

**EXOGENOUS OCHRONOSIS MASQUERADING
REFRACTORY MELASMA**Swati Sharma¹, Raghavendra Rao²¹Department of Pathology, Kasturba Medical College, Manipal, Karnataka, India²Department of Dermatology, Kasturba Medical College, Manipal, Karnataka, India

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Abstract

Exogenous ochronosis is an infrequent dermatosis characterized by dark blue hyperpigmentation. It may be caused largely by hydroquinone, a fenolic compound which is used in the treatment of melasma and other skin hyperpigmentation. The exact etiopathology is still not understood and the results of various treatments offered are unsatisfactory. We present a case of exogenous ochronosis which resembled melasma but clinicopathologic evaluation led to the correct diagnosis. We also emphasize the need to restrict the indiscriminate use of hydroquinone containing compounds without medical prescription.

Key words: ochronosis; hydroquinone; alkaptonuria**Cite this article:**Sharma S, Rao R. Exogenous ochronosis masquerading refractory melasma. *Our Dermatol Online*. 2014; 5(4):398-400.**Introduction**

The term 'ochronosis' was first described by Virchow [1] in 1866 as a brownish-yellow pigment that gets deposited in the connective tissue of various organs. Ochronosis can be endogenous or exogenous in origin. Endogenous ochronosis also called as alkaptonuria is caused by deficiency of the enzyme homogentisic acid oxidase which causes deposition of ochronotic pigments [2]. In contrast, exogenous ochronosis presents as gray-brown or blue-black macules, hyperchromic, pinpoint papules in photo-exposed regions in a symmetrical pattern. It can occur secondary to the topical application of hydroquinone, phenol, resorcinol, or even by oral administration of antimalarials [3].

Case Report

A 47 year old female complaints of black pigmentation over bilateral cheeks for last 6 years which has aggravated for the past 2 years. Symptoms started with redness and gradually progressed to black pigmentation and it gets worsened by sun exposure. Patient has been applying a skin lightening cream over the cheeks for last 7 years on her own without consulting any doctor. For the present symptoms local doctor prescribed topical steroids but her condition did not improve. There was no history of itching, arthralgia, alteration in the colour of urine, hyperpigmentation of sclera, axillae or genitalia. She was started on antidepressants recently. On examination

hyperpigmented macules with peripheral erythema was noted at malar area on both the cheeks (Fig. 1). Clinical differentials included pseudo ochronosis, refractory melasma and topical steroid induced telangiectasia. Skin biopsy of the lesion on histopathology revealed acanthotic epidermis overlying dermis showing accumulation of yellow brown pigment causing homogenization and swelling of collagen fibres (Figs 2, 3). A diagnosis of pseudo-ochronosis was given. Patient has been started on sunscreen cream, hydroquinone free and steroid free depigmenting ointments. She is on regular follow up.

Discussion

Exogenous ochronosis was first related by Pick [4] in 1906. Beddard and Plunter [5] described it in a patient using phenol for an ulcer treatment in 1912. However, ochronosis secondary to the use of hydroquinone in topical bleaching agents was first described by Finlay in 1975 [6].

The exact incidence of exogenous ochronosis is unknown due to inability to recognize symptoms at an early stage and inappropriate and indiscriminate use of these topical agents by the patients. It was thought that use of high concentrations of hydroquinone above 4% for a long period of time is responsible for development of exogenous ochronosis. However, recent reports of exogenous ochronosis even in patients using hydroquinone in low concentrations (2%) and for periods as short as 3 months have been described [2,3]



Figure 1. Erythematous plaque on left malar area.

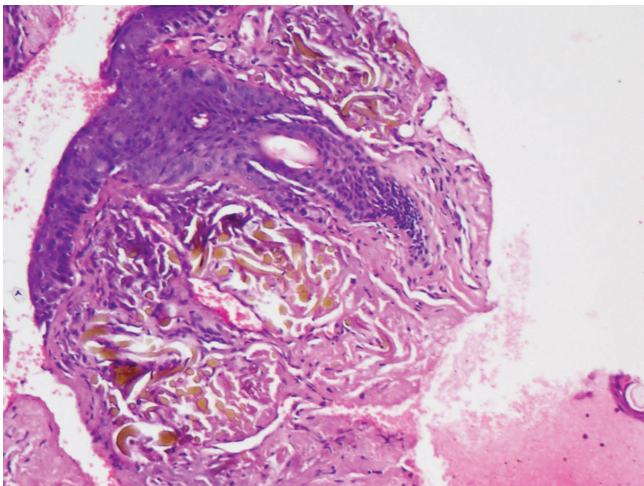


Figure 2. Accumulation of yellow-brown pigment in the dermis. H&E X100

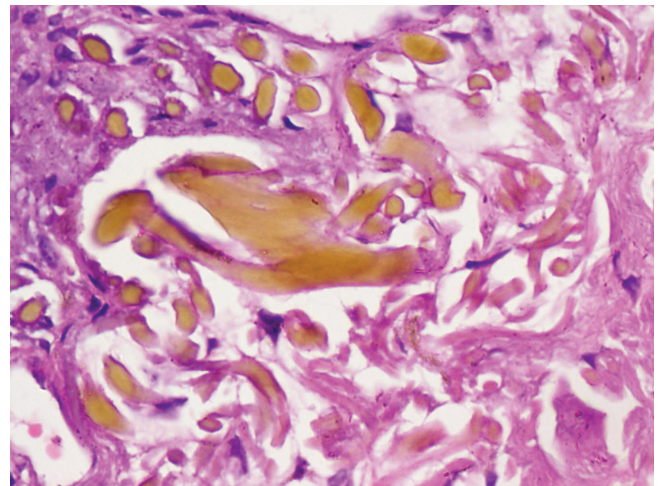


Figure 3. Homogenization and swelling of collagen fibres. H&E X400

The other predisposing factors mentioned in literature include Fitzpatrick's System high phototype, lack of sun protection, skin irritation and vigorous friction [7]. Out of the various theories described the most accepted one is Penneys [8] who attributed the hyperpigmentation due to the inhibition of the enzyme homogentisic acid oxidase by hydroquinone. This leads to the accumulation of homogentisic acid which further polymerizes to form 'ochre' pigment in the dermis. According to Dogliotte and Leibowitz [9] exogenous ochronosis has three clinical stages, first as initial erythema and mild pigmentary change; second hyperpigmentation, black colloid milia, and atrophy; and third as development of papulonodules [3]. Hydroquinone has been used for treating hypermelanosis, senile lentigo, pigmented areas of vitiligo and melasma. It acts by inhibiting production of melanin. Its chronic use causes

depigmentation confetti type, exogenous ochronosis, dermatitis, squamous cell carcinoma on the exogenous ochronosis site, reduction of the healing capacity of the skin, pigmentation of sclera and nails and even cataract [2].

Important clinical differential is melasma which can be confirmed on histopathologic examination. Histopathology of ochronosis is characterized by yellow brown, banana-shaped pigment fibers in the dermis in its early stages. As it progresses to the third papulonodular stage, the ochronotic fibers degenerate and form a colloid milium. Some lesions may form sarcoid-like granulomas surrounding the ochronotic fibers [3]. In contrast, melasma shows a significant increase in the amount of melanin in all epidermal layers which can be confirmed in Masson-Fontanna stain.

Pigment incontinence, presence of melanophages and solar elastosis can be seen in both the lesions. Exogenous ochronosis is usually superimposed on the skin affected by melasma. Most importantly there are no ochre fibers in melasma, which is the characteristic finding in ochronosis [10]. Reports of electron microscopy and dermatoscopy differentiation of the two are also well documented [2].

Exogenous ochronosis is refractory to treatment and results are not uniform with the use of topical agents like retinoic acid, azelaic acid, kojic acid; dermabrasion; cryotherapy; laser with CO₂, ruby laser Q; sunscreens and corticosteroids. Since the treatment is not easy, hence prevention is very important and suggested. The use of lower concentrations of hydroquinone under medical supervision, sun protection and early diagnosis of symptoms clinically are recommended [2,3,7].

Discussion

Exogenous ochronosis is a rare, cosmetically disfiguring lesion. It usually occurs as a potential side effect of topical use of hydroquinone, which is employed clinically to treat melasma or most of the times self prescribed by the patient as seen in our case. Since this is difficult to treat, it needs early diagnosis and immediate discontinuation of the hydroquinone. One should ensure not to increase its concentration in an attempt to clear the hyperpigmentation. The prescription of hydroquinone for any patient should be accompanied by information of this possible side-effect and also the indiscriminate use of hydroquinone containing compounds without medical prescription should be restricted.

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