Generalized facial pigmentation: An uncommon presentation of cutaneous lupus erythematosus

Sir,

Post-inflammatory hyperpigmentation occurs when the basement membrane of the skin is damaged and this is seen in many inflammatory skin diseases such as lupus erythematosus. It appears in the late phase of many skin lesions and hampers the identification of specific histological features which are characteristic of the triggering disease.[1]

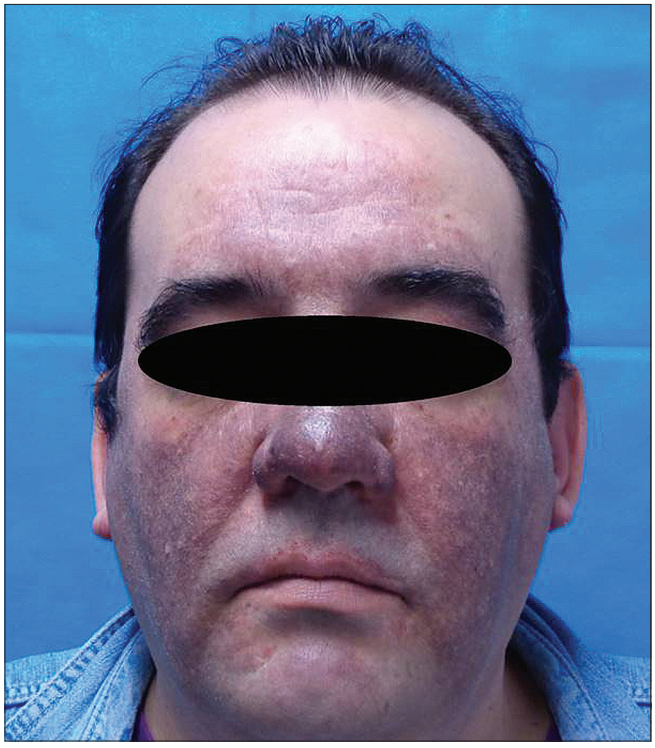

Figure 1: Patient 1 with diffuse slate-grey pigmentation on face with mild erythema

Post-inflammatory pigmentation is widely seen in the periphery of the skin lesions of discoid lupus erythematosus or in the late phase of acute cutaneous lupus erythematosus. However, cutaneous lupus erythematosus presenting predominantly with macular pigmentation is uncommon and often misdiagnosed.[2,3]

We present six patients who came with diffuse cutaneous facial pigmentation, as the main manifestation of cutaneous lupus erythematosus, showing histological features of cutaneous lupus.

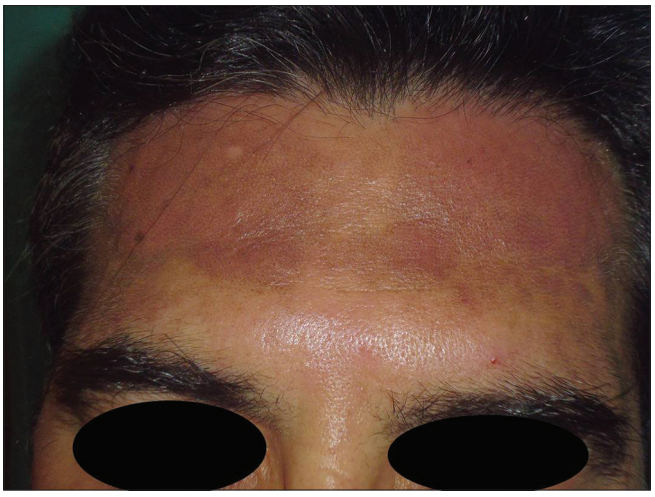

Figure 2: Patient 2 with brownish pigmentation on the forehead with marked erythema

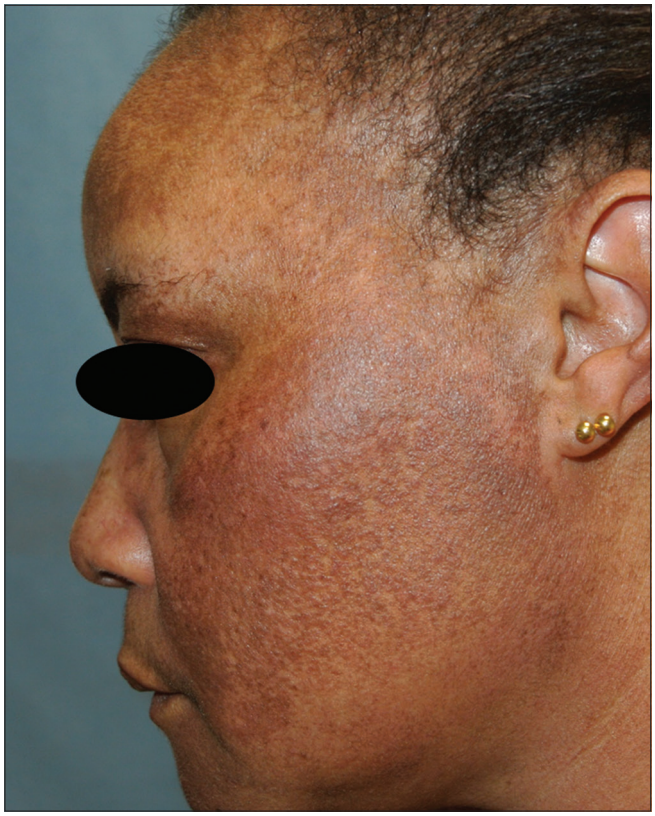

Figure 3a: Patient 4 with brown reticulated pigmentation on forehead, eyelids and malar area

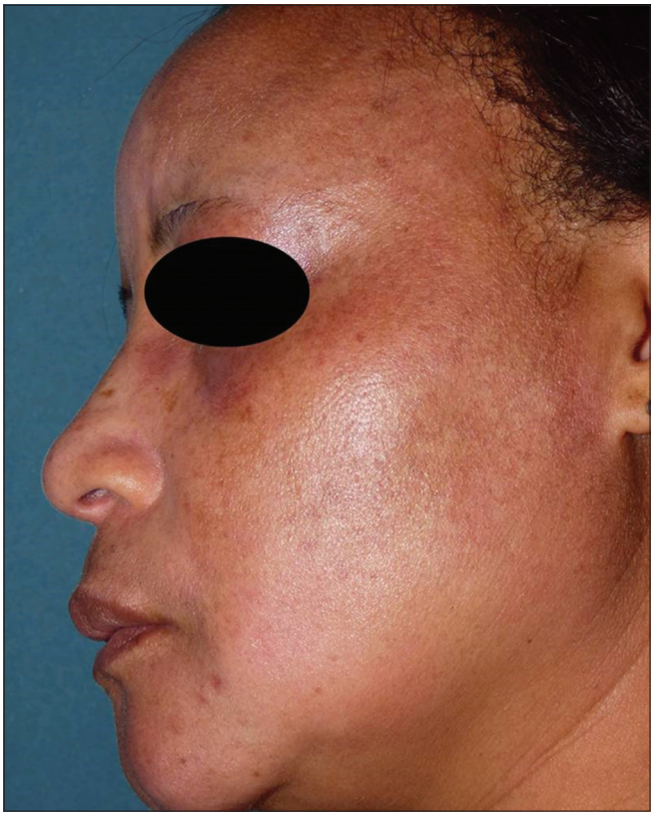

Figure 3b: Patient no. 4 after treatment

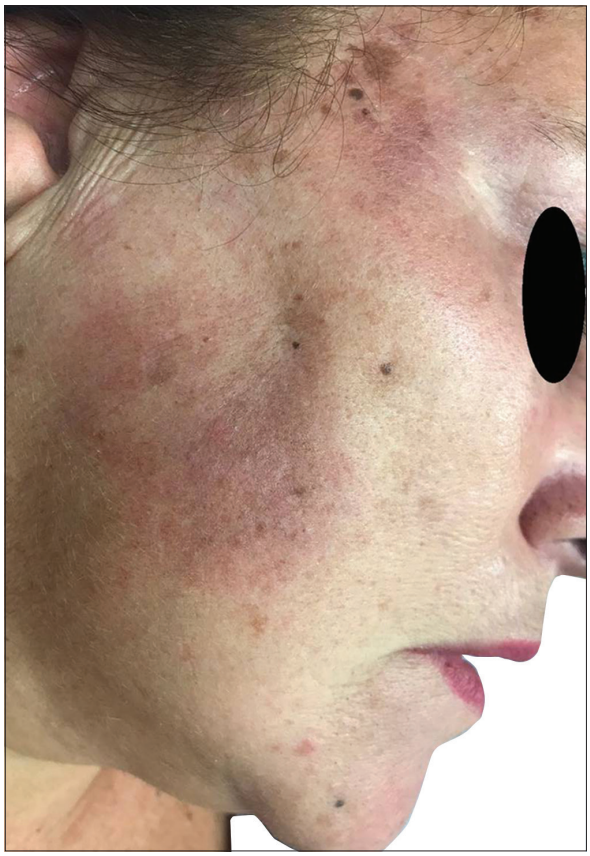

Figure 4: Patient 6 with brownish pigmentation limited to malar and mandibular area with marked skin erythema

Our patients included four men and two women from Hospital 12 de Octubre and Hospital Fundación Jiménez Díaz (Madrid, Spain) with an average age of 51.33 years and medium-dark phototypes (III-V). Time until diagnosis ranged from 3 months to 10 years.

Clinically, they showed a diffuse, non well-demarcated grey-brown pigmentation, mainly on the forehead, temples and cheeks [Figures 1-4]. Patient no. 1 showed involvement of the ear lobes and patient no. 4 had pigmentation in the V area of the neck as well. Five cases showed concomitant facial erythema, although pigmentation was the predominant feature in all of them. In patient no. 4, who had features of systemic lupus erythematosus, the worsening of pigmentation was observed concurrently with disease outbreaks and the onset of other general manifestations, particularly joint-related symptoms. Besides, this patient had subcutaneous nodules in buttocks and thighs concurrently with one of the outbreaks of the systemic disease. Lupus panniculitis was suspected; however, the biopsy did not show any specific finding. All the patients showed positive autoimmunity markers [Table 1].

In all cases, drug-induced skin pigmentation was ruled out and epicutaneous patch tests were performed with GEIDAC's (Spanish Research Group on Contact Dermatitis and Cutaneous Allergy) standard battery which showed negative results.

Table 1: Clinical and serological features of the patients

Patient	1	2	3	4	5	6
Age (years)	50	45	71	43	38	61
Sex	Male	Male	Male	Female	Male	Female
Skin phototypes	III	III	IV	V	III	III
Facial erythema	Yes	Yes	No	Yes	Yes	Yes
Time until diagnosis	4 years	10 years	2 years	6 months	3 years	1 year
Cutaneous pigmentation	Diffuse slate-grey pigmentation on face	Brownish pigmentation on the forehead.	Brownish pigmentation on the forehead	Brown reticulated pigmentation on forehead, eyelids and malar area	Brown patched pigmentation on forehead and malar area	Brownish pigmentation limited to malar and mandibular area
Cutaneous manifestations	None	None	Light sensitivity	Subcutaneous nodules	Light sensitivity	Light sensitivity
Other autoimmune diseases	Sjogren's syndrome	Antiphospholipid syndrome	No	No	No	Sjogren's syndrome and Rheumatoid arthritis
Autoimmunity markers	Positive lupus anticoagulant test. Negative for ANA, anti-DNAds, anti-RNP, anti-SM, anti-SSA/Ro, antiSSB/La, and rhreumatoid factor	Positive lupus anticoagulant test. Negative for ANA, anti-DNAds, anti-RNP, anti-SM, anti-SSA/Ro, antiSSB/La, and rhreumatoid factor	Positive: ANA 1/320 and anti-RNP antibodies	Positive: ANA 1/640 (ANA method test: screening Multiplex and indirect immunofluorescence), anti-DNAds, anti-RNP and anti-SM antibodies	Positive lupus anticoagulant test. Negative for ANA, anti-DNAds, anti-RNP, anti-SM, anti-SSA/Ro, antiSSB/La, and rhreumatoid factor	Positive: ANA 1/160 (ANA method test: screening Multiplex and indirect immunofluorescence), anti-dsDNA, anti-Sjögren's syndrome-related antigen A (anti-SSA/Ro), anti-La protein antibodies (anti-SSB/La) and rheumatoid factor
Inflammatory markers	Lymphopenia, High erythrocyte sedimentation rate	None	None	Leukopenia, Lymphopenia, High erythrocyte sedimentation rate, High C-reactive protein	High C-reactive protein	None
Histopathological findings	Vacuolar interface dermatitis. Dense lympho-mononuclear perivascular and perifollicular infiltrate. Melanin incontinence	Lympho-mononuclear infiltrate. Effacement of dermoepidermal interface with vacuolar degeneration of basal cells and melanophages	Perifollicular lymphocytic infiltrate. Vacuolar degeneration of the basal cells and melanin deposits in the papillary dermis	Focal interface dermatitis. Periadnexal lymphocytic infiltrate with dermal melanin deposits	Vacuolar degeneration of the basal cells. Lympho-mononuclear periadnexal infiltrate and abundant melanophages in the papillary dermis	Dense lympho-mononuclear perivascular and perifollicular infiltrate and vacuolar interface dermatitis
Systemic LE criteria	No (only positive lupus anticoagulant test)	No (only positive lupus anticoagulant test)	No (only light sensitivity)	Yes (acute cutaneous lupus erythematosus, synovitis, leukopenia, positive anti nuclear Antibodies, Anti-dsDNA and anti-smantibodies)	No (only light sensitivity and positive lupus anticoagulant test)	No (only light sensitivity and positive anti nuclear Antibodies, Anti-dsDNA antibodies)
Treatment given and response	Hydroxychloroquine Photoprotection Improvement of Pigmentation	Hydroxychloroquine Photoprotection Pigmentation: stability achieved	Hydroxychloroquine Photoprotection Pigmentation: modest improvement	Hydroxychloroquine Photoprotection Systemic steroids, Methotrexate Mepacrine Intravenous immunoglobulin Recalcitrant course	Hydroxychloroquine Photoprotection Pigmentation: stability achieved	Hydroxychloroquine Photoprotection Pigmentation: modest improvement

ANA: antinuclear antibodies, anti-RNP: anti ribonucleoprotein, Anti-dsDNA: anti-double-stranded DNA, Anti-sm: anti-Smith

The area of skin which showed maximum pigmentation was selected for skin biopsy. Histological examination was carried out in all cases and it revealed interface dermatitis with vacuolar degeneration of the basal cells, a dense lympho-mononuclear perivascular and perifollicular infiltrate with abundant melanophages in the papillary and

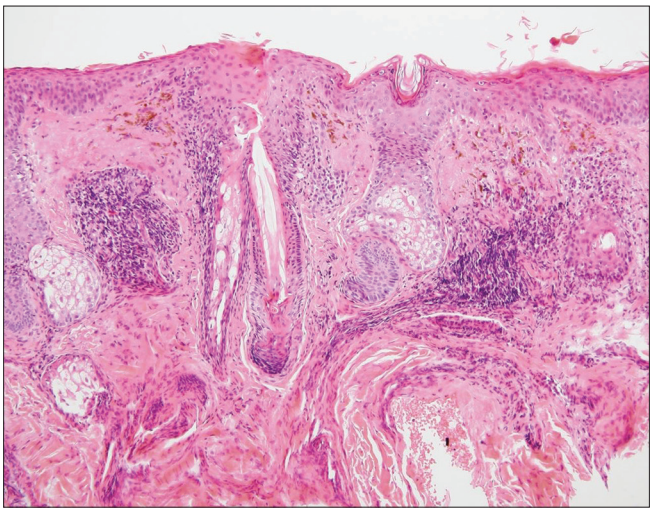

Figure 5: Patient 1: Histopathological examination showing vacuolar interface dermatitis with dense lympho-mononuclear perivascular and perifollicular infiltrate and melanin incontinence (H and E, ×40)

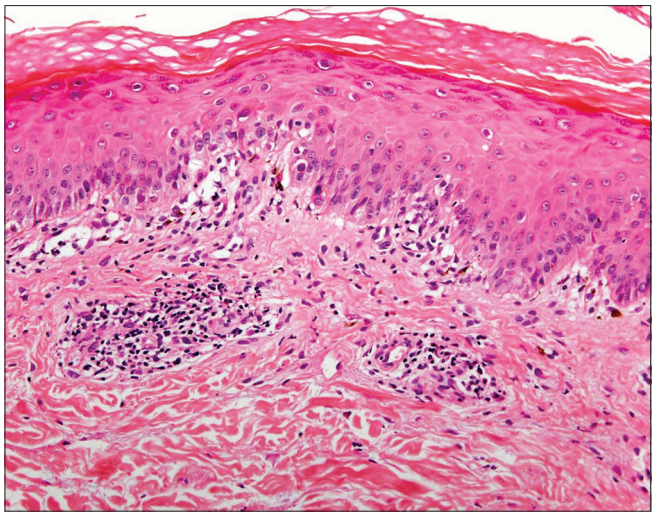

Figure 6: Patient 4: Histopathological examination showing focal interface dermatitis and superficial perivascular lymphocytic infiltrate in papillary dermis with melanin deposits (H and E, ×400)

high reticular dermis. The colloidal iron technique revealed mucin deposits in the dermis in all cases. This was compatible with pigmented lupus erythematosus [Figures 5 and 6]. More than one biopsy was needed to reach the diagnosis in three of the patients. Due to the nonavailability of the direct immunofluorescence technique at our hospital, this procedure was not performed. Each of the patient received hydroxychloroquine at a dose of 400 mg daily, together with strict photoprotection. Pigmentation on the forehead of patient no. 1 improved with hydroxychloroquine and strict photoprotection by wearing a hat. Pigmentation also improved in patient no. 3, but in rest of the patients pigmentation remained unchanged. Patient no. 4 had a recalcitrant clinical course which was controlled only with intravenous immunoglobulin infusions. She received 16 monthly cycles of intravenous immunoglobulin at a dose of 400 mg/kg/day for 5 consecutive days, achieving non-pregression of the facial pigmentation [Figures 3b and 3b].

Although not often recognized, cutaneous lupus erythematosus may present itself with diffuse facial pigmentation as the predominant disease manifestation. Boyd reported eleven patients who presented with solitary pigmented macules with histological features of discoid lupus erythematosus. These authors conclude that this peculiar presentation occurs in older patients and shows a good response to topical corticosteroids.[4] Later, Taddio *et al*. reported the case of a 14-year-old girl with diffuse facial pigmentation showing histological characteristics of cutaneous lupus erythematosus in the context of a first systemic disease outbreak which was resolved with specific treatment.[5]

Recently, Khullar *et al*. reported three patients with generalized brownish-grey facial pigmentation with a diagnosis of pigmented lupus erythematosus.[6]

Reaching this diagnosis can be tricky and other causes of post-inflammatory pigmentation such as Riehl's melanosis, lichen planus pigmentosus and drug-related pigmentation should be included in the differential diagnosis. It is especially relevant to exclude hydroxychloroquine-associated pigmentation since it can lead to discontinuation of a beneficial treatment. Histopathological examination is the key and would show granular deposits of yellow-brown pigment and no inflammation.

We believe our patients have a true form of cutaneous lupus erythematosus whose main dermatological manifestation is pigmentation. Our series suggests that this feature is more common among patients with medium-dark phototypes and being the predominant skin manifestation it could be a marker of cutaneous lupus activity in such patients. There is a great clinical variability in the degree and distribution of pigmentation. The most common pigmentation pattern is a spotted or reticular brown pigmentation on the forehead, temples and malar areas. However, sometimes the lesions have a scattered pattern. This heterogeneity makes the patient's clinical context and skin biopsy essential for diagnosis.

In conclusion, when we come across a patient with generalized facial pigmentation, pigmented lupus erythematosus should always be consdered and histological evaluation should be done to confirm this diagnosis. Dermatologists should be aware of this possibility since it can be the only feature of lupus erythematosus.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that

their names and initials will not be published and due efforts will be made to conceal their identity but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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