Clinical, Cosmetic and Investigational Dermatology

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CASE REPORT

Non-Insulated Microneedle Radiofrequency for the Treatment of Hydroquinone-Induced Exogenous Ochronosis: A Case Report and Literature Review

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Purpose: Exogenous ochronosis is a challenging condition that requires multifaceted modalities. This investigation delineates a case of hydroquinone-induced exogenous ochronosis that improved following treatments with a bipolar non-insulated microneedle radiofrequency (MNRF). To report the efficacy and safety of microneedle radiofrequency as a novel treatment for exogenous ochronosis, and to review the role of energy-based devices as treatment options for this condition.

Patients and Methods: A 63-year-old patient with a history of long-term application of hydroquinone-containing products for the treatment of melasma gradually developed hyperpigmented lesions on the face, which were later confirmed the diagnosis of exogenous ochronosis by skin biopsy. Three sessions of bipolar non-insulated MNRF with four-week intervals were employed to treat the affected areas. The clinical improvement of the ochronotic lesion was assessed by digital photograph and Trica facial analysis instrumentation.

Results: There was a discernible enhancement in exogenous ochronosis and preexisting melasma within one month after the initial session of bipolar non-insulated MNRF. Following three sessions of MNRF, the patient also demonstrated a further diminution of ochronotic substances and a substantial improvement in the overall dermal texture of the treated regions as assessed by the Trica facial analysis system. Adverse effects were mild erythema and edema, which were transient and self-resolving within four to five days. No post-inflammatory hyperpigmentation, hypopigmentation, or prolonged erythema was detected after the intervention.

Conclusion: This case of exogenous ochronosis demonstrates the role of bipolar non-insulated MNRF as a viable and safe therapeutic option for the management of hydroquinone-induced exogenous ochronosis.

Keywords: ochronosis, melasma, energy-based devices, radiofrequency, microneedle radiofrequency

Introduction

Exogenous ochronosis (EO) is an acquired hyperpigmented disorder characterized by bluish-grey skin discoloration on the face, neck, back, or extensor surfaces of the extremities. EO demonstrates histopathological characteristics of ochre-colored banana-shaped deposits in the dermis with collagen and elastic fiber degeneration. While hydroquinone is the most common cause of EO, resorcinol, phenol, and mercury can also contribute to this condition. The pathophysiology of hydroquinone-induced exogenous ochronosis remains unclear and has been proposed by numerous theories. However, the most widely accepted explanation is that topically applied hydroquinone inhibits the local action of the enzyme homogentisic acid oxidase within the dermis, resulting in the accumulation of homogentisic acid, which has the propensity to form ochronotic pigment.[1]

EO requires a multimodal treatment approach and is usually refractory and unresponsive to standard treatments. This includes ceasing the offending agent, avoiding sun exposure, oral medication, and topical medication.[1] Recent reports have been integrating lasers and light therapies to manage EO. Previous light-based treatments, such as ablative lasers

Received: 3 June 2025
Accepted: 15 October 2025
Published: 22 October 2025

including CO2 lasers and Erbium lasers, Q-switched lasers, fractional lasers, and intense pulsed light (IPL), have been reported to be efficacious. Nevertheless, these treatments are sometimes associated with post-inflammatory hyperpigmentation (PIH).[1] Consequently, energy-based devices as radiofrequency (RF) has garnered attention as an alternative treatment for hyperpigmented disease owing to their safety profile, characterized by minimal scattering effects and absence of chromophore absorption, resulting in fewer complications compared to traditional laser-based approaches. However, none of the previous literature documents the usage of the energy-based device for treating EO. Hence, we present the first case of EO successfully treated with bipolar non-insulated microneedle radiofrequency (MNRF).

Case Report

A 63-year-old Thai female with Fitzpatrick's skin type IV presented with multiple greyish macules and papules on the face for 10 years. She was diagnosed with melasma and had been treated with a regimen comprising a combination of whitening agents containing hydroquinone, chemical peels, and unspecified laser treatments. Over the past decade, she developed slight erythema in the malar regions, gradually progressing to multiple tiny black dots on the preexisting melasma. Dermatological examination revealed multiple tiny pinpoint dark brown macules and papules mixed with reticulate brown to grey patches with some telangiectasia on the forehead, bilateral cheeks, nose, and chin (Figure 1A). Dermatoscopy showed brownish to greyish caviar-like macules and papules with an ill-defined brown reticular network with telangiectasia (Figure 1B). A 3-mm punch biopsy performed on the left nasolabial fold revealed multiple brownish banana-shaped materials deposited in the upper dermis, which were compatible with exogenous ochronosis (Figure 2).

The patient was treated with three sessions of bipolar non-insulated MNRF (Sylfirm X plus, Viol, Gyeonggi, South Korea) with a disposable tip composed of 25 non-insulated microneedles in 5×5 arrays. She was instructed to apply topical anesthetic cream containing 5% lidocaine and 5% prilocaine cream (Racser®, Galentic Pharma, Navi Mumbai, India) 30 minutes before the procedure. She was given a treatment in pulsed-wave mode at the forehead, malar areas, nose, and chin for treating EO and melasma; meanwhile, continuous-wave mode was performed at infraorbital, malar, and jawline areas for skin tightening. The specific parameters for each area are described in Table 1. The same setting of the MNRF device was performed for all three sessions with a 4-week interval. She was also instructed to apply sunscreen, moisturizer, and avoid sun exposure after each treatment.

Results

At the 4-week follow-up after a single treatment, clinical improvement of the lightening of the lesion was observed compared to baseline (Figure 3A and B). The noticeable reduction of ochronotic pigments, telangiectasia, and preexisting melasma was significantly observed at 8 weeks follow-up (Figure 3C). After three sessions, the lesion clearance continued, and overall skin texture improved (Figure 3D). Facial analysis machine (Trica3D, Qingdao Xiaoyou

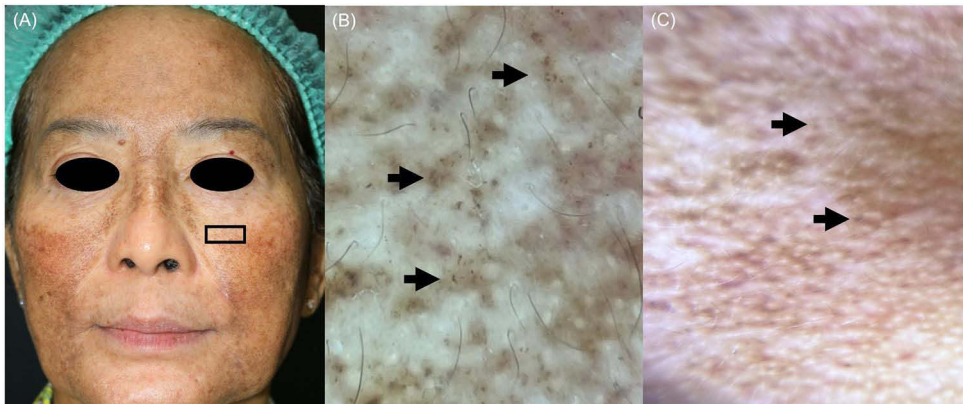

Figure 1 Digital photograph (**A**) by digital camera (D5100 model, Nikon Corporation, Japan) revealed exogenous ochronosis as multiple tiny black dots at bilateral malar, nose, forehead, and chin on top of preexisting melasma. The black box labeled the area of dermatoscopic examination. Dermatoscopic examination (**B**) showed tiny pinpoint carvial dark brown papules (arrows) throughout the lesion and the overlying melasma before treatment. (**C**) Dermatoscopic image at 12-week follow-up after three sessions of non-insulated microneedle radiofrequency, showing marked reduction in papular pigmentation (arrows) and background hyperpigmentation.

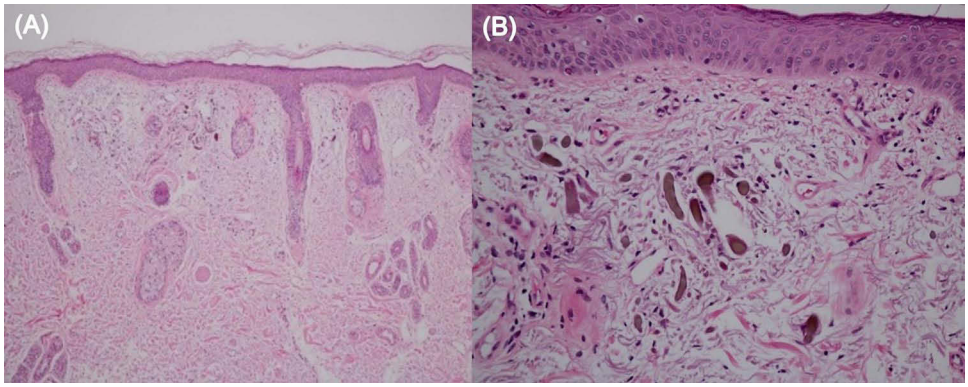

Figure 2 H&E stain from punch biopsy at left nasolabial fold at 100x magnification (**A**) and 400x magnification (**B**) revealed superficial perivascular infiltration with lymphocytes and ochronotic materials in brown banana-shaped deposits at the upper dermis. The measured depth of ochronotic material is 0.5 mm below the epidermis. Solar elastosis and telangiectasia were also noted.

Intelligent Technology, China) revealed lesion lightening from baseline to 12 weeks (Figure 3E–H). Brown field mode was also utilized to enhance brown pigment, indicating a notable improvement of hyperpigmented lesions, especially at the nose and bilateral malar regions (Figure 3I–L). The red area mode also noted the significant improvement of telangiectasia (Figure 3M–P). In each session, the patient reported mild pain. Side effects, including transient redness and mild swelling, were self-limited and resolved within 4–5 days. Post-inflammatory hyper- or hypopigmentation or prolonged erythema were not observed. The patient expressed high satisfaction with the treatment outcome.

Discussion

EO is a challenging dermatological condition that causes significant physical and psychological burdens for affected individuals. Exogenous ochronosis (EO) may mimic melasma in its early stages, but differs by showing gray-blue to blue-black macules with "caviar-like" papules and pathognomonic banana-shaped fibers on histology. In contrast, melasma presents with brown reticular macules and epidermal pigmentation.[2] Dermoscopy may assist, but a biopsy remains the definitive method. Importantly, early recognition or suspicion of EO is critical, as misdiagnosis as melasma often leads to continued hydroquinone use, which can aggravate EO and worsen outcomes. Various treatment modalities, including topical and oral medications, light-based treatments, and laser interventions, have been explored to manage the disease. While avoiding exposure to the causative agents alone results in minimal disease improvement. Topical therapies, such as retinoic acid, have shown different responses and lead to transient hyperpigmentation in some cases. A combination of retinoic acid with chemical peels has also shown no significant benefit. The efficacy of topical low-potency corticosteroids (1 to 2.5 percentage of hydrocortisone) appears to be minimal in terms of lightening effects.[1]

The first report of laser treatment in EO was introduced in 1990, with a combination of dermabrasion and CO_2 laser revealed to be effective and provided a satisfying result.[3] Ablative lasers such as CO_2 laser[4] and Erbium-doped yttrium aluminium garnet (Er:YAG) ablative laser (2,940 nm)[5] has been reported to effectively lighten lesions by removing the

Table 1 Summarized Protocol of Treatment with Bipolar Non-Insulated MNRF Throughout All Sessions

Continuous-wave mode (CW)	
Infraorbital	CW 2, depth 0.5 mm, power level 4, 1 pass
Malar areas	CW 2, depth 2.0 mm, power level 4, 1 pass
Jawline	CW 2, depth 3.0 mm, power level 4, 2 passes
Pulsed-wave mode (PW)	
Exogenous ochronosis lesions (forehead, malar areas, nose, chin)	PW 2, depth 0.5 mm, power level 3, 1 pass

https://doi.org/10.2147/CCID.S544338

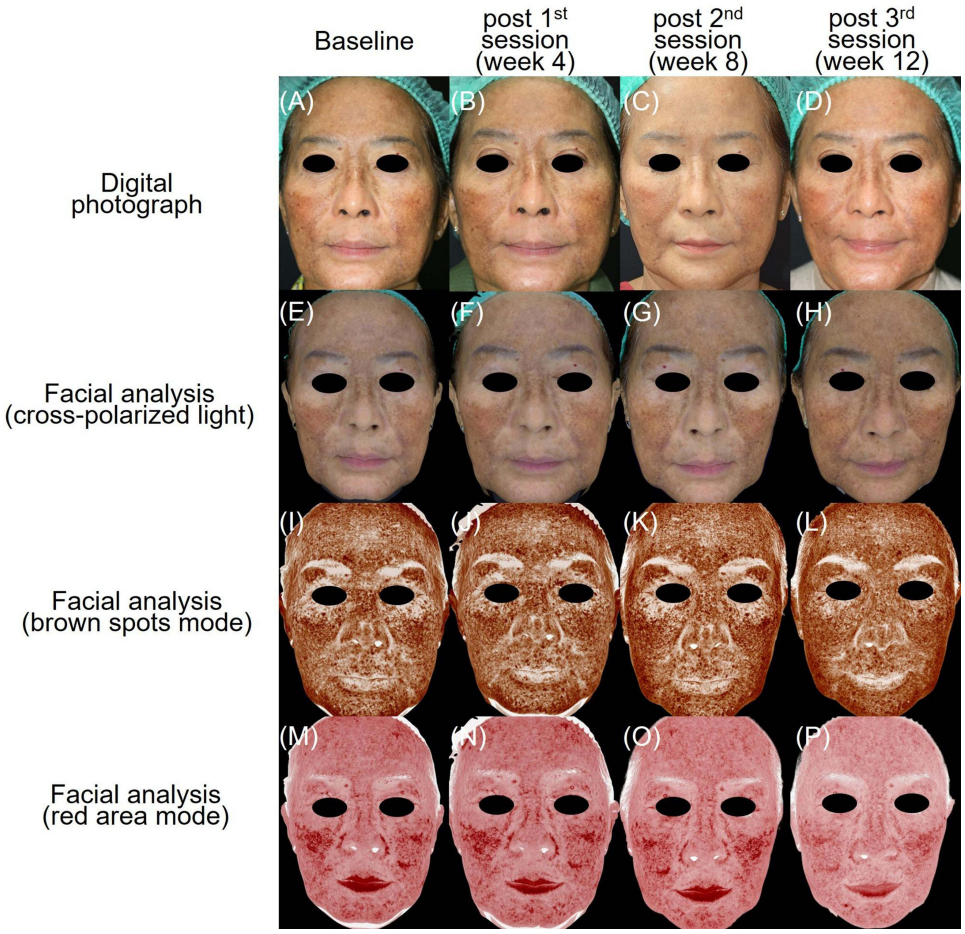

Figure 3 Clinical photographs and facial analysis reveal significant improvement of exogenous ochronosis and overall skin quality from baseline to week 12 post-treatment (**A**–**D**). The improvement of pigmented lesions is observed in facial analysis in cross-polarized light (**E**–**H**) and brown spots mode (**I**–**L**). Significant improvement of telangiectasia is noted in the red area mode (**M**–**P**).

damaged tissue through vaporization process. This process, while effective, typically results in a longer recovery time and may cause discomfort or pain for the patient during treatment. Subsequently, studies have explored the efficacy of pigment-specific lasers as a monotherapy, including Q-switch Ruby, Alexandrite, and Nd:YAG lasers. These lasers are effective, but multiple treatment sessions were often required to obtain optimal results.[6–10] The combination of Q-switch laser, especially 1,064-nm Nd:YAG, with other treatments has also shown significant improvement. However, PIH usually occurs in cases with dark skin type.[11–13] More recently, Picosecond lasers (755 nm and 1,064 nm) were also reported to be useful in EO without any side effects.[14,15] The mechanism of action of the laser therapies involves the laser's ability to deliver high-energy light to target ochronotic pigments, causing them to shatter and subsequently be eliminated through the lymphatic system or via trans-epidermal elimination.[15] IPL devices also reported to be effective for treating EO by causing melanosomes elimination together with necrotic keratinocytes induced by thermal heating.[16,17]

The summarized data of light-based and laser devices for EO treatment is reported in Table 2.

Following advances in the laser and light-based therapies, RF devices have emerged as a promising alternative modality for treating pigmentary disorders. Microneedle radiofrequency (MNRF) delivers RF energy via insulated or non-insulated microneedles in monopolar, bipolar, or fractional modes, inducing dermal remodeling through bulk heating. By directly targeting dermal pathological structures while sparing the epidermis, minimizing surface disruption.[18] Beyond its physical effects, RF-induced thermal effects have been shown to reduce senescent fibroblasts and restore basement membrane integrity.[19] In vitro studies further demonstrated that RF irradiation enhances the expression of genes that inhibit tyrosinase activity and promote lymphangiogenesis, addressing histopathological features

Table 2 Efficacy of Lasers and Light-Based Therapy as Treatment for Ochronosis

Reference	Year	Number of Patients, Gender, Age (Years), and Fitzpatrick Skin Type	Treatment(s)	Treatment Parameter	Number of Treatments and Interval	Clinical Efficacy	Side Effect
Monotherapy							
Carvalho et al[4]	2016	1, Male, 46 Skin type V	CO_2 laser	Energy 120 mJ, density set at 150 points per cm^2	Twelve sessions with a one-month interval	Excellent response	NA
Chaptini and Huilgol[5]	2014	1, Female, 54 Skin type II	Er: YAG ablative laser 2,940 nm	A 100 μm ablation with scanner sizes 3 to 8 with 2 to 8 passes	Two sessions with a nine-month interval	Marked improvement with excellent result	No
Kramer et al[6]	2000	1, Female, 50 Skin type IV	Q-Switched 694 nm Ruby laser	Fluence 7 J/cm^2, spot size 5 mm	NA	Effective	NA
Bellew and Alster[7]	2004	2, Female, 46 and 47 Skin type IV	Q-Switched 755 nm Alexandrite laser	Fluence 6 to 7 J/cm^2, spot size 3 mm (non-overlapping collimated spot)	Four sessions with a bimonthly and a four-month interval	Effective	PIH in 1 patient
Charlin et al[8]	2007	1, Female, 56 Skin type V	Q-switched Nd:YAG 1,064 nm laser	NA	NA	No improvement	NA
Tan[9]	2013	6, Females, 37 to 63 Skin types III and IV	Q-switched Nd:YAG 1,064 nm laser	Fluence 1.2 J/cm^2, spot size 8 mm, 4 passes (for melasma and exogenous ochronosis) Fluence 4 to 6 J/cm^2, spot size 4 mm, 2 to 3 passes (additional for exogenous ochronosis)	Eight to sixteen sessions with a fortnightly time interval	Improvement	No
Liu et al[10]	2014	1, Male, 50 Skin type IV	Q-switched Nd:YAG 1,064 nm laser	Fluence 6–9 J/cm^2	Six sessions	No improvement	NA
Mendez et al[14]	2018	1, Female, 55 Skin type V	Fractional picosecond 1,064/532 nm laser	Wavelength of 1,064/532 nm, fluence 1.30/0.18 J/cm^2 and increasing by 0.20/0.02 J/cm^2 each session until reaching 2.90/0.30 $J/cm^{2,}$ spot size of 6 mm	Nine sessions with a bimonthly interval	Clear improvement in the color of lesions and improvement in skin texture	NA
Almutairi et al[15]	2024	1, Male, 52 Skin type IV	Picosecond 755 nm Alexandrite laser	Fluence 0.3 J/cm^2, spot size 10 mm (flat lens) then fluence 0.45 J/cm^2, spot size 8 mm (fractional) at first session Fluence 0.3 J/cm^2, spot size 10 mm (flat lens) then fluence 0.7 $J/cm^{2,}$ spot size 8 mm (fractional)	Three sessions with a six-week interval	Significant resolution of pigmentation	No
Gil et al[16]	2010	1, Female, 63 Skin type V	IPL 645 nm	Fluence 20 to 22 J/cm^2 Pulse duration 6 ms	Six sessions in two months	Mild clearing, no significant difference	NA

(*Continued*)

Table 2 (Continued).

Reference	Year	Number of Patients, Gender, Age (Years), and Fitzpatrick Skin Type	Treatment(s)	Treatment Parameter	Number of Treatments and Interval	Clinical Efficacy	Side Effect
Lee and Weiss[17]	2014	1, Female, 48 Skin type IV	IPL 570 nm	Fluence 12 J/cm^2 Pulse duration 15 ms	NA session with a six-week interval	Fading of hyperpigmentation after the first treatment	No
Combined therapy							
Diven et al[3]	1990	1, Female, 53 Skin type IV	Dermabrasion and CO_2 laser	Full face except for periorbital and nasal area (Dermabrasion: diamond fraise) Three to four passes for eyes, nose, and forehead (CO_2 laser)	NA	Effective and satisfying result	NA
Franca et al[11]	2010	1, Female, 40 Skin type III	Combination of Q-switched Nd:YAG 1,064 nm laser, Ultrapulse CO_2 laser, Microdermabrasion with chemical peeling, IPL, and 20% TCA peel	Fluence 2.9 to 3.05 J/cm^2, spot size of 4 mm, (Q-switched Nd:YAG 1,064 nm. laser) Fluence 5 watts (Ultrapulse CO_2 laser) Fluence 36 J/cm^2, pulse duration 10 ms (IPL) Microdermabrasion and chemical peeling (5% hydroquinone + 5% retinoic acid + 14% salicylic acid) Fluence 36 J/cm^2, pulse duration 10 ms (IPL) Trichloroacetic acid 20% (TCA) peels	Four sessions (Q-switched Nd:YAG 1,064 nm. laser) Six sessions with a thirty-day interval (Ultrapulse CO_2 laser) One session One session Three sessions with a thirty-day interval One session	Completely resolved lesion (modest success after 4 sessions of Q-switched Nd: YAG laser)	NA
Kanechorn-Na-Ayuthaya et al[12]	2013	3, Females, 58 to 67 Skin type III, IV, V	Combination of Q-switched Nd:YAG 1,064 nm and Fractional CO_2 laser	Fluence 1.9 to 2.2 J/cm^2 at multiple passes (Q-switched Nd:YAG 1,064) NA (CO_2 laser)	Two to four sessions with two-, one-, and four-month interval (Q-switched Nd: YAG 1,064 nm laser) One session after the third session of Q-switched Nd: YAG 1,064 nm laser (CO_2 laser)	Successful lightening of ochronosis together with improvement of skin texture and tone	Transient purpura and PIH
Ceglio et al[13]	2021	1, Male, 52 Skin type V	Combination of Q-switched Nd:YAG 1,064 nm Laser, IPL 580 nm, and fractional CO_2 laser	Toning mode, fluence 1 to 1.3 J/cm^2, spot size of 8 mm, frequency of 10 Hz, and fluence 4 to 5 J/cm^2, spot size of 5 mm (Q-switched Nd: YAG 1,064 nm laser) Wavelength of 580 nm, fluence 15 J/cm^2, pulse duration 15 ms (IPL) Wavelength of 10,600 nm, a 120 nm tip, 80 to 100 mJ, density 50 MTZ/cm^2 (fractional CO_2 laser)	Eight sessions in two months and four sessions in one month. (Q-switched Nd: YAG 1064 nm. laser) Seven sessions with a one-month interval. (IPL) Five sessions with a bimonthly time interval. (fractional CO_2 laser)	Significant lesion improvement	No

Abbreviations: CO2, Carbon dioxide; Er:YAG, Erbium-doped yttrium aluminium garnet; IPL, Intense pulsed light; mm, millimeter; ms, millisecond; NA, not applicable; Nd, YAG: Neodymium-doped yttrium aluminium garnet; nm, nanometer; PIH, post-inflammatory hyperpigmentation; μm, micrometer.

commonly observed in melasma, including increased senescent fibroblasts, basement membrane disruption, pendulous melanocytes, and neovascularization.[20,21] Clinically, MNRF has demonstrated superior efficacy in recalcitrant melasma when combined with Q-switched Nd:YAG lasers, as shown in split-face trials compared with QS-Nd:YAG alone.[22–24] The combination group showed greater clinical improvement with minimal adverse effects. These outcomes are thought to result from a combination of dermal remodeling and pigment clearance mediated through transepidermal elimination and lymphatic drainage.

In non-insulated bipolar systems, RF energy is emitted between two adjacent active electrodes, generating localized thermal reactions that propagate upward from the distal part of each needle tip. This results in a teardrop- or cocoon-shaped coagulation zone within the dermis with minimal epidermal reaction, known as the "Na effect". The selective extension of RF energy based on tissue impedance ensures that low-impedance structures, such as the epidermis, are relatively preserved, thereby reducing the risk of post-inflammatory complications.[18,25] Beyond solely thermal effects, non-insulated electrodes in bipolar systems can also induce electromagnetic-selective tissue reactions, leading to vascular modulation and remodeling of dermal structures.[26] These combined thermo-selective and electromagnetic effects enable broader dermal engagement compared to insulated electrodes, which confine energy only to the needle tips and predominantly generate localized coagulation. As a result, this pattern is particularly beneficial for EO, where ochronotic pigment deposits and dermal pathology are located throughout the upper to mid-dermis. As melasma and EO share key pathological features such as dermal pigment deposition, basement membrane disruption, and superficial telangiectasia, the therapeutic benefits of MNRF demonstrated in melasma may extend to EO through similar mechanisms.

We selected non-insulated bipolar MNRF (Sylfirm X plus, Viol, Gyeonggi, South Korea) for treating EO with underlying melasma. This machine allows precise needle depth adjustment from 0.3 to 4.0 mm, facilitating targeted delivery of RF energy directly into the dermis, corresponding to the typical depth of ochronotic pigment. PW mode was used to restore basement membrane disruption, enhance dermal microenvironment, and target pathological pigment deposits at histopathologically identified depths, promoting the elimination of scattered pigment via the transepidermal and lymphatic system. Meanwhile, CW mode, characterized by a longer duration RF energy delivery, was utilized to promote neocollagenesis, addressing the patient's additional concerns related to skin texture and laxity. Furthermore, since MNRF does not interfere with chromophore absorption, it poses a lower risk of complications such as post-inflammatory hyper or hypopigmentation, which is common among patients with dark skin tones like EO patients. The treatment session is brief, well-tolerated, and requires minimal downtime.

This case highlights the MNRF's potential in targeting hyperpigmented diseases by addressing key pathological factors within the upper dermis and basement membrane, including the basement membrane disruption, neovascularization, and senescent fibroblasts. The patient remained free of recurrence during the 12-week follow-up; however, the relatively short duration is a limitation. This case report only represents one patient, and longer observation is necessary to establish the durability of treatment outcomes. A repeat biopsy was not performed due to ethical and patient comfort considerations. Further research should investigate the association between exogenous ochronosis and dermal pathology while validating MNRF as a treatment option for this condition.

Conclusion

This is the first report using MNRF for exogenous ochronosis. After three sessions of dual-wave bipolar non-insulated MNRF, a noticeable reduction of ochronotic pigments and improvement in overall skin quality with no serious side effects were observed. Non-insulated MNRF may be valuable for patients with darker skin types at higher risk of laser complications.

Ethics Approval and Informed Consent

This case report was approved by the Institutional Review Board of Human Rights related to the case report protocol, Ramathibodi Hospital, Mahidol University (Protocol number MURA2025/24) in accordance with the Declaration of Helsinki and approved by Thai Clinical Trials Registry (TCTR20250126002). Written informed consent was obtained from the patient for the publication of this case report and any accompanying images as per our standard institutional rules.

Funding

The authors received no financial support for this research.

Disclosure

The authors declare no conflicts of interest in this work.

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