Spared Supravenous Pigmentation in a Patient of Systemic Sclerosis: A Sign of Progressive Disease with Systemic Involvement

Dear Editor,

Systemic sclerosis (SSc) is a chronic autoimmune disease with variable clinical presentations. The most characteristic feature of systemic sclerosis (SSc) is progressive fibrosis of the skin and other organs resulting from excessive deposition of the extracellular matrix.[1-3] Pigmentary changes such as salt-and-pepper pigmentation and diffuse generalized, and photoaccentuated hyperpigmentation are commonly associated with SSc.[1] These changes may help in early diagnosis and subsequent appropriation of the treatment.

We are discussing a case of SSc with myopathy, typical skin changes including salt-and-pepper pigmentation, and a rarely described pattern of spared pigmentation over superficial veins of the frontal scalp (serpentine supravenous hyperpigmentation; SSH).

A-27-year-old patient presented with one-year history of increasing tightening of the skin over the face, trunk, and distal extremities associated with progressive arthralgia, myalgia, and restricted movements of limbs. On examination, there were numerous, 1–3 mm depigmented macules interspersed within areas of normal pigmentation around the follicles suggestive of salt-and-pepper pigmentation over the forehead, nape of neck, and bony prominences including postauricular, supraclavicular, suprascapular over spine and bilateral shin [Figures 1 and 2]. There was a striking presence of retained pigmentation over the supra-trochlear and supraorbital veins and their immediate branches [Figure 3]. Patient revealed a history of photosensitivity, exertional dyspnea, and difficulty in swallowing (solid foods) for 5–6 months. Clinical history and features suggestive of puffy fingers, digital ulcerations, calcinosis cutis, periodontitis, gingivitis, microstomia, and Raynaud's phenomenon were absent. Patient was normotensive, and there was no history of chest pain, lightheadedness, chronic cough, and syncope.There was no familial history of a similar skin condition or history of chronic chemical exposure in this case. Laboratory investigations revealed normal white blood cell count, electrolytes, fasting blood sugar, creatinine, liver, and thyroid function tests. Erythrocyte sedimentation rate of 33 mm/hour (0–20 mm/hour), an elevated serum creatine kinase at 367 mcg/L (10–120 mcg/L), and positive antinuclear antibody (ANA) with coarse-speckled pattern and anti-topoisomerase I (anti-Scl-70) antibodies were detected. Histopathological findings from a 4-mm skin punch biopsy are depicted in Figure 4. Decreased esophageal motility was detected on barium swallow. Pulmonary function tests could not be performed as the patient was unable to hold breath. High-resolution computerized tomography revealed normal lung architecture except few small areas of scattered ground glass opacities in the peripheral aspect of bilateral lower lobes. Cardiac evaluation including electrocardiogram and 2-D echocardiography was normal. Routine and microscopic urine examination was normal. Based on the clinical feature and diagnostic workup, diffuse cutaneous systemic sclerosis (dSSc) with myopathy was considered the final diagnosis.The patient was started on monthly intravenous methylprednisolone pulse therapy along with daily oral cyclophosphamide. Intravenous immunoglobulin therapy was considered as an adjuvant due to rapidly progressing

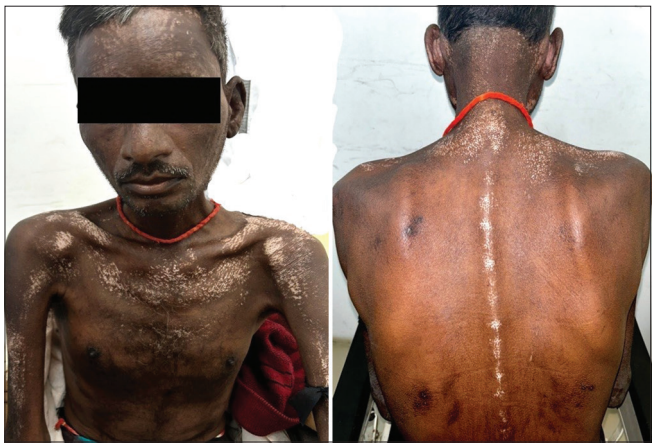

Figure 1: Numerous, 1–3 mm depigmented macules interspersed with areas of normal pigmentation around the follicles suggestive of salt-and-pepper pigmentation over the forehead, nape of neck, and bony prominences including supraclavicular, suprascapular areas, and over spine

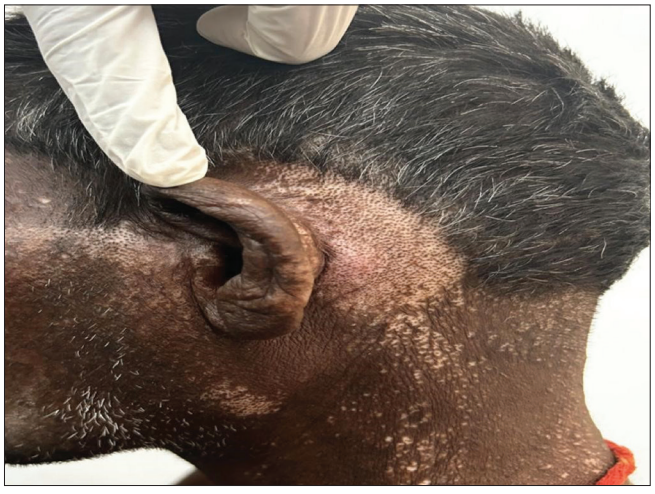

Figure 2:Classical salt-and-pepper pattern of dyspigmentation in postauricular area

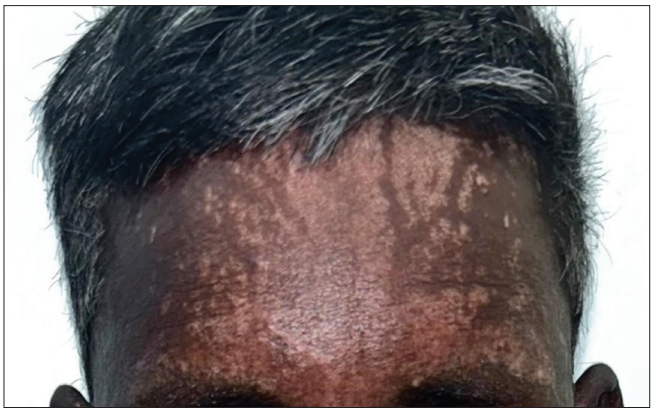

Figure 3: Streaky/serpentine supravenous spared pigmentation over the forehead

muscular symptoms and its corticosteroid-sparing ability but could not be given due to financial constraints. To ensure regular follow-up, the patient was adequately counseled about the nature/course of the disease and the possible therapy outcomes.

In most cases, diagnosis of sclerosis is straightforward aided by distinctive clinical features such as increasing tightening of skin (most perceptible over limbs and face), characteristic patterns of pigmentary alteration, and symptoms related to involvement of respiratory and gastrointestinal tract. Currently, there are five described patterns of pigmentary alteration in SSc, which are (a) diffuse generalized hyperpigmentation, similar to Addison's disease,[1-3] (b) focal depigmentation with perifollicular hyperpigmentation (salt-and-pepper pattern),[1-4] (c) localized hypo- and hyperpigmentation in localized sclerotic skin,[1-4] (d) streaky hyperpigmentation over blood vessels on a background of depigmentation on the legs and temporal scalp,[3,5-7] and (e) reticulate hyperpigmented scleroderma.[2,3] Some of these pigmentary changes have been considered as a surrogate tool for early diagnosis of SSc.[4]

Serpentine supravenous hyperpigmentation (SSH) on a background of depigmentation in patients of diffuse cutaneous SSc has been rarely described in literature. We could find a handful of case reports/series[6,7] describing such occurrences in SSc including two recent case reports.[5,7] Supraventine pigmentation secondary to intravenous infusion of certain chemotherapy agents including 5-fluorouracil, docetaxel, cyclophosphamide, bleomycin, and vinca alkaloids is different from SSH in SSc as SSH is a retained form of normal pigmentation whereas chemotherapeutic agents impart the pigmentation due to their deposition, direct toxicity, or inflammation.[5,7]

Preservation of normal pigment overlying the superficial veins within the areas of "salt-and-pepper" pigmentation is quite rare and has been attributed to the warm skin overlying superficial veins.[5,6] Jawitz *et al*.[6] had

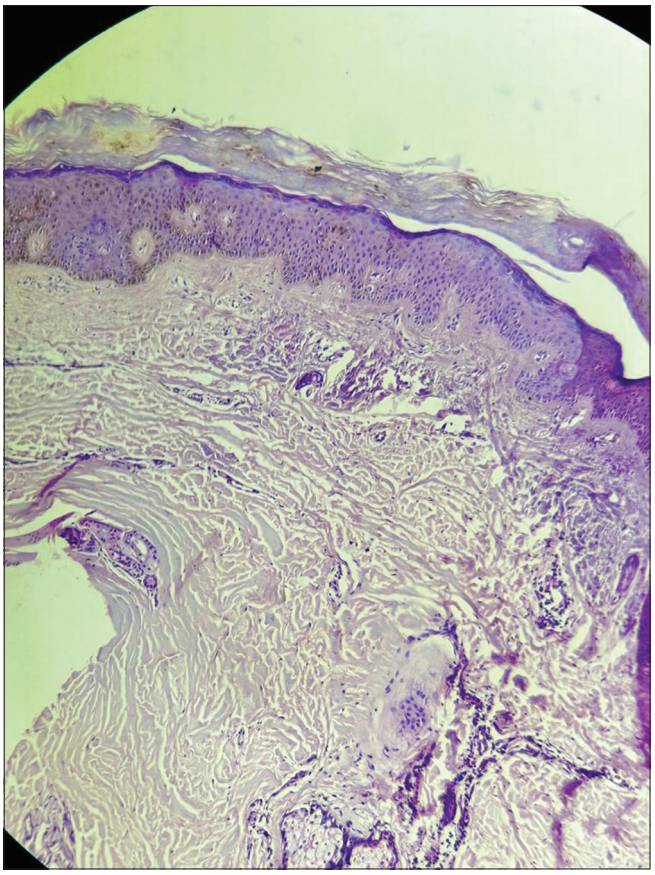

Figure 4: Section prepared from the dorsal aspect of right forearm showing hyperkeratosis and epidermal atrophy at some places along with increased basal cell melanization. Homegenization of collagen bundles, atrophic adnexa, and sparse mononuclear perivascular and periappendigeal infiltrate is seen. (H and E, 10x)

demonstrated a temperature gradient of 0.5–1.5°C between the supravenous areas as compared to the surrounding skin.[5,6] Possibility of thermal stimulus in SSH is further supported by perifollicular sparing of the pigment in the "salt-and-pepper pattern" as hair follicles possess a richer capillary network that warms the perifollicular skin and preserves melanogenesis leading to perifollicular pigment retention in patients of SSc.[8]

Muscular symptoms can be observed in both dSSc and dSSc-myositis overlap. However, dSSc-myositis overlap is also known to involve other organs such as heart, lungs, and gastrointestinal tract more frequently and more severely. Raynaud's phenomenon and digital ulcerations are also more common in dSSc-myositis overlap.[9] In this case, lack of cardiovascular involvement, absence of definitive features of interstitial lung disease on high-resolution computerized tomography, and lack of digital ischemic sequelae suggests the possible absence of overlap syndrome. However, it can't be completely ruled out as overlap syndromes are well known to develop a wide range of varying clinical features.

Interestingly, all the cases with SSH were finally diagnosed as progressive, diffuse cutaneous SSc. Association of SSH

with progressive SSc in all described cases [5-7] and also in our patient may serve as a prefatory note for considering SSH as a cutaneous sign of progressive diseases activity with a high possibility of already existing systemic involvement warranting an extensive systemic evaluation and appropriation of the treatments.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/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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