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Treatment With Mycophenolate Mofetil for Salt-and-Pepper Dyspigmentation Caused by Autoimmune Sclerosing Disease

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To the Editor: Systemic sclerosis (SSc), an autoimmune disease that leads to fibrosis of skin and internal organs, may present with pigmentary changes.[1] Vitiligo-like depigmentation with perifollicular pigment retention, or salt-and-pepper dyspigmentation (S&P), is classically associated with severe SSc.[1] Histopathology reveals that pigment alterations occur in areas of cutaneous sclerosis;[2] therefore, S&P can occur in other autoimmune sclerosing conditions including mixed connective tissue disease (MCTD) with scleroderma features.[3]

Unfortunately, such pigmentary changes are disproportionately seen in Black patients, and they are a leading cause of body image dissatisfaction.[4] Yet, SSc clinical studies often neglect studying S&P.[1] Herein, we report 3 African American patients with either SSc or MCTD with scleroderma features who suffered from S&P that responded to mycophenolate mofetil (MMF).

Patient 1

An African American woman in her 30s presented with SSc complicated by scleroderma renal crisis and Raynaud's phenomenon (RP) with digital ulceration. On examination, extensive skin tightening was noted on her face, trunk, and extremities, resulting in limited mobility of her upper extremities. S&P was observed in several areas of cutaneous sclerosis, including her upper back, chest, and dorsal hands (Figure 1A). Work-up revealed high-titer anti-nuclear antibody (ANA) (>1:10240, nucleolar pattern). She was started on

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MMF, titrated to 3 g/day. A year later, cutaneous sclerosis and range of motion improved dramatically, and S&P nearly resolved (Figure 1B).

Patient 2

An African American man in his 20s presented with a year of focal depigmentation. He denied RP but had digital pitting of his fingertips. On exam, S&P was present on his face, retroauricular and posterior scalp, dorsal hands, and scrotum (Figure 1C). He also had mild skin tightening of his hands and dorsal forearms. Work-up revealed high-titer ANA (>1:5120, nucleolar pattern). Soon after, skin tightening spread to his chest and thighs. He was diagnosed with SSc, and MMF 2g/day was initiated. Within 2 months, slight improvements in cutaneous sclerosis and dyspigmentation were observed. S&P improved approximately 50% in 6 months, nearly resolving after several years of MMF treatment (Figure 1D).

Patient 3

An African American woman in her 40s with MCTD with scleroderma features, complicated by cytopenias, perimyocarditis, and RP, presented with a year of dyspigmentation. Examination revealed S&P on her scalp, face, neck, chest, upper back, and upper arms (Figure 2A). Her chest, neck, and arms were shiny in appearance, consistent with sclerosis, and finger edema was noted. Work-up identified high-titer ANA (1:2560, speckled pattern) and ribonucleoprotein antibody. She was treated with MMF 2g/day, and S&P dramatically improved just 2 months later. Although MMF was eventually decreased to 1.5g/day due to leukopenia and anemia, the patient's S&P continued to improve over a year later (Figure 2B).

MMF has emerged as a treatment of choice for SSc, demonstrating efficacy for SSc-associated interstitial lung disease and cutaneous sclerosis.[1,5,6] It is thought to have anti-sclerosing effects by inhibiting TGF-β, fibroblast proliferation, and collagen deposition,[5] likely explaining its efficacy in MCTD with scleroderma features as well. Because S&P occurs in areas of cutaneous sclerosis,[2] treating underlying sclerosis would hypothetically improve overlying S&P. However, data is extremely limited regarding S&P treatment despite its known impact on quality of life.[4] Existing data includes a cohort of 9 SSc patients in which methotrexate improved mottled pigmentation by 25% in most subjects and one case report that suggested suplatast tosilate, an antiallergic Th2-suppressing drug, as potential therapy.[1]

Data supporting the efficacy of MMF in treating S&P in SSc and MCTD is lacking. In our cohort, all 3 patients experienced >75% improvement of S&P with MMF. Given the impact on quality of life in patients who suffer from S&P,[4] this observation supports an additional reason to consider MMF in patients with autoimmune sclerosing conditions.

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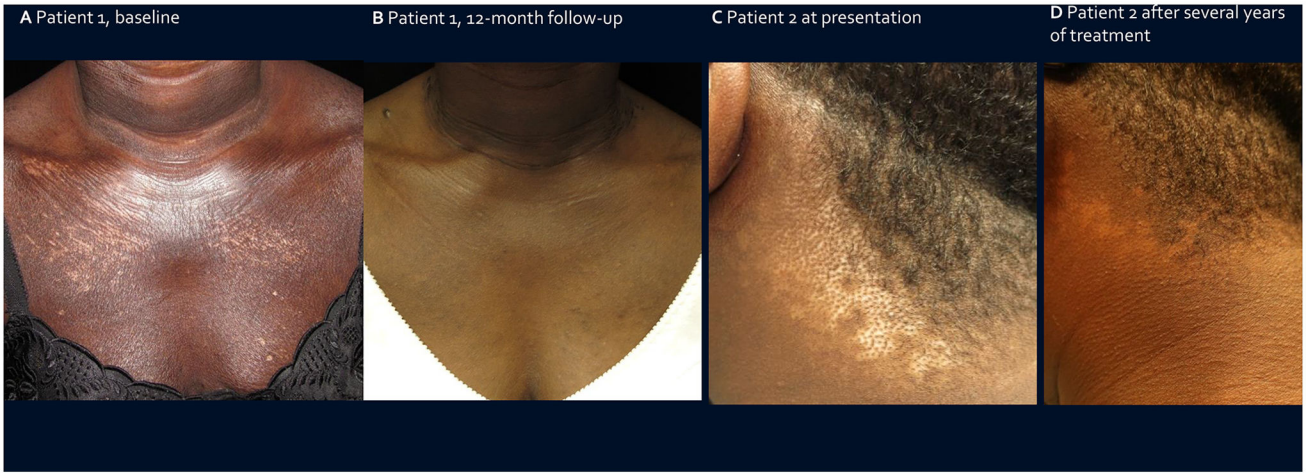

Figure 1.

A, Patient 1 noted prominent salt-and-pepper dyspigmentation on her upper back, chest, and hands at baseline. B, Patient 1 had noticeable improvement in dyspigmentation 2 months after treatment with mycophenolate mofetil, 3 grams, daily. At her follow-up visit in 12 months, she exhibited nearly complete resolution of dyspigmentation. C, Patient 2 presented with salt-and-pepper dyspigmentation on his face, retroauricular and posterior scalp, dorsal hands, and scrotum at baseline. D, Patient 2 had slight improvement in dyspigmentation just 2 months after receiving treatment with mycophenolate mofetil, approximately 50% improvement in 6 months, and near complete resolution several years into treatment.

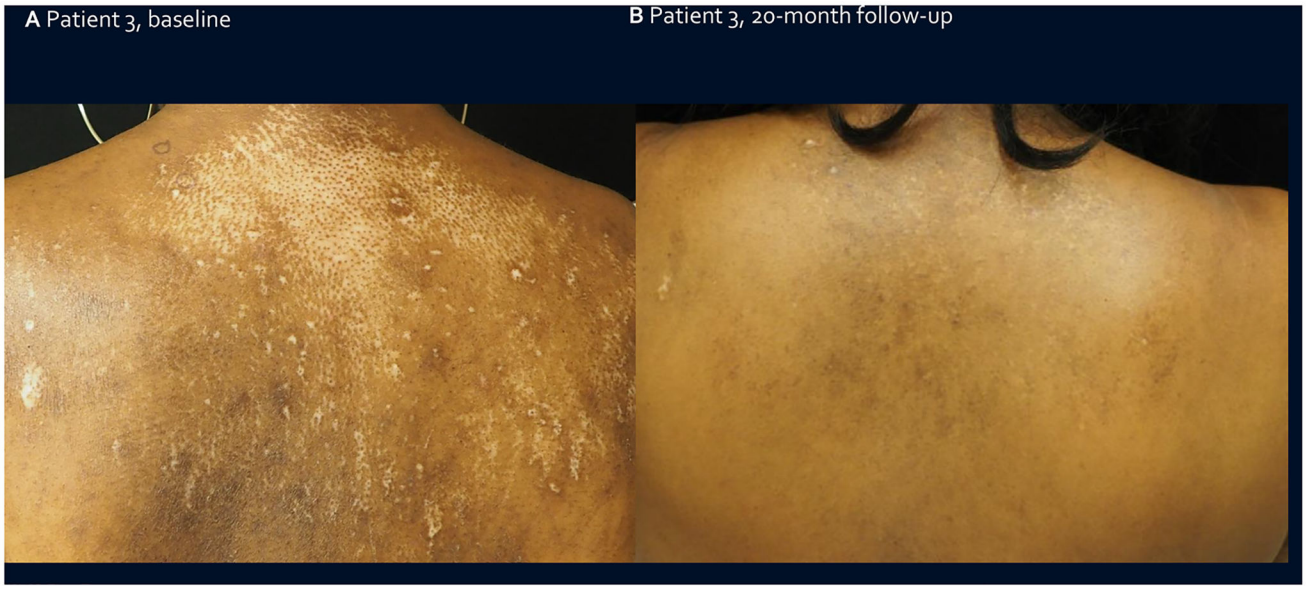

Figure 2.

A, Patient 3 noted salt-and-pepper dyspigmentation on her scalp, face, neck, chest, upper back, and upper arms at baseline. B, Patient 3 noted nearly full resolution of dyspigmentation at follow-up nearly 20 months after beginning treatment withmycophenolate mofetil.