

Hydroquinone-Induced Exogenous Ochronosis in Filipino Patients: Clinical and Therapeutic Insights from a Case Series

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ABSTRACT: Exogenous ochronosis (EO) is an uncommon but increasingly recognised acquired pigmented disorder associated with prolonged topical hydroquinone use, particularly among individuals with darker skin phototypes. Despite the widespread availability of skin-lightening agents in the Philippines, local data on hydroquinone-induced EO remain limited. This case series describes the clinical, dermoscopic, histopathologic, and therapeutic findings in eight Filipino women with Fitzpatrick skin type IV diagnosed with hydroquinone-induced EO between November 2021 and April 2025. Patients, aged 43–65 years (mean, 55.4 years), presented with progressive bluish-grey to black facial hyperpigmentation after 10–25 years of unsupervised use of 2% hydroquinone, commonly in combination with tretinoin 0.05%. Dermoscopy consistently demonstrated reddish-brown reticular structures obliterating follicular openings, black dots, and elongated serpentine vessels, while histopathology in 6 biopsied cases revealed characteristic ochre-colored globules, degenerated collagen fibers, dilated vessels, and prominent solar elastosis. Following diagnosis, hydroquinone was discontinued, strict photoprotection was advised, and treatment with safer skin lightening agents was initiated. In addition, selected patients underwent laser therapy, with significant clinical improvement observed in one patient following sequential 1064 nm Q-switched Nd:YAG (QSNY) laser and 675 nm laser treatment, whereas 577 nm laser produced modest responses. These findings highlight the characteristic clinical, dermoscopic, and histopathological features of hydroquinone-induced EO in Filipino women, which may facilitate early recognition of EO in individuals with darker skin phototypes. Dermoscopy may aid clinical recognition, while histopathology can provide confirmation when indicated. Prompt discontinuation of hydroquinone and an individualised approach to treatment may be considered in the management of EO.

Keywords: Exogenous ochronosis, Hydroquinone, Clinical, Dermoscopy, Histopathology, Therapy

INTRODUCTION

Exogenous ochronosis (EO) is a facial pigmented disorder characterised by asymptomatic blue-black and grey-black hyperpigmented macules and patches with changes in skin texture, typically on the face, neck, back, and extensor surfaces of the extremities [1]. It is more commonly reported in individuals with darker skin phototypes, particularly among Black South Africans and Hispanic populations with prolonged use of hydroquinone-containing skin-lightening products. However, increasing numbers of cases have also been reported in individuals with lighter skin tones, including those of East Indian, Asian, and European descent [2]. Historically, the condition has been primarily associated with prolonged use of high-concentration hydroquinone

and other compounds, such as phenol, resorcinol, and quinine, with unprotected sun exposure as an exacerbating factor [1]. Dermoscopy and skin biopsy can aid in diagnosis, with histopathological examination providing confirmation when indicated. Management involves discontinuing the offending agent, strict photoprotection, and considering topical or procedural therapies; however, no treatment has been consistently proven to be universally effective [1].

An earlier case series of EO in Filipino patients has been reported, with a focus on describing the dermoscopic findings of EO to aid diagnosis [3]. In contrast, the present case series describes the clinical, dermoscopic, and histopathological findings, as well as treatment approaches. The patients in the present case series are distinct from those in the previously published

cohort, with no overlap between the two patient populations. This case series provides additional local clinical experience with EO associated with prolonged, unsupervised hydroquinone use, including its diagnosis and management.

METHODOLOGY

Participants

We present a series of eight Filipino female patients diagnosed with EO and Fitzpatrick skin type IV who consulted at our institution between November 2021 and April 2025 (**Table 1**). Written informed consent for publication, including the use of clinical photographs, was obtained from all patients. Patients were aged 43 to 65 years, with a mean age of 55.4 years. None exhibited features of endogenous ochronosis, such as dark urine, arthralgia, scleral hyperpigmentation, or thickened cartilage. All cases presented with progressive facial hyperpigmentation persisting for 2 to 10 years. Notably, all had a history of prolonged use, ranging from 10 to 25 years, of 2% hydroquinone in solution and cream formulations, some of which also contained tretinoin 0.05%. Photoprotection practices varied. The baseline severity of facial hyperpigmentation, assessed using the mMASI [4], ranged from 4.2 to 18.0 (mean, 10.5).

Dermoscopic Assessment

The patients presented with bluish-grey to black facial hyperpigmentation, most pronounced over the malar and zygomatic areas. Closer inspection revealed caviar-like papules (2 cases) and confetti-like depigmentation (all cases) (**Figure 1**). Dermoscopy (HEINE Optotechnik GmbH & Co. KG, Herrsching, Germany) showed reddish-brown reticular structures obliterating follicular

openings, black dots, interspersed elongated serpentine vessels, and confetti-like depigmentation. Histopathology was performed in 6 cases, while 2 patients declined biopsy. The biopsied cases showed ochre-coloured globules, dilated vessels, degenerated collagen fibres, and prominent solar elastosis. Histopathological examination of areas with confetti-like depigmentation revealed fibrosis and ochronotic pigment, suggesting scarring (**Figure 2**).

Management and Outcome

All patients were prescribed topical therapy aimed at promoting collagen remodelling and skin repair and were advised to discontinue hydroquinone and use daily photoprotection. One patient (case 5) underwent sequential treatment with a 1064 nm Q-switched Nd:YAG (QSNY) laser (Tri-Beam Premium, Jeisys Medical, Korea), under topical anaesthesia with 10.56% lidocaine occlusion (fluence, 4–6 J/cm²; spot size, 4 mm; frequency, 2–6 Hz; pulse duration, 5–10 ns; single pass), followed by a 675 nm laser (RedTouch, DEKA Laser, Italy; power, 6.0 W; dwell time, 150 ms; spacing, 2000 µm). Significant clinical improvement was observed after 4 sessions of QSNY laser followed by 6 sessions of the 675 nm laser. The mMASI score decreased from 14.7 at baseline to 5.4 after treatment, representing a 63.3% reduction (**Figure 3**). Two patients (cases 1 and 2) were treated with the 577 nm ProYellow laser (Asclepion Laser Technologies GmbH, Jena, Germany), resulting in mild improvement after 2 to 3 sessions. Laser therapy was administered at monthly intervals. No adverse effects were reported during treatment. The remaining five patients who received conservative management without additional laser therapy, were subsequently lost to follow-up; therefore, treatment outcomes could not be assessed.

Table 1. Demographic and clinical characteristics of the patients.

Patient no.	Sex	Age (years)	Hydroquinone use (2%)	Sun protection	mMASI (baseline)	Additional treatment
1	Female	55	10 years	Yes	5.4	577 nm ProYellow laser (3 sessions)
2	Female	54	10 years	Occasional	6.9	577 nm ProYellow laser (2 sessions)
3	Female	60	25 years	None	16.2	-
4	Female	43	10 years	Occasional	4.2	-
5	Female	61	10 years	Occasional	14.7	1064 nm QSNY laser (4 sessions) 675 nm laser (6 sessions)
6	Female	54	20 years	Occasional	9.9	-
7	Female	51	10 years	None	18.0	-
8	Female	65	10 years	Yes	9.0	-

Modified MASI total score = 0.3 A(f) D(f) + 0.3 A(lm) D(lm) + 0.3 A(rm) D(rm) + 0.1 A(c) D(c)

The range of the total score is 0 to 24.

Area and darkness are scored as follows:

Area of involvement: 0 = absent, 1 = <10%, 2 = 10%-29%, 3 = 30%-49%, 4 = 50%-69%, 5 = 70%-89%, and 6 = 90%-100%;

Darkness: 0 = absent, 1 = slight, 2 = mild, 3 = marked, and 4 = severe.

Area (A), Darkness (D), forehead (f), left malar (lm), right malar (rm), and chin (c).



Figure 1. Clinical presentation of eight cases at baseline showing bluish-grey to black facial hyperpigmentation, most prominent over the malar and zygomatic areas, with confetti-like depigmentation. **A**, case 1; **B**, case 2; **C**, case 3 with additional caviar-like papules; **D**, case 4; **E**, case 5; **F**, case 6; **G**, case 7 with additional caviar-like papules; **H**, case 8.

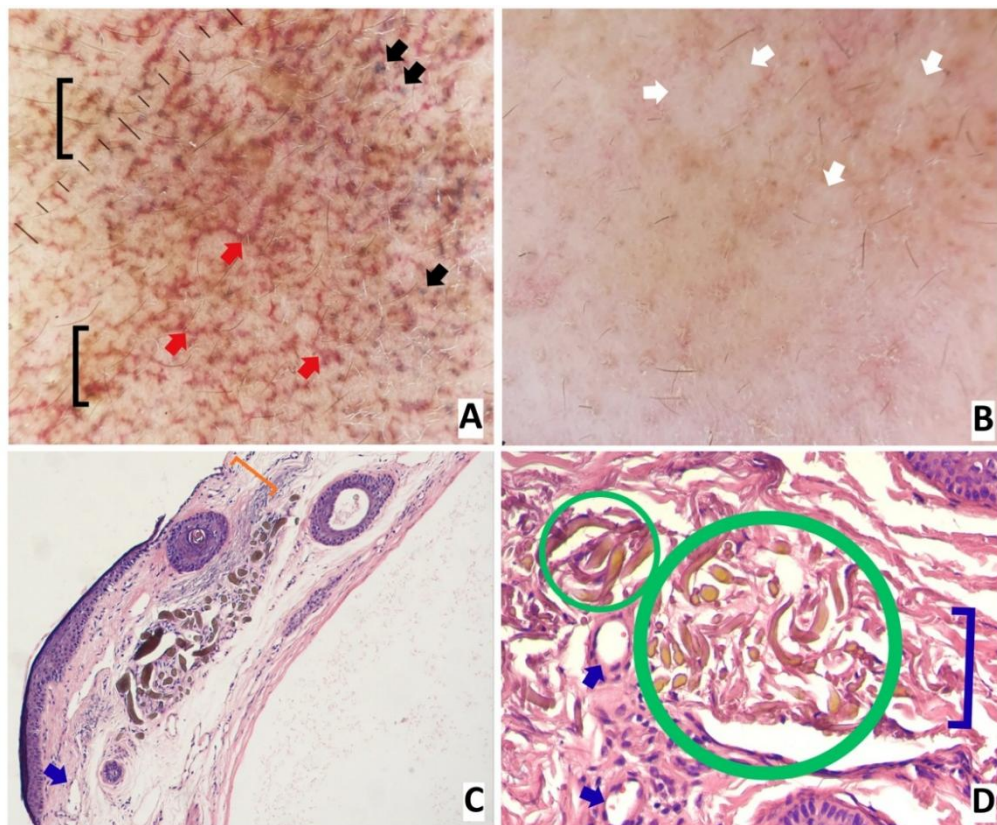


Figure 2. Dermoscopy showing (A) reddish-brown reticular structures obliterating follicular openings (black bracket), black dots (black arrow), interspersed elongated serpentine vessels (red arrow), and (B) confetti-like depigmentation (white arrow). Histopathology showing (C) prominent solar elastosis (orange bracket) [case 3, H&E, $\times 10$] and (D) ochre-coloured globules (green circle), dilated vessels (blue arrow), and degenerated collagen fibres (blue bracket) [case 4, H&E, $\times 40$]. Biopsy site: preauricular area. The preauricular area was selected to minimise visible scarring.



Figure 3. Case 5. Clinical response to sequential laser therapy in hydroquinone-induced EO. (A) Baseline showing grey-black facial hyperpigmentation involving the forehead, malar, zygomatic, and chin regions (mMASI, 14.7); (B) Improvement in facial pigmentation after 4 sessions of 1064 nm QSNY laser treatment; (C) Further reduction in facial hyperpigmentation following 6 sessions of a 675 nm laser as sequential treatment (mMASI, 5.4).

DISCUSSION

EO is a rare but potentially irreversible complication of prolonged topical hydroquinone use. The proposed pathogenesis of EO is prolonged hydroquinone exposure inhibits homogentisate 1,2-dioxygenase, resulting in localized accumulation and polymerization of homogentisic acid within altered elastic fibers [2], a process that may further be potentiated by chronic ultraviolet exposure. Although traditionally associated

with high-concentration formulations, accumulating evidence indicates that EO may also develop following long-term use of 2% hydroquinone [2,5,6], particularly in the absence of physician supervision and consistent photoprotection. Earlier reports likewise proposed that extended duration of hydroquinone exposure, rather than concentration alone, is the principal factor in the development of EO. It has also been suggested that the percentage of hydroquinone stated by a manufacturer may not necessarily represent the actual concentration

of hydroquinone in a product [7]. Similarly, in the present case series, all patients had prolonged exposure to products labelled as containing 2% hydroquinone before disease onset. These observations are consistent with earlier findings that chronic exposure to hydroquinone-containing regimens, together with inconsistent photoprotection, may contribute to the development of EO. However, the actual hydroquinone concentrations of the products used by our patients were not independently verified and may have differed from the concentrations stated by the manufacturers.

The clinical, dermoscopic, and histopathological findings in the present series were consistent with those previously reported in Filipino patients with EO [3]. Dermoscopy in our patients demonstrated reddish-brown reticular structures with obliteration of follicular openings, black dots, elongated serpentine vessels, and confetti-like depigmentation. Similarly, Belizario et al. reported blue-gray and black dots, annular and arcuate structures, reddish- to dark-brown curvilinear structures, obliteration of follicular openings, telangiectasias, and confetti-like depigmentation [3]. The similarity of these dermoscopic features, particularly the presence of pigmentary structures associated with obliteration of follicular openings, may aid in distinguishing EO from other facial hyperpigmentation disorders such as melasma. Histopathologically, our findings of ochre-colored deposits, solar elastosis, and degenerated collagen were likewise consistent with previous reports, in which ochre-colored bodies in the papillary dermis were the characteristic finding, accompanied variably by solar elastosis, telangiectasia, and inflammatory changes [3].

Management of EO remains challenging because no therapy has consistently demonstrated predictable efficacy. Current treatment is centred on discontinuation of the offending agent, strict photoprotection, and individualised use of topical or procedural therapies [2,5]. In the present case series, in addition to discontinuation of hydroquinone and photoprotection, selected patients received laser therapy, including sequential treatment with a 1064 nm QSNY laser followed by a 675 nm laser in one patient and a 577 nm yellow laser in 2 patients. Laser therapy was offered as an additional treatment; however, only three patients proceeded because the remaining patients were unable to afford the associated costs and opted for topical therapy.

The 1064 nm QSNY laser has been reported to improve pigmentation in EO through fragmentation of dermal ochronotic pigment, thereby facilitating its clearance by dermal macrophages and lymphatics [8]. In our patient, the subsequent use of the 675-nm laser was intended to promote dermal collagen remodelling and improve skin texture after pigment reduction, as this wavelength has been shown to stimulate neocollagenesis and extracellular matrix remodelling [9]. To our knowledge, there are currently no published reports describing the use of the 675 nm laser for the treatment

of EO, particularly as a sequential modality following QSNY laser therapy. The 577 nm yellow laser was selected to target associated facial erythema and telangiectasia [10]. Although favourable clinical improvement was observed in the patient who received sequential QSNY and 675-nm laser treatment, further studies are warranted to evaluate the therapeutic efficacy, safety profile, optimal treatment parameters, and long-term outcomes of this sequential laser approach in the management of EO. In case 5, mMASI was used to assess treatment outcome. Although mMASI was developed and validated for melasma and has not been validated for EO, it was used as an exploratory measure to provide standardised quantitative documentation of facial pigment burden, despite the absence of a disease-specific severity index for EO.

Recent clinical guidance continues to recognise hydroquinone as the gold-standard topical depigmenting agent when prescribed appropriately [6]. Rather than discouraging its use, current recommendations advocate limiting treatment duration, ensuring physician supervision, and transitioning to maintenance regimens or alternative depigmenting agents, including azelaic acid, tranexamic acid, thiamidol, kojic acid, niacinamide, and arbutin, when clinically appropriate [6]. More recently, 2-mercaptopyridine-5-yl glycine has emerged as a promising non-hydroquinone depigmenting agent, demonstrating efficacy comparable to 4% hydroquinone with improved tolerability in patients with facial melasma, making it a potential alternative for long-term pigmentary management [11].

Collectively, our findings highlight the potential association between prolonged, unsupervised hydroquinone use and the development of EO, underscoring the importance of patient education, regular follow-up, and clinical monitoring for early signs of EO to minimise irreversible pigmentary sequelae. This study is limited by its small sample size, uncontrolled design, and incomplete follow-up, while the actual hydroquinone concentrations of products labelled as 2% were not independently verified and may have differed from the manufacturers' stated concentrations.

CONCLUSION

EO is a potentially preventable complication of prolonged, unsupervised use of topical hydroquinone-containing skin-lightening products. Our findings show that hydroquinone-induced EO may occur following long-term use of products containing 2% hydroquinone and highlight the value of dermoscopy and histopathology for clinical recognition and diagnosis. Prompt discontinuation of hydroquinone, strict photoprotection, and individualised management remain the cornerstones of treatment, although therapeutic outcomes, including those with laser therapy, are variable. Physician oversight, patient education, and adherence to recommended treatment duration may help reduce the risk of EO.

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CONFLICT OF INTEREST

The authors declare no potential conflicts of interest.

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