A Case Report on The Use of Topical Cysteamine 5% Cream in the Management of Refractory Post-Inflammatory Hyperpigmentation (PIH) Resistant to Triple Combination Cream (hydroquinone, topical corticosteroids and retinoids)

N Mathe[1], M Balogun[1], J Yoo[1]

[1]Department of Dermatology, University Hospitals Birmingham, U.K

Corresponding author:

Dr Jinah Yoo, (MBChB, MRCP, MSc)

Department of Dermatology,

University Hospitals Birmingham

Mindelsohn Way

Birmingham B15 2TH

Email: jyoo@doctors.org.uk

Telephone: 0121 371 5124

Authors:

Dr Nomathamsanqa Mathe (BMedSci, BMBS, MRCP(UK)(Derm))

Dr Mariam Balogun (MBBS, BMedSci, PgMedEd, MRCP(UK)(Derm))

Any conflict of interest disclosures: None to be declared

Funding: None to report

Data availability statement: The data that support the findings of this report are available from the corresponding author upon reasonable request

DR. NOMATHAMSANQA MATHE (Orcid ID : 0000-0002-7864-0193)

Article type : Master Case Presentation

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Article Keywords: hyperpigmentation, post-inflammatory hyperpigmentation, management, cysteamine

Running head: Cysteamine 5% cream in PIH

Abstract

Background: Post-inflammatory hyperpigmentation (PIH) occurs as a result of different inflammatory dermatoses and exogenous factors in individuals with darker skin types. With current skin lightening treatments, there are concerns about irritation leading to worsening of their underlying inflammatory skin condition or worsening of PIH.

Case: A 20-year-old woman with Fitzpatrick skin type (FST) V presented with facial hyperpigmented patches since childhood following an intermittent erythematous, pruritic facial rash. Skin biopsy confirmed PIH secondary to possible burnt-out morphea. Treatment with topical adapalene 0.1% gel and triple combination cream (containing hydroquinone, topical corticosteroids and retinoids) proved unsuccessful. Treatment with cysteamine 5% cream over 4 months resulted in significant improvement with a reduction in the melanin index.

Discussion: The current recommendation for first-line treatment in PIH is hydroquinone or triple combination cream containing hydroquinone, which can be associated with significant short- and long-term side effects. Cysteamine 5% cream is one of the latest cosmetic skin

lightening products. It is hypothesised that cysteamine reduces melanin production by inhibiting key melanogenic enzymes required in melanogenesis. Its efficacy and tolerability have been demonstrated in two randomised controlled trials against placebo in patients with melasma. This report demonstrates a successful use of cysteamine 5% cream in a patient with chronic severe PIH.

Background

PIH occurs as a sequela of a wide variety of cutaneous dermatoses, and exogenous insults, more commonly on the skin of individuals with FST III-VI. An overdrive of melanogenesis is by the inflammatory reaction damaging the cell membrane leading to the release of arachidonic acid and oxidation to prostaglandins and leukotrienes. Furthermore, it has been suggested that the basal vacuolar changes and increased matrix metalloproteinase -2 expression potentially contribute to impairing the basal layer and deeper dermal pigmentation in PIH lesional skin.[1,2] A UK-dermatologist online survey revealed that 67% of dermatologists manage their patients with PIH conservatively[3] and the psychological and social impact is often underestimated by clinicians.

Case

A 20-year-old Bangladeshi woman presented with longstanding facial hyperpigmentation, which had developed aged 7 months as an intermittent, pruritic, erythematous rash and resolved aged 5 years; with resultant PIH. She reports that a biopsy carried out in Bangladesh aged 11 years had been inconclusive and the hyperpigmented patches remained asymptomatic without any signs of inflammation. Examination revealed dark hyperpigmented patches in a centrofacial distribution with skin atrophy around the perioral area (Fig. 1a). Histology from a skin biopsy from the left forehead showed basal hyperpigmentation, occasional lightly pigmented keratinocytes within the mid epidermis, pigment incontinence and scattered melanophages within fibrotic dermis which was consistent with PIH. Direct immunofluorescence and serum autoantibodies were negative. Based on the clinical features and skin biopsy, a diagnosis of PIH secondary to burnt-out morphea was made. Initial treatment with adapalene 0.1% gel for 4 months was not effective. Subsequent treatment with triple combination cream (hydroquinone 5%, hydrocortisone 1%

and tretinoin 0.1% cream) for 3 months with strict photoprotection resulted in transient improvement before it has worsened immediately on discontinuation of the cream. She was then commenced on cysteamine 5% cream once daily for 4 months, along with strict photoprotection. This resulted in significant improvement in hyperpigmentation with reduction in melanin index from 904 to 818, measured from central forehead (SkinColorCatch, Delfin technologies, Finland) without any side effects (Fig. 1b&1c).

Discussion

Navigating the management of PIH in patients with darker FST remains a tightrope between efficacy of proposed treatment and favourable risk-benefit profile. There are fewer controlled studies in PIH compared to melasma. The possible reasons may include spontaneous resolution after months or years and lack of validated objective measurement tool. Many review articles suggest similar approach in the treatment of PIH to melasma in addition to strict control of active inflammation. The current recommendation for first-line treatment is hydroquinone or triple combination cream containing hydroquinone, topical corticosteroids and retinoids.[4] Despite its efficacy, significant side effects associated with its use include: irritation, skin atrophy, and post inflammatory hypo/hyperpigmentation. Long-term side effects such as exogenous ochronosis, particularly after prolonged use, and concerns over carcinogenicity, as observed in animal models, show there is an unmet need for safe skin lightening treatment. Other alternative topical treatments include azelaic acid, tranexamic acid, vitamin C or topical retinoid but they often cause irritation. Several lasers and light energy devices, such as quick-switched (QS)-lasers, fractional non-ablative lasers and intense pulsed light, have been used in the treatment of various hyperpigmentary disorders. However, its efficacy is doubtful and there is increased risk of PIH, especially in darker skin type.[4]

Cysteamine 5% cream is one of the latest additions to cosmetic skin lightening products. Cysteamine is physiologically synthesised by all mammalian cells from the essential amino-acid cysteine into the strong natural antioxidant with its highest concentration found in mammalian milk. The skin lightening effect of cysteamine is postulated to be due to its inherent antioxidant properties causing a lightening effect in the stratum corneum. Furthermore, as a thiol compound, it is hypothesised that cysteamine reduces melanin production by inhibiting key melanogenic enzymes, tyrosinase and peroxidase, as well as chelating copper ions required in melanogenesis.[5] Its efficacy in melasma patients has been

demonstrated by two randomised controlled trials against placebo with a 67% reduction in melanin index (p=0.001) in patients with melasma using cysteamine 5% cream, with the Melasma Area Severity Index (MASI) score being significantly lower in the cysteamine group versus the placebo group (p=0.02).[6,7] Furthermore, there is an ongoing multi-centre randomised-controlled trial comparing cysteamine 5% cream against 4% hydroquinone cream in melasma which will help us to assess the potential use of cysteamine 5% cream as an alternative safe option to hydroquinone.[8] The side effects associated with cysteamine 5% cream are often mild and include erythema, dryness, irritation and burning sensation of the skin which resolve on cessation of application. Although its efficacy in melasma has been reported in several studies, there has not been any literatures reporting its successful use in PIH. This report demonstrates a successful use of cysteamine 5% cream in a patient with chronic severe PIH which was well-tolerated even in sensitive areas such as periorbital skin and its potential use as a long-term maintenance treatment.

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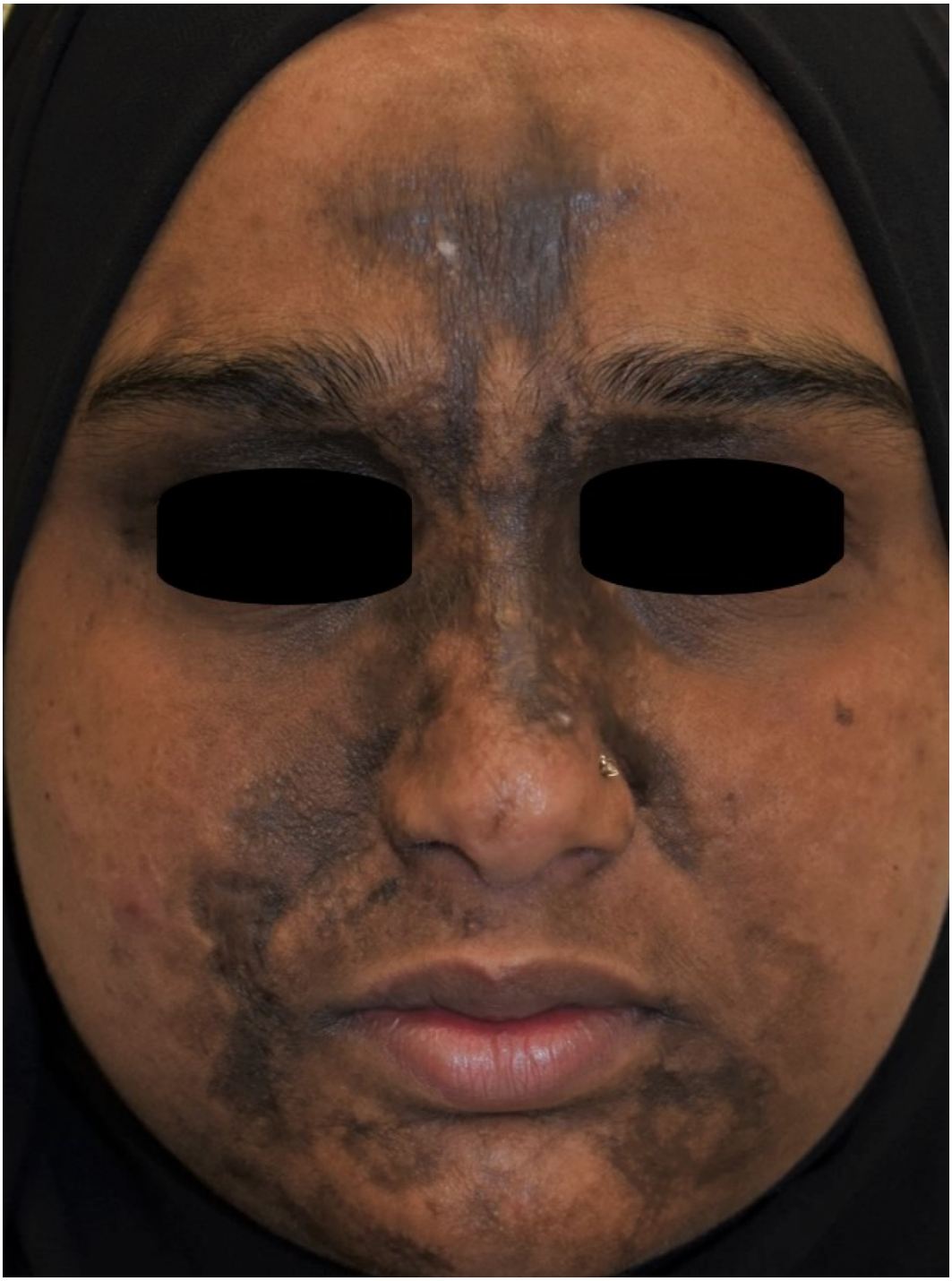
Data Citation : The data that support the findings of this report are available from the corresponding author upon reasonable request

Fig 1 Clinical photograph of facial hyperpigmentation (a) at baseline, (b) in 2 months after starting cysteamine 5% cream, (c) in 4 months after starting cysteamine 5% cream



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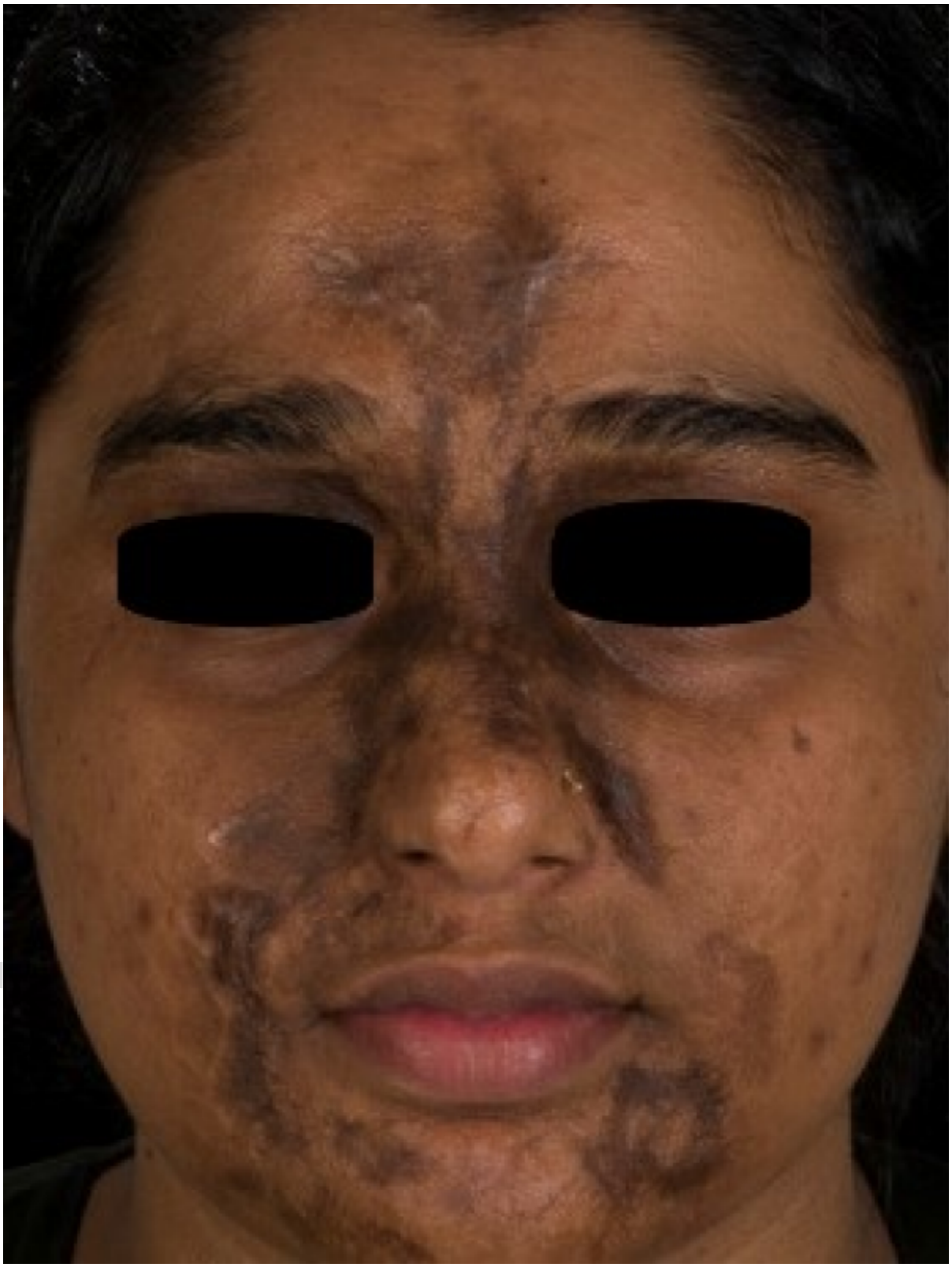

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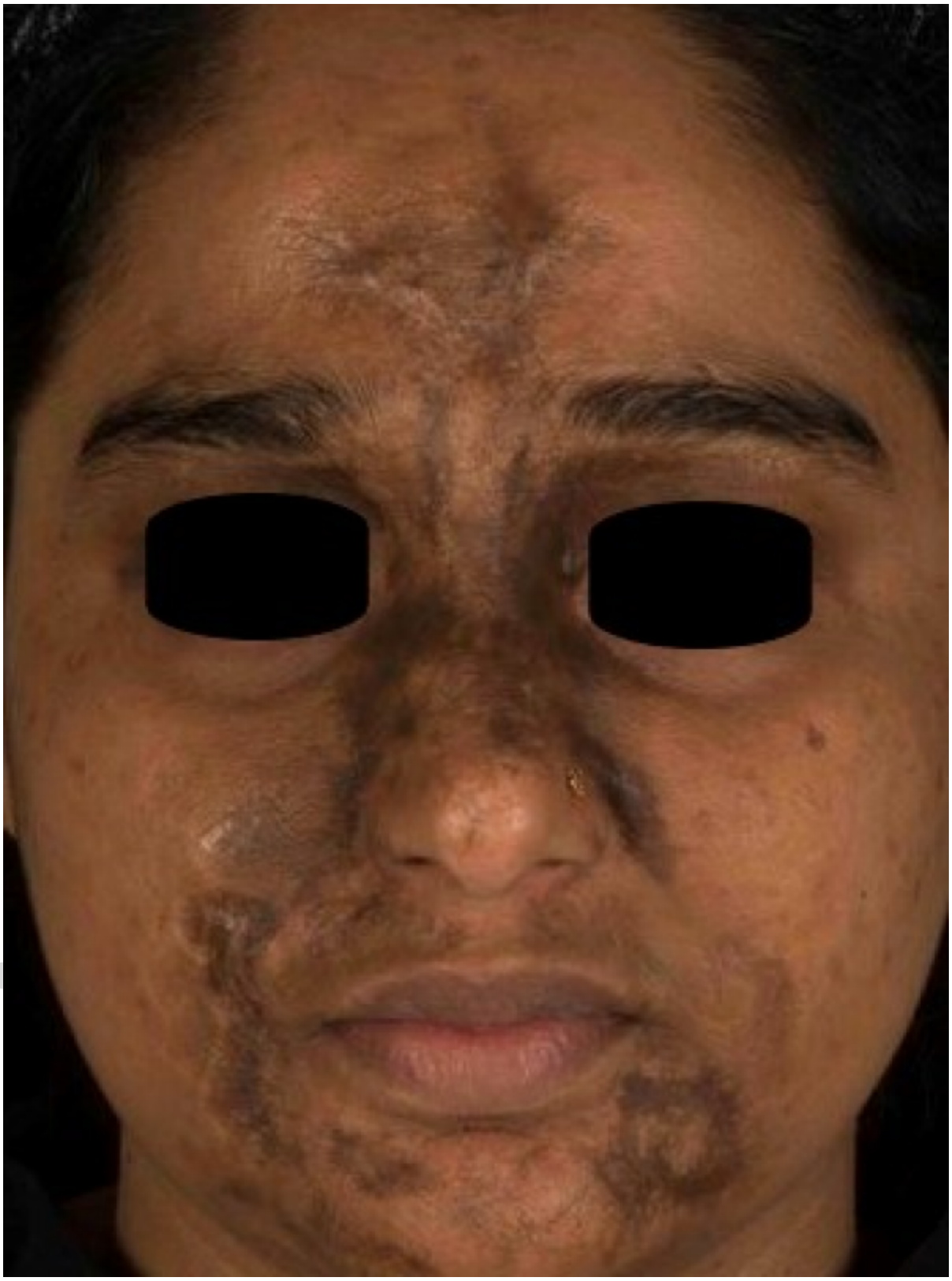

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