IADVL

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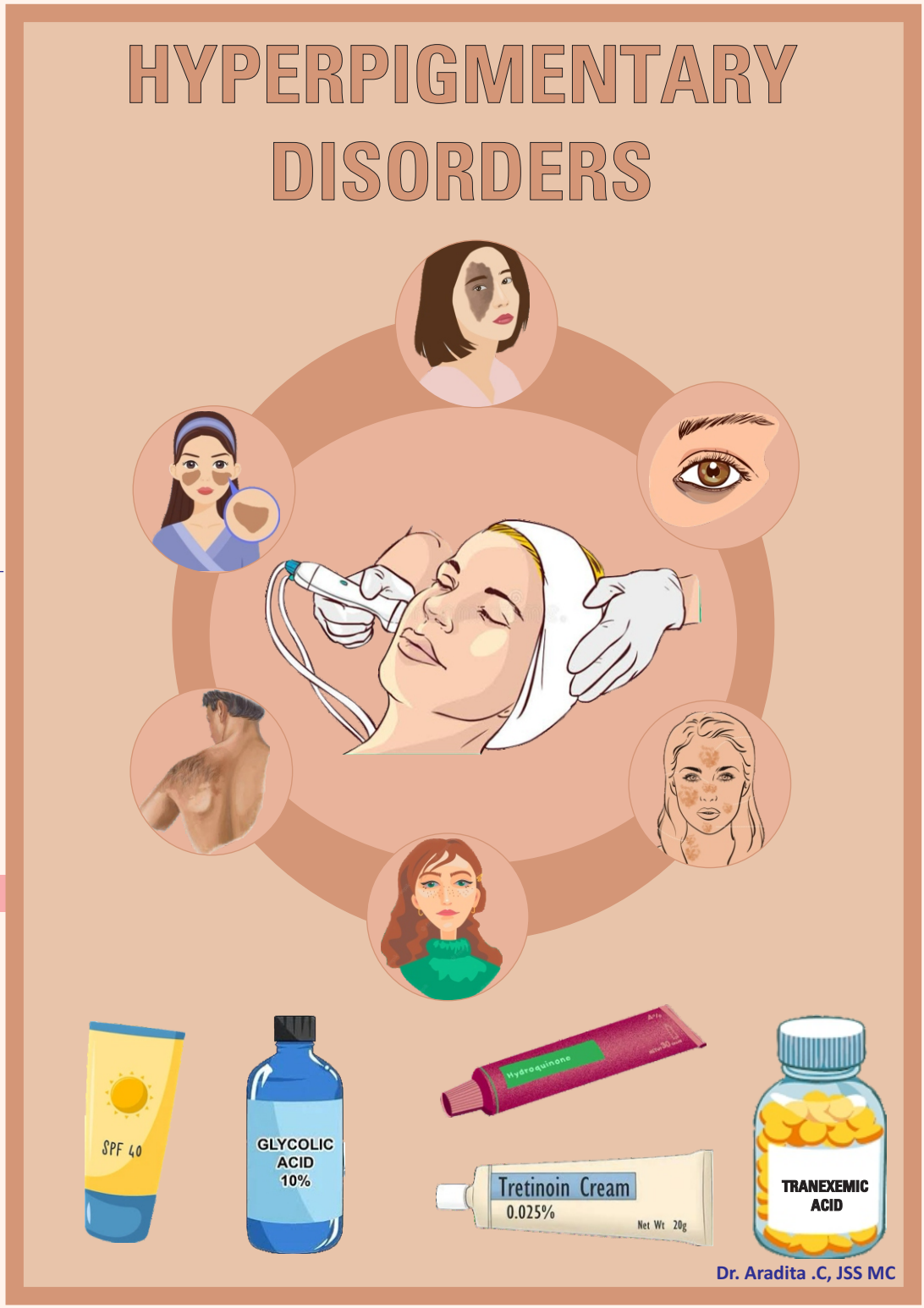

Dr. Aradita .C, JSS MC

PREFACE

Dr. Rashmi Sarkar, MD,FAMS

Dear IADVL Members,

Season's greetings for a Happy and Healthy New Year!

Amongst the various academic groups of IADVL,SIG Pigmentary Disorder has been very active in 2022 in carrying out physical CMEs with state branches and working on a News Bulletin.We are very fortunate to have a hard working IADVL SIG Pigmentary Disorders (IADVL Academy) under Dr Sendhil Kumaran,Coordinator and Dr Chethana Gurumurthy,Convener who have made sure to carry out several activities throughout the year in 2022 along with their team members.I congratulate them and the entire task force for coming up with a newsletter on hyperpigmentation.

Long live IADVL!

Dr Rashmi Sarkar
President IADVL 2022
LM/ND/1543

Acquired Dermal Macular Hyperpigmentation: An Update

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Uniform Nomenclature

Acquired dermal macular hyperpigmentation (ADMH) is an umbrella term that includes disorders clinically characterized by small and large pigmented macules or patches and histopathologically showing an evidence of current or resolved interface dermatitis with pigment incontinence, without clinically significant prior inflammatory phase. The term intends to include diseases previously described in the literature as lichen planus pigmentosus, Riehl's melanosis, pigmented contact dermatitis, ashy dermatosis and erythema dyschromicum perstans. The nomenclature and origin of these disorders have always been a matter of discussion. These disorders share many clinicopathological similarities, are difficult to treat and adversely affect the quality of life. Recent consensus points towards the need for a unifying term to facilitate research and therapeutic trials. This article aims to provide a comprehensive review of the recent advances in ADMH[1].

A Delphi consensus on the nomenclature and diagnosis of lichen planus pigmentosus and related entities[2]

Sixteen researchers representing 12 different universities across India and Australia agreed to be part of this Delphi exercise. At the end of three rounds, a consensus of >80% was reached on usage of the umbrella term 'acquired dermal macular hyperpigmentation'. It was agreed that there were minimal differences, if any, among the disorders previously defined as ashy dermatosis, erythema dyschromicum perstans, Riehl's melanosis and pigmented contact dermatitis. It was also agreed that lichen planus pigmentosus, erythema dyschromicum perstans and ashy dermatosis did not differ significantly apart from the sites of involvement, as historically described in the literature. Exposure to hair colours, sunlight and cosmetics was associated with these disorders in a significant proportion of patients. Participants agreed that both histopathology and dermatoscopy could diagnose dermal pigmentation characteristic of acquired dermal macular hyperpigmentation but could not differentiate the individual entities of ashy dermatosis, erythema dyschromicum perstans, Riehl's melanosis, lichen planus pigmentosus and pigmented contact dermatitis. Acquired dermal macular hyperpigmentation could be an appropriate conglomerate terminology for acquired dermatoses characterised by idiopathic or multifactorial non-inflammatory macular dermal hyperpigmentation.

Quality of life

Psychosocial burden of lichen planus pigmentosus is similar to vitiligo, but greater than melasma: A cross-sectional study from a tertiary-care center in north India[3]

In this study the mean DLQI scores in patients with lichen planus pigmentosus, vitiligo and melasma were 10.9 ± 5.95, 9.73 ± 6.51 and 8.39 ± 5.92, respectively, the difference being statistically significant only between lichen planus pigmentosus and melasma ($P < 0.001$). The corresponding mean modified VIS-22/VIS-22 scores were 26.82 ± 11.89, 25.82 ± 14.03 and 18.87 ± 11.84, respectively. This difference was statistically significant between lichen planus pigmentosus and melasma, and between vitiligo and melasma ($P < 0.001$ for both). As compared to vitiligo, patients with lichen planus pigmentosus had a significantly greater impact on "symptoms and feelings" domain ($P < 0.001$) on DLQI, and on "social interactions" ($P = 0.02$) and "depression" ($P = 0.04$) domains on VIS-22. As compared to melasma, patients with lichen planus pigmentosus had significantly higher scores for "symptoms and feelings," "daily activities," "leisure" and "work and school" domains of DLQI, and all domains of VIS-22. Female gender was more associated with impairment in quality of life in patients with lichen planus pigmentosus, while lower education, marriage, younger age and increasing disease duration showed a directional trend. Patients with lichen planus pigmentosus have a significantly impaired quality of life. The psychosocial burden of lichen planus pigmentosus is quantitatively similar to that of vitiligo, but significantly greater than melasma.

New scoring system

Reliability assessment and validation of the dermal pigmentation area and severity index: a new scoring method for acquired dermal macular hyperpigmentation[4]

Dermal pigmentation area and severity score (DPASI) was a recently proposed scoring system for acquired dermal macular hyperpigmentation (ADMH). After standardized training, three researchers independently rated 55 patients with ADMH on two consecutive days within 1 week, to determine intra-rater and inter-rater reliability. Validation was performed by comparing DPASI with the physician global assessment score.Test-retest reliability of individual raters tested by Pearson's r showed good correlation for all three raters ($r = 0.984$, $P < 0.0001$; $r = 0.983$, $P < 0.000$ and $r = 0.970$, $P < 0.0001$). Inter-rater agreement computed by intra-class correlation coefficient also showed good correlation (ICC = 0.997, $P < 0.0001$). Internal consistency as measured by Cronbach's alpha was 0.997. The score faired well in face and content validity (I-CVI of 0.87). On usability assessment, the scale had a median score of 4 on a scale from 1 to 5. The meantime taken to score the patients were 307.2 ± 83, 308.9 ± 84.4, 350.15 ± 91.8 s by three observers, respectively.The DPASI is a reliable measure of ADMH severity. The use of dermoscopy decreases inter and intra-observer variation resulting in a more objective score.

Investigations options

Contact sensitization to hair colours in acquired dermal macular hyperpigmentation: Results from a patch and photo-patch test study of 108 patients[5]

Detailed clinical examination, skin biopsies, and patch and photo-patch testing with Indian standard series and patient's own cosmetic products were performed. In this study, thirty-nine (36.1%) patients were found to demonstrate a positive patch/photo-patch test with 35/39 reacting to their own products (all were hair colours) and 16/39 reacting to antigens from commercial series (commonly paraphenylenediamine). Fourteen patients developed delayed hyperpigmentation on positive patch-test sites at 1 month. Higher mean age, symptomatic pigmentation (pruritus, burning and photosensitivity), hair margins involvement (outer surface, helix and lobule of ear; temples and preauricular area), ill-defined lesions, epidermal atrophy and epidermal melanization extending >3 layers were significantly common in patch-test-positive patients. Well-defined lesions, perioral involvement and associated lichen planus were clinical pointers towards patch-test negativity.Index study exemplifies that patch-test results have distinct clinical and histopathological correlates in ADMH. Hair dye contact sensitization appears to be an important aetiological factor in about one-third patients presenting with ADMH.

Treatment options

Optimizing Q-switched lasers for melasma and acquired dermal melanoses[6]

The Q-switched Nd:YAG laser is an established modality of treatment for epidermal and dermal pigmented lesions. The dual wavelengths of 1064nm and 532nm are suited for the darker skin tones encountered in India. Though this laser has become the one of choice for conditions such as nevus of Ota, Hori's nevus and tattoos, its role in the management of melasma and other acquired dermal melanoses is not clear. Despite several studies having been done on the Q-switched Nd:YAG laser in melasma, there is no consensus on the protocol or number of sessions required. Acquired dermal melanoses are heterogenous entities with the common features of pigment incontinence and dermal melanophages resulting in greyish macular hyperpigmentation. As the pathology is primarily dermal or mixed epidermal-dermal in these conditions, the longer wavelength of 1064nm is preferred due to its deeper penetration. Generally multiple sessions are needed for successful outcomes. Low fluence Q-switched Nd:YAG laser at 1064nm utilizing the multi-pass technique with a large spot size has been suggested as a modality to treat melasma. Varying degrees of success have been reported but recurrences are common on discontinuing laser therapy. Adverse effects such as mottled hypopigmentation have been reported following laser toning; these can be minimized by using larger spot sizes of 8 to 10mm with longer intervals (2 weeks) between sessions.

Oral mycophenolate mofetil in the treatment of acquired dermal macular hyperpigmentation: An open-label pilot study[7]

In this open-label, pilot study, patients of acquired dermal macular hyperpigmentation affecting at least the face and/or neck were included. Each participant was treated with mycophenolate mofetil 2 g/day for 24 weeks, with a follow-up of 12 weeks. Two aspects of disease severity were measured: activity (appearance of new lesions/extension of existing lesions), and degree of hyperpigmentation (measured using 'dermal pigmentation area and severity index'). Patient satisfaction was assessed on a scale of 0-10. Forty-three of 46 patients who were prescribed mycophenolate, completed the study (40 females, 6 males; mean disease duration 2.8 ± 1.4 years). Amongst 20 (43.5%) patients with active disease, stability was achieved in 17, after a mean duration of 6.1 ± 2.5 weeks (range 4-12 weeks; median 4; IQR 4 weeks). Mean dermal pigmentation area and severity index at baseline was 18.8 ± 7.1 and decreased to 13.7 ± 6.3 at 24th week (27.5 ± 14.7%; P < 0.001). A significant decreasing trend in dermal pigmentation area and severity index (P < 0.001) was observed, and first significant difference from baseline was noted at the 16th week (P 0.008). Less than 10%, >10-20%, >20%-30%, >30%-40%, >40%-50%, and >50% reduction in dermal pigmentation area and severity index was observed in 8, 5, 4, 15, 10 and 1 patients/patient respectively. The maximum mean grade of pre-treatment dermatoscopic severity was 3 ± 0.7, and decreased to 2.1 ± 0.8 on the face (P < 0.001) and 2.4 ± 0.7 on the neck (P < 0.001) post-treatment. There were 9 (20.1%) non-responders. Self-assessment scores of the rest of the patients fell in the range of moderate/fair improvement (>5 to 7). No significant correlation was seen between patient satisfaction score and degree of reduction in dermal pigmentation area and severity index (r -0.39). Three developed adverse effects (leucopenia, n = 1; transaminitis and hyperbilirubinemia, n = 2) that resolved following discontinuation of mycophenolate. Mycophenolate mofetil appears to be a promising treatment option in acquired dermal macular hyperpigmentation.

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MELASMA - UPDATE ON PATHOGENESIS & TREATMENT

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Melasma is the most common pigmentation disorder among Indians and is associated with treatment challenges. At least 90% of those affected are women. It is mostly observed in the facial area of darker-complexioned individuals (skin types IV–VI) exposed to intense ultraviolet (UV) radiation and shorter wavelengths of visible light. Melasma is characterized by symmetrically oriented hyperpigmented macules and patches, with varying presentations including blotchy, irregular, arcuate, and polycyclic. Melasma is frequently associated with a considerable emotional burden due to facial disfigurement.

Genetic component:

The pathogenesis of melasma is multifactorial and not well defined. Patients exhibit different clinical and histological features, suggesting the involvement of multiple mechanisms. Transcriptional analysis of melasma lesional skin revealed almost 300 genes as being differentially regulated in melasma, highlighting the complexity of the disorder.[1] Such complexity and heterogeneity have implications on the treatment of the condition, which is notoriously difficult.

Immune dysregulation:

In a study by Rodríguez-Arámbula et al, conducted on 20 female patients with malar melasma, histopathological examination revealed significantly higher inflammatory infiltration of CD4+ T cells, CD68+ macrophages and mast cells, as compared to unaffected skin. Additionally, genetic and immunohistochemical analyses showed significant elevations in the expression of IL-17 and COX-2. This indicates that malar melasma contains chronic inflammatory cells and mediators which can be exacerbated by environmental stimuli, of which cumulative sun exposure is the most important. This might explain the recurrence of melasma as well as the favourable responses to topical anti-inflammatory treatments.[3]

Multifactorial pathogenesis:

It is now thought that melasma is the result of a complex interaction between epidermal melanocytes, keratinocytes, dermal fibroblasts, mast cells, vascular endothelial cells, and hormonal, genetic, as well as UV influence. Histopathologically, melasma is characterized by solar elastosis, basement membrane disruption, increased vascularization and increased mast cell count, which strongly indicate that melasma should also be regarded as a photoaging skin disorder.[3]

Triggers:

Common triggers include pregnancy, hormonal therapies (including oral contraceptives), phototoxic and anti-epileptic medications, intense sun exposure and genetic predisposition. More than 30 % cases in women and most cases in men are idiopathic.[2]

Due to these multiple possible risk factors, innumerable therapeutic options targeting the various pathways of melanin synthesis as well as physical modalities to remove the melanin have come forth for the relief of this refractory disorder.[4]

Therapeutic management:

It is challenging, given its chronicity and recurrence rates. No single treatment is universally efficacious. Thus, combination treatment should be applied, along with avoidance ofexacerbating factors such as use of hormonal contraception and UV light exposure.

The existing modalities which are used include hydroquinone, retinoic acid, kojic acid, azelaic acid, and peeling agents like glycolic, trichloroacetic acid, salicylic and lactic acid. Physical agents like lasers and dermabrasion have also been tried with limited success. Combination therapies, either in double or triple combinations yielded the best results when compared to single therapies.

Topical treatment

Topical treatments have been the mainstay of melasma treatment. Photoprotection is the most important and it has been used as an adjuvant to other melasma treatments, since both UV and visible light can cause sustained hyperpigmentation in all skin types. Hydroquinone (HQ) has been considered a first-line treatment for melasma and triple combination creams containing hydroquinone have become increasingly popular, as they yielded superior results.

Many other active ingredients have been studied, of which 1% flutamide and thiamidol 0.2% seem to have superior results to HQ, with no adverse events reported. Tranexamic acid (TXA) 5%, lignin peroxidase, petroselium crispum solution, silymarin cream, 4% diacetyl boldine serum and cosmetic product combination cream had comparable results to HQ cream formulas, which make them a valid alternative to HQ. Furthermore, TXA combinations seem to be more efficacious against hypervascular, inflammatory melasma. Also, azelaic acid 10% combined with d-panthenol 10% had better results than other azelaic acid formulas[7]

Systemic treatment:

Nowadays there are many systemic therapies that can be used as an adjuvant in melasma treatment. Oral polypodium leucotomos is one of the a valid options. Further studies are necessary in order to assess the recurrence rates and the possibility of maintaining the systemic treatment with after topical treatment cessation, in order to avoid relapses.[10]

Transexamic acid:

Oral TXA had better results than placebo, although not statistically significant. Oral TXA in combination with HQ 4% cream, as well as TC cream, rendered superior results than the topical treatment alone. In terms of delivery methods, oralTXA seems to have better results than microneedling.[5] Additionally, in terms of TXA dosage,no significant differences were found between the use of either 500 mg, 750 mg, 1000 mg or 1500 mg daily.[8]

Others:

Dietary carotenoids, melatonin, either topical or systemic or both, as well as procyanidin + vitamins A, C E seem the least effective of the systemic treatments. However, additional studies following patients for longer periods might be useful.

Microneedling

Microneedling is a minimally invasive, collagen induction therapy that consists in delivery of fine needles into the skin. It enhances transdermal drug delivery It has shown results even after as early as 7 days, from a histological viewpoint.

Microneedling with TXA:

Rendered inferior results to GA peeling, silymarin cream, HQ 4% cream and similar results to microneedling with vitamin C 40%. In the oral versus intradermaldelivery of TXA, the former yielded superior results in an Indian cohort. The addition of glutathione to TXA cocktails used for microneedling procedures rendered superior results and zero recurrence rates.[9]

Microneedling with glutathione: In a study by Feng et al, microneedling with glutathione in combination with TXA was superior to HQ topical application.[6]

Microneedling has also been used as combination therapy with HQ 4% cream, Q switched Nd YAG laser and the results were superior to both topical and laser therapy alone.

Microneedling is a useful adjuvant to topical therapy in melasma and can be used as a step up option in patients refractory to topical treatment, before using other therapies like peels, lasers and systemic medications.

Platelet Rich Plasma:

A split face study using PRP & hydroquinone on one side & HQ alone on the other side showed that PRP exerts enhanced benefits in the management of melasma. [11]

Lasers and Light Therapy

Among laser devices, QSNYL is the preferred choice for dermal and mixed types of melasma. LFQSNYL, also known as laser toning, uses a low-fluence, multi-pass technique is another addition to the list.

A new class of lasers that generate picosecond- domain pulses, available in different wavelengths, of 532 nm, 755 nm and 1064 nm, determine melanin fragmentation by photoacoustic, rather than photothermal effect, thus determining even less inflammation than the LFQSNYL. Lee et al demonstrated picosecond 755 laser superiority to QSNYL. Fractional resurfacing lasers, either ablative or non-ablative, creates different columns of microthermal damage in the skin, which determines lower inflammation and risk of dyspigmentation. As an antivascular treatment in melasma, PDL, QSNYL and IPL, either as monotherapy or combined with systemic or topical TXA, seems to be efficacious in cases of melasma with increased vascularity.[12]

In conclusion PLE and TXA have been demonstrated to be an efficacious treatment, especially in association with topical HQ and TCC. (Triple combintion cheams)

Microneedling with a combination of TXA and glutathione has new and encouraging results that might prove superior to the gold standard so far, HQ cream and might also lower the recurrence rates. Additionally, oral TXA seems to have superior results to intradermal TXA in patients with dermal and mixed types of melasma

Chemical peeling have demonstrated high efficacy when combined with either topical or laser therapy.

There is a lack of studies following melasma patients on the long term. Treatment choice should be made after Wood's lamp examination, as well as dermatoscopic evaluation, in order to determinate the epidermal, dermal or mixed type of melasma, as well as the degree of vascularity.

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RARE CASE SCENARIOS

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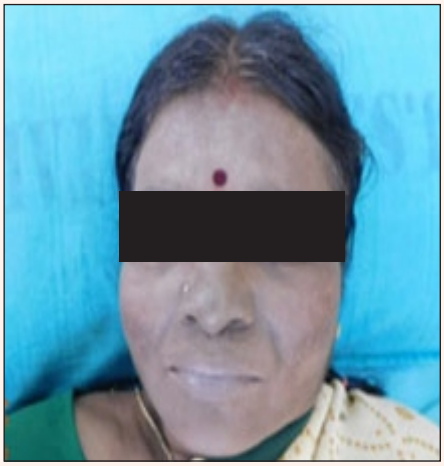
Case 1 – BLUE LADY

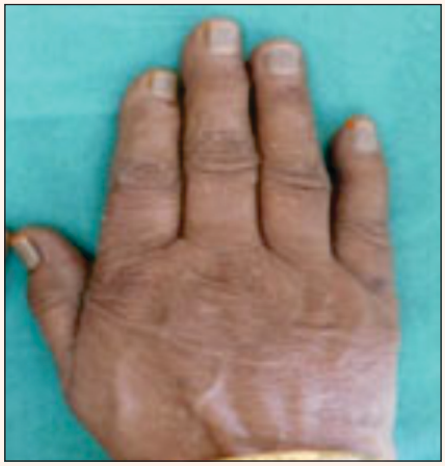
A 67-year-old female came with asymptomatic greyish blue pigmentation predominantly over the exposed areas of the skin for the past 6 months. It started over the face and then spread to involve whole body in a span of 2 months.

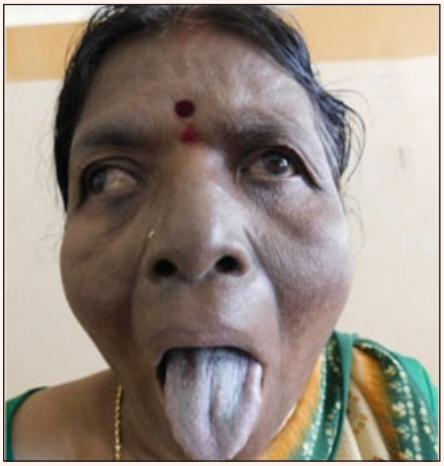
There was no history of any treatment taken for the same.

She was a known case of type 2 diabetes mellitus on oral hypoglycaemic drugs and was also on some ayurvedic medication for back pain since 2 years. There was no change in medications prior to onset of pigmentation.

On examination there was greyish blue pigmentation involving face, trunk, upper and lower limbs. In addition to skin there was pigmentation involving both finger and toe nails, ocular conjunctiva and tongue. Systemic examination was within normal limits.

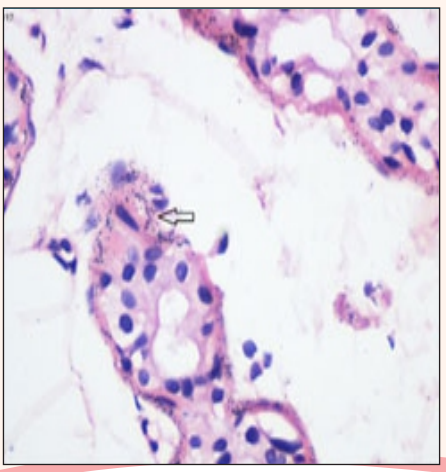






With this clinical information the various differentials thought were Drug induced pigmentation, Lichen planus pigmentosus (LPP), Addison's disease.

Accordingly she was investigated. Complete blood investigation with liver & renal function test, thyroid function test, vitamin B12 levels, ultrasound abdomen were within normal limits. Histopathological examination showed epidermis displaying focal thinning and mild edema and perivascular lymphocytic infiltrate in dermis. The basement membrane of adnexal structures and vessels showed deposition of fine brownish black granules. Features were consistent with Argyria.



On detailed enquiry an ayurvedic medication consumed by the patient for back pain for about 2 years contained silver. Hence, it was concluded as drug induced Argyria and was started on oral hydroxychloroquine.

Disease	History and clinical	Dermascopy	Histopathology	Treatment
Acquired dermal macular hyperpigmentation (ADMH)	Greyish brown asymptomatic pigmentation usually seen in middle aged	Pigment dots, globules and blotches sparing eccrine and follicular openings	Basal cell degeneration, pigment incontinence and sparse dermal inflammatory infiltrate	Topical steroid, tacrolimus. Oral retinoids, cyclosporine. Q switched Nd YAG laser.
Drug and heavy metals induced pigmentation	History of drug (antimalarials, minocycline) and heavy metals (gold, bismuth)	Blue grey peppering in a reticular or hexagonal pattern	Brown granules within the macrophages and basal cells of eccrine glands.	Drug withdrawal. Q switched Nd YAG laser.
Addison's disease	Bronzing hyperpigmentation more over sun exposed area , pressure points, palmar creases and mucous membrane.	Not defined	Basal melanin hyper melanosis and superficial dermal	Oral Corticosteroids
Alkaptonuria	Dark colored urine and other body secretions Bluish grey pigmentation of palms, malar area of face, ear	White globular structures with greyish blue structureless areas	Epidermal thinning with deposition of ochre bodies with collagen degeneration in dermis.	Nitisinone and Vitamin C is beneficial in some cases.

Silver is a naturally occurring element hence it is found in lower concentration of up to 3microgram/litre in a normal healthy individual. Exposure to large amounts of silver results in toxicity. Sudden exposure to large doses of inorganic silver leads to acute toxicity manifesting as vomiting, diarrhoea, decreased blood pressure and respiration ultimately leading to convulsions and shock. However, chronic low dose exposure leads to precipitation of silver in soft tissue like skin, liver, spleen and adrenal glands known as argyria. The use of silver in the form of dietary supplement and as a constituent of alternative therapies has lead to resurgence of localised as well as generalised argyria.1 Ash of silver is widely used in ayurveda, one of the Indian traditional system of medicine. 2 Several neuropathic medications also contain silver leading to generalised argyria. 3 Another cause of localised argyria is through use of mega endoprosthesis containing silver for reconstructive surgeries.4 Clinically it manifests as slate grey pigmentation involving skin more over sun exposed areas and oral, ocular mucosa. It needs to be differentiated from other causes of pigmentation Histopathology of skin shows deposition of fine brown black granules in basal lamina of secretory portion of eccrine glands. Treatment includes cessation of silver exposure and sun protection to avoid further increase in pigmentation. Q-switched Nd-YAG laser might be useful in reducing the pigmentation.

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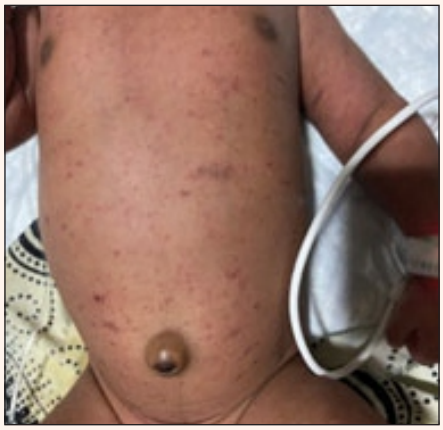
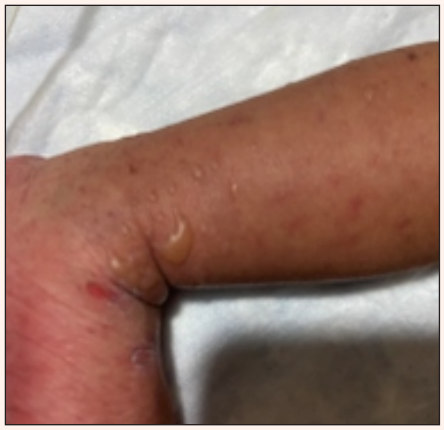
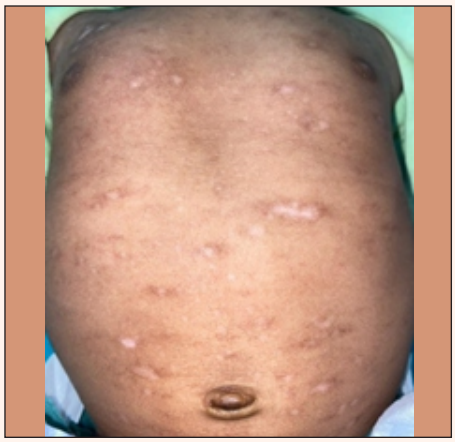
Case 2: INFANT WITH CHIK SIGN.

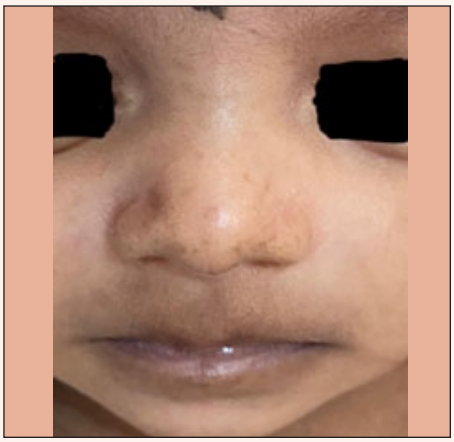
A 45 days old male baby was brought to hospital with history of fever and reddish rashes all over body since 2days. The rashes initially appeared over trunk and then spread to involve extremities in span of 24hours. There was no history of excessive crying, sleep or feeding disturbance since last 2 days. Baby's immunisation status was complete till date. Mother had history of mild grade fever associated with joint pain for 2 days which subsided with symptomatic treatment. On examination temperature was 100oF, heartrate was 126beats per minute and respiratory rate was 42 per minute. Cutaneous examination revealed erythematous macules involving trunk and extremities. Systemic examination was within normal limits. On day 3 of admission baby developed tiny superficial vesicles over lower limbs and few over abdomen which resolved with exfoliation in 4 days. Routine blood investigations were within normal limits, COVID RT-PCR was negative in both mother and baby. Tests for dengue, chikungunya and Leptospira ware negative. Skin biopsy was taken from the vesicle and it showed intraepidermal bullae and dermal lymphocytic infiltrate. Baby was treated with antipyretics and antibiotics, following which baby was symptomatically better and was discharged on day 6.





During its follow up period on day 15, baby had developed hypopigmented and hyperpigmented macules all over body and also over the tip of the nose(chik sign). With this as a clue, test for chikungunya was repeated and it showed positive for IgM antibodies.





Chikungunya is an arboviral disease transmitted by mosquitoes. Ever since 1963 several outbreaks are being reported in India. Incubation period is short ranging from 3-7days. Following which individuals will present with sudden onset of fever with chills and rigor. Anorexia, vomiting and arthralgia are the other features.[1] Cutaneous manifestation was seen in 77% of patients[2] and in almost all affected infants. Cutaneous manifestations include generalised erythema and maculopapular rash which initially starts over trunk and then spreads centrifugally. These rashes occur within 2-3 days of fever and resolve by 6-7 days. The most common skin involvement is by brownish black pigmentation. Freckle like macules occur in majority of the cases and it may or may not be preceded by maculopapular rash.[3] The cause for this may be due to intraepidermal dispersion of melanin

triggered by the virus. Pruritus may be an associated symptom.[4]

Cutaneous manifestation in infants are different compared to adults. Vesiculobullous lesions are most commonly seen in infants than adults. Tiny superficial vesicles develop initially over the extremities by 2-3 days of fever and resolve with exfoliation and hypo or hyperpigmentation. Vesicles are secondary to focal necrosis and ballooning degeneration of cells caused by viral replication.[5]

This needs to be differentiated from other causes of fever with rash. Hyperpigmented macules gives us a clue towards diagnosis.

Confirmation is done by testing for IgM antibodies in the serum of affected individuals. However, this test might be negative in the initial few days of the infection. Other tests include RT-PCR.[4] Chikungunya is a self-limiting disease, which resolves in 7-8days. Symptomatic treatment and supportive therapy will help in faster recovery.[1]

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THE PSYCHOSOCIAL IMPACT OF MELASMA AND ACQUIRED DERMAL MACULAR HYPERPIGMENTATION

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Pigmentary disorders constitute 4-8% of patients presenting to dermatology outpatient departments in India. Though often regarded as of being only 'cosmetic' significance, pigmentary disturbances lends a considerable psychosocial impact; perhaps the basis on which these entities merit the label of 'diseases'. Darker ethnic groups are known to have greater tendency for hyperpigmentation, an unfortunate reality for a country that culturally associates lighter skin types with better socio-economic status, employability and beauty.

Melasma is the most common, among the acquired hyperpigmentary disorders, affecting upto 30% middle-aged women in a population-based study.[1] Acquired dermal macular hyperpigmentation (ADMH), is less common, and is an umbrella term including many closely related and overlapping entities such as lichen planus pigmentosus, pigmented contact dermatitis/Riehl's melanoses and ashy dermatoses/erythema dyschromicum perstans. These entities present as asymptomatic slate grey to brown macules, varying from well-defined round lesions to ill-defined or coalescing areas of hyperpigmentation over face, trunk and upper limbs.

These disorders of hyperpigmentation have been shown to exert a moderate to large negative effect on patient's lives. A study from India reported that about 42% patients with lichen planus pigmentosus (n = 7) and pigmented cosmetic dermatitis (n = 10) had large effect on the quality of life as estimated by the DLQI (Dermatology Life Quality Index).[2] Two recent separate large studies from tertiary care institutes in north India have been shown the DLQI scores in patients with lichen planus pigmentosus and ADMH to be 10.9 and 9.16 respectively, and 7.10-8.39 in patients with melasma.[3,4] The prevalence of anxiety disorder in patients with melasma and ADMH has been shown to be 11.6% and 18.7% respectively. Depression was seen in 12.8% of melasma patients, and in nearly twice as many patients with ADMH (24.1%).[4] In fact, the psychosocial impact of lichen planus pigmentosus was greater than melasma and comparable to vitiligo, despite the lack of cultural stigma and misconceptions that are prevalent with regard to the latter.[3] The worst impact was seen in those belonging to age groups 18-30 year and unmarried females, likely reflecting the direct cosmetic impact. Disease-specific quality of life scales have been developed for melasma, but similar scales are currently lacking for ADMH. MELASQoL (Melasma Quality of Life) scale comprises 8 domains, in which social life, recreation and leisure, and emotional well-being has been found to have the largest impact. Patients with lichen planus pigmentosus report feeling embarrassed about meeting new people, worried about the spread of disease and preoccupied with thoughts about the disease. Expenditure for treatment as well as unsolicited advice regarding treatment from family members further add to the emotional distress.[3]

The saga of treatment in these recalcitrant conditions is often a story of many pages, commonly spreading across modern and alternative medicine; with patients morosely pulling out photographs of how they looked like before their pigmentary alterations. A meta-analysis evaluating the quality of life among melasma patients has shown higher MELASQol scores in patients who received previous treatment for melasma[5] While this may reflect greater treatment-seeking behaviour in those distressed, it may also reflect the exhaustion and frustration from treatments which require monetary input and prolonged compliance and yet do not drastically modify the disease. However, when treatments are successful, it has been shown to improve the quality of life in melasma patients. At the same time, the 'success' of a treatment is often measured quantitatively in terms of colorimetry, spectrophotometry, severity indices or photographic assessment, and expressed in terms of 'statistical significance'. It is important to translate these outcomes to clinically meaningful differences to the patients. A meta-analysis of 22 studies showed that there was no statistically significant difference in quality of life scores

among patients experiencing ≤50% improvement in melasma severity, but patients experiencing >50% improvement in melasma severity experienced an additional 14% improvement in quality of life compared to the other patients. When studies were pooled according to baseline melasma severity, treatment of severe melasma was associated with a moderate improvement in quality of life whereas the treatment of mild to moderate melasma was not.[6] There are contradictory studies regarding correlation of baseline disease severity and quality of life, though seven of 12 studies in a meta analysis on quality of life amongst melasma patients demonstrated no statistical correlation between MASI and MELASQol. In general, it is well-established that the clinical severity of a disfigurement may not always be a good predictor of how patients see it. Factors such as a person's general outlook towards life, role of appearance in self-esteem or self-concept, and societal factors including media, advertisements and family support contribute to a person's well being, and are thus amenable to change through psychological intervention. However, current facilities for dedicated psychodermatology interventions are limited, and it thus falls on the treating dermatologist to address this important disease aspect.

Data for effective treatment options and natural course of ADMH are much more scarce, with some patients even showing spontaneous resolution within a few months to years while others struggle with a chronic and persistent disease. The lack of a reliable prognosis and difficulty in treating a disease of which we have little understanding, leads to doctor-shopping. Herein dives the ever-growing pharmaceutical expanse of skin lightening products, currently representing 50% of India's entire skincare market, with estimates of its worth varying between $US 450–535 million![7] About 37.6% of urban population between 16-60 years reported using skin fairness products, women being twice more likely to use them than men. Many of these are unregulated, and not uncommonly lead to steroid induced side effects or even pigmented contact dermatitis, thus perpetuating the cycle. Camouflage options such as safe colour-matched cosmetics or tinted sunscreens provide an even tone to the skin, and should be offered to patients. Use of these has been shown to improve quality of life in patients with pigmentary diseases, with significant reduction in the impact of dermatological condition on interpersonal relationships. Counselling and psychotherapy are other interventions, the first administrable by a dermatologist with some training, as the patients may be reluctant to visit a psychiatrist straight-up. Counselling requires empathy, positive regard and a non-judgemental attitude to relate to the patient.

As dermatologists, we often tend to focus on the 'visible' aspect of skin disease. What may not be as visible to our eyes, but nonetheless a burden on the patient's mind, tends to get sidelined. It does well to remember the basic definition of disease when we find ourselves faced with an 'insignificant' complaint amidst a busy practice of much more symptomatic or emergent conditions - 'a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity'. Recognizing the psychosocial impact of pigmentary diseases, including melasma and ADMH will allow us to provide a more holistic treatment to our patients.

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MCQ's QUIZ

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1. Crisaborole , a novel topical agent used in atopic dermatitis inhibits which subtype of phosphodiesterase enzyme.
   a. PDE 1 b. PDE2 c. PDE3 d. PDE4.

2. Hem like pattern on dermatoscopy is characteristic of which of the following.
   a. Reihl's melanoses. b. Lichen Planus Pigmentosus.
   c. Pigmented contact dermatitis. d. Pigmentary demarcation lines.

3. Black urine disease is name given for which of these disease.
   a. Argyria. b. Chrysiasis. c. Alkaptonuria. d.Hydragyrism

4. Dirty skin syndrome is linked to which drug
   a. Amiodarone. b. Chloroquine. c. Minocycline. d.Phenytoin .

5. Flagellate dermatitis is seen in all except
   a. Jellyfish stings. b. Still's disease.
   c. Docetaxel d. Doxorubicin.

6. Jellinek's Sign is seen in
   a. Addison's disease b. Scleroderma
   c. Hyper thyroidism d. Alkaptonuria

Answers.

1. d. Crisaborole acts by inhibiting PDE 4 and produces anti inflammatory effect.

2. b. Slate gray to blue globules deposited in peri follicular and peri eccrine areas gives hem like pattern.

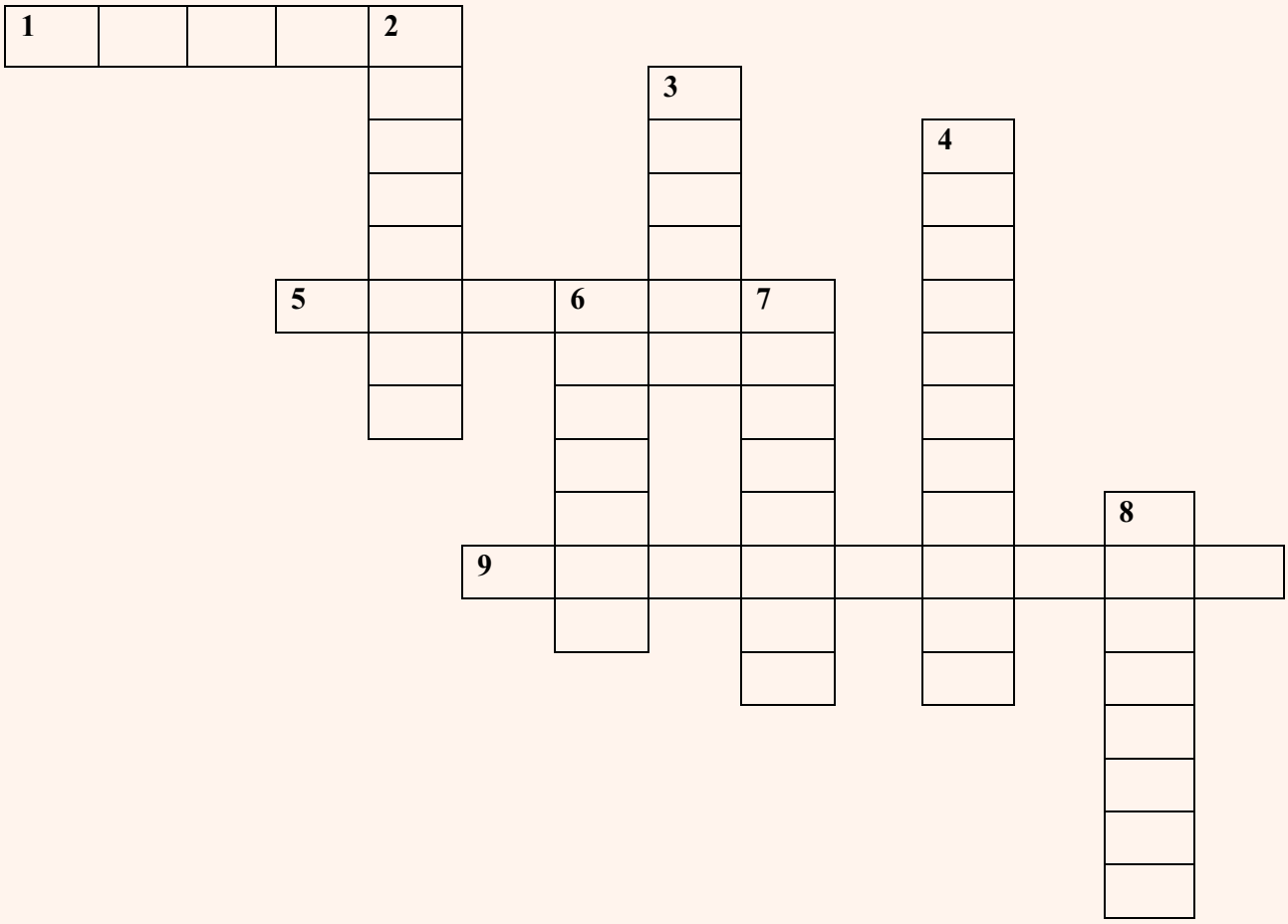
3. c. In alkaptonuria, homogentisic acid is oxidized to form a pigment like polymeric material responsible for the black color of standing urine.

4. c. Dirty skin syndrome is muddy brown discoloration in sun exposed areas, typically the face caused by minocycline.

5. d. Flagellate dermatoses characterised by linear or curvilinear arrangement simulating the marks of whiplashes.

6. c. Pigmentation of eyelids seen in hyperthyroidism is called Jellinek's sign.

CROSSWORD PUZZLE



CLUES

Across

1. Disease due to mercury poisoning named after a colour.
5. Characteristic bodies due to long term use of hydroquinone.
9. Therapeutic agent in melanoma which produce vitiligo as side effect.

Down

2. Mushroom responsible for flagellate dermatitis.
3. Disease with eyeliner sign on histopathology.
4.Vitiligo associated with congenital megacolon.
6. Metal poisoning which gives raindrop appearance.
7. Disease with oral pigmentation associated with hypotension.
8. Nail change in darrier disease named after snack.

Answer key :

1. PINK'S disease.
2. SHIITAKE mushroom.
3. BOWEN'S disease
4. WAARDENBURG (type 4)
5. BANANA bodies.
6. ARSENIC.
7. ADDISON'S disease.
8. SANDWICH nails.
9. NIVOLUMAB.

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