated with the hydroquinone, with global data pertaining to number of individual case safety reports reported till date that is less than ten from the reported events to the WHO-UMC database.¹¹ Although it is believed that application of high concentrations of hydroquinone after applying for a prolonged period causes exogenous ochronosis. In this case patient applied 4% of hydroquinone for a period of 3 months and developed exogenous ochronosis which suggests that usage of Hydroquinone 4% cream for as little as three months duration can also cause exogenous ochronosis.

CONCLUSION

When dermatologists prescribe patients with hydroquinone for skin lightening, pigmentation, and melasma, the patients apply the cream more frequently than required anticipating better recovery or improvement for the disease conditions. They do not understand the possibility of causing some of the serious adverse effects like exogenous ochronosis, and finally they end up with distress and depression. Hence prescriptions containing hydroquinone should be dispensed only after a proper orientation about the possible side effects and should be counselled to use for a limited period of time as required.

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