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Case report

Sclerodermoid lesions in a patient with multiple transplants and porphyria cutanea tarda

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Abstract

Patients with chronic graft versus host disease may exhibit a range of sclerotic features. Herein we present a patient with confirmed porphyria cutanea tarda who subsequently developed chronic graft versus host disease.

Introduction

Chronic graft versus host disease (cGVHD) can present with a range of sclerotic features, from smooth, waxy and thickened skin to a morphea-like form featuring patchy areas of shiny skin with dyspigmentation and leather like consistency [1]. Porphyria cutanea tarda (PCT) also has a sclerotic form and classically affects photo-exposed areas, such as the back of the hands [2]. We describe a patient with a history of PCT and multiple transplants who presented with new disfiguring sclerotic plaques and ulcers over his face, scalp and arms. Although initial urine studies confirmed PCT, cGVHD was suspected given his transplant history. His immunosuppressive regimen was increased and the lesions improved. Given the photodistributed nature of the cGVHD lesions, we hypothesized that PCT acted as a photosensitizing co-stimulant for the development of sclerodermoid cGVHD in this patient. Distinguishing these two entities can be challenging and requires a high index of suspicion, lab work, and close follow-up.

Key words: Sclerodermoid, porphyria cutanea tarda, chronic graft versus host disease, ulcers

Case synopsis

A 50-year-old man presented with progressive skin tightening and ulceration on his face, ears, scalp, dorsal hands, and forearms. Although the lesions were fixed and limited to his hands for several years, three months prior to presentation, he began to have involvement of his face. He had a history of hepatitis C, complicated by cirrhosis and hepatorenal syndrome, for which he had a combined liver, renal, and pancreatic transplant ten years prior. The renal transplant failed two years ago, and he was then managed on hemodialysis. On evaluation, the patient reported a history of a blistering rash on his hands that appeared before his

transplants and later resolved. He denied fevers, diarrhea, or a family history of skin disorders. His medications included tacrolimus, prednisone, nifedipine, levothyroxine, intravenous iron, and sevelamer.

On exam, there were sclerotic, atrophic, dyspigmented plaques with several areas of hemorrhagic erosions affecting most of his face, ears, and scalp. Alopecia with loss of follicular ostia was noted on the scalp**.** Multiple irregular and crusted ulcers with surrounding atrophic plaques covered his dorsal hands and forearms (Figure 1A,1B). His fingernails were brittle and dystrophic with onycholysis. There was sparing of sun-protected areas and his trunk and lower extremities were clear. Given the photodistributed nature of the lesions, porphyria cutanea tarda (PCT) was suspected.

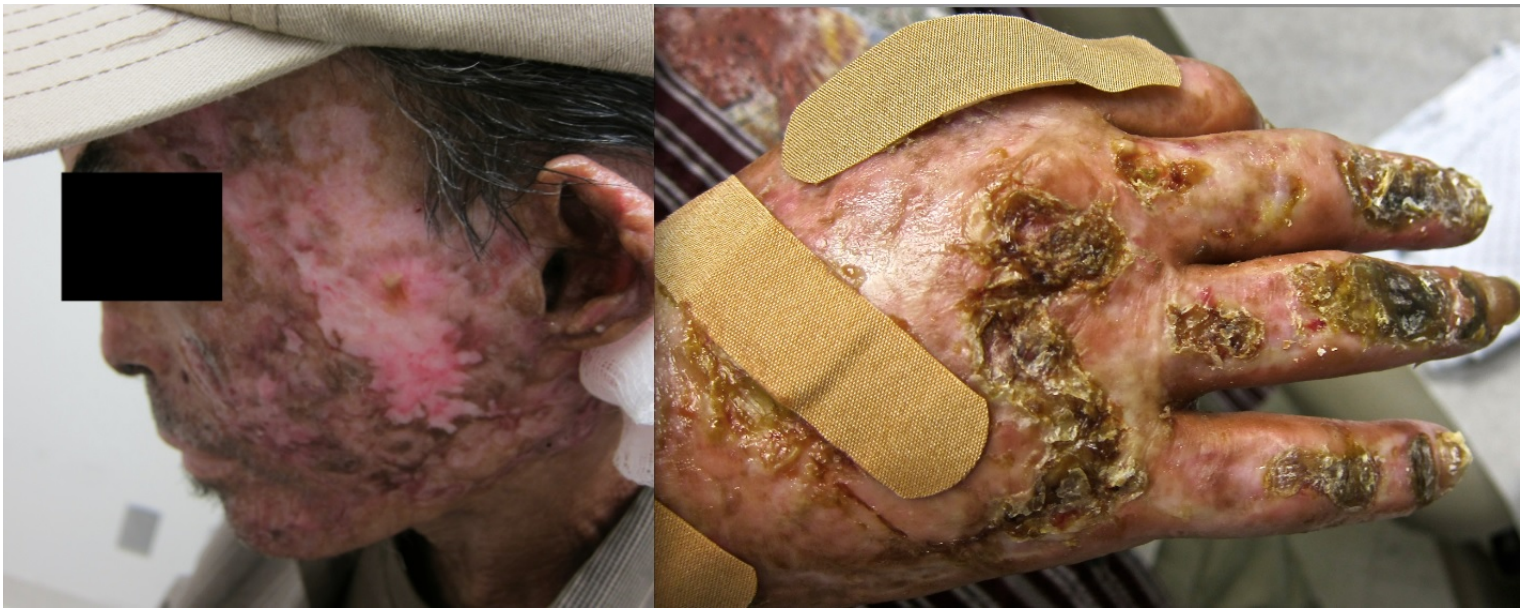

Figure 1. 1A:Sclerotic, atrophic, dyspigmented plaques overlying the face and ear (left) 1B: Multiple crusted ulcers with surrounding atrophic plaques covered his dorsal hands and forearms (right)

The biopsy from the left posterior auricular area showed hyperkeratosis with extensive full-thickness dermal sclerosis obliterating normal upper dermal architecture. There were sparse perivascular lymphoid infiltrates and occasional plasma cells, neutrophils, and eosinophils (Figure 2). Additionally, there was mild interface vacuolopathy with a few necrotic keratinocytes (Figure 3). Bullae and thickening of the basement membrane and vessels were not noted, and direct immunofluorescence (DIF) was negative. Although the histopathologic findings were consistent with the differential diagnoses of sclerodermoid graft-versus-host-disease (GVHD), sclerodermoid PCT, and nephrogenic systemic fibrosis (NSF), sclerodermoid GVHD was favored owing to the presence of interface dermatitis, one of the hallmark features of GVHD, which is not seen in NSF or PCT [3]. In addition, the lack of immunostaining with CD34 of the interstitial mesenchymal cells was not consistent with NSF [4]. PCT was also ruled out given the lack of subepidermal bullae, the absence of PAS positive thickening around blood vessels and negative DIF [3].

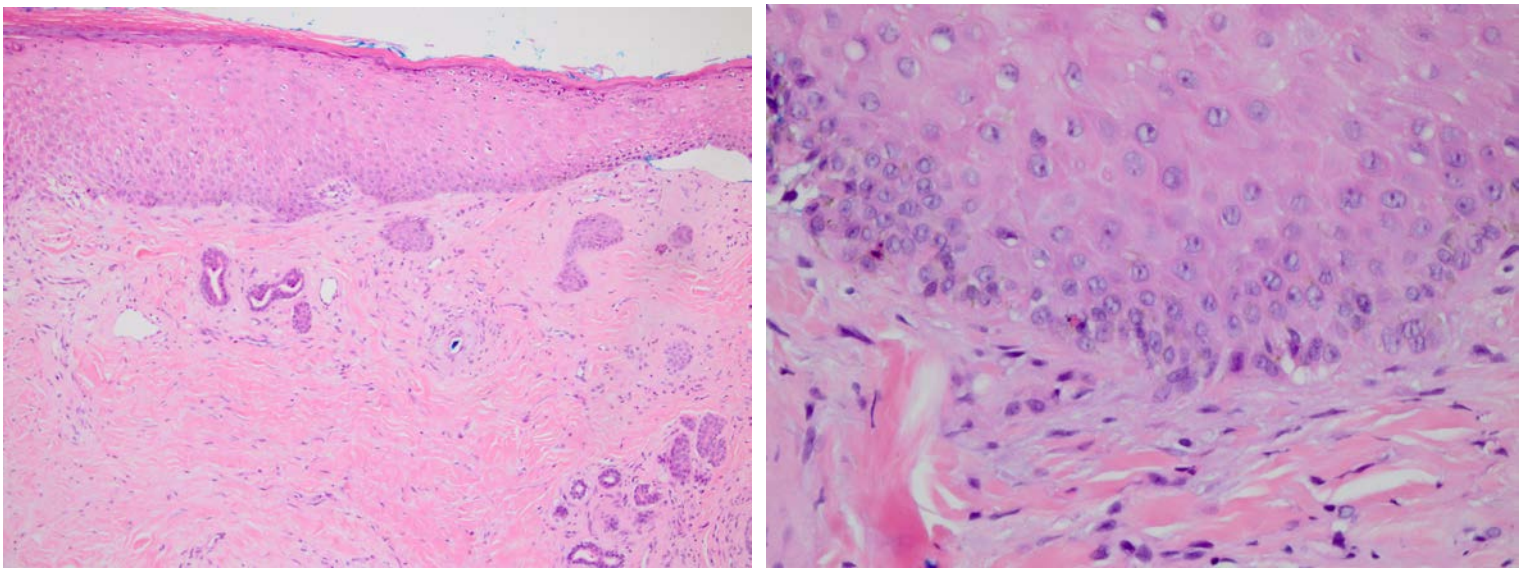

Figure 2. Biopsy of left posterior auricular area: Hyperkeratosis with extensive full-thickness dermal sclerosis and sparse perivascular lymphoid infiltrates. **Figure 3.** Biopsy of left posterior auricular area: Mild interface vacuolopathy with a few necrotic keratinocytes

Urine analysis revealed markedly elevated uroporphyrin (1389 mcg/L), hepta-carboxyl (1020 mcg/L), hexa-carboxyl (13mcg/L), penta-carboxyl (20mcg/L), and mildly elevated total whole blood porphyrins (147 mcg/dL) consistent with PCT. Further laboratory analysis revealed a mild normocytic anemia (hemoglobin 11.5 g/dL) and mildly elevated aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase. Antinuclear, double-stranded DNA, SCL-70, U1RNP, and other autoantibodies were unremarkable. Donor human leukocyte antigens were not detected in the patient's blood and a liver biopsy showed no evidence of rejection or graft-versus-host disease.

His immunosuppressive regimen was increased, iron supplementation was discontinued, strict photoprotection was emphasized, and diligent wound care was implemented. This intervention resulted in symptomatic and clinical improvement (Figure 4A,4B)

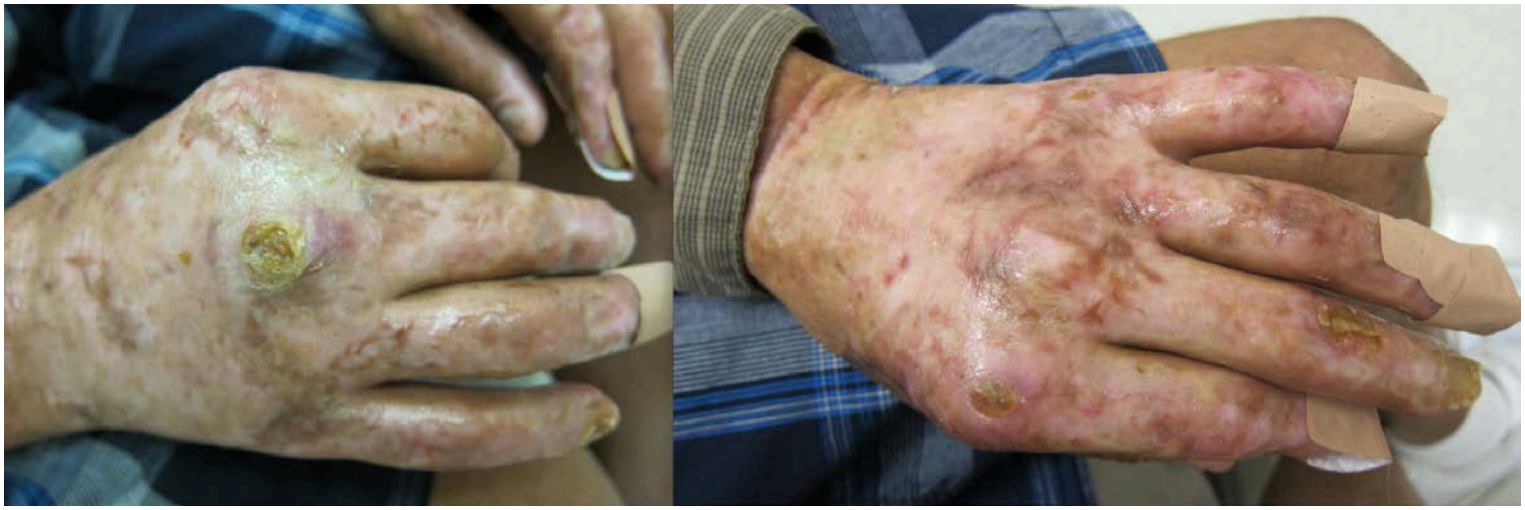

Figure 4. Crusted ulcer before (left) and after change in immunosuppressive regimen

Discussion

Sclerodermoid lesions in a patient with multiple transplants and laboratory evidence of PCT present a diagnostic dilemma. GVHD after solid organ transplant is uncommon, with an estimated incidence of one to two percent after liver transplantation [5]. The diagnosis of cutaneous chronic GVHD (cGVHD) requires at least one diagnostic or distinctive manifestation plus biopsy, laboratory testing, or imaging confirmation in the same or another organ [6]. The diagnostic mucocutaneous manifestations are lichen planus-like lesions, lichen sclerosus-like lesions, morphea-like lesions, poikiloderma, lichenoid-type features, oral hyperkeratotic plaques, and restriction of mouth opening owing to sclerosis. Distinctive manifestations include depigmentation, nail changes (dystrophy, longitudinal ridging, splitting or brittle features, pterygium unguis, onycholysis, nail loss), scalp involvement (scarring and non-scarring alopecia, papulosquamous lesions, scaling), and oral lesions (mucoceles, oral mucosal atrophy, ulcers, pseudomembranes, xerostomia). Our patient had evidence of sclerotic lesions, a diagnostic manifestation, and depigmentation, scarring alopecia, nail dystrophy--all distinctive manifestations. Additionally, cGVHD associated ulcers of the limbs, similar to those in our patient, has been reported [7]. Furthermore, the patient's skin biopsy demonstrated features more consistent with sclerodermoid cGVHD over NSF and PCT. In addition, the elevated uroporphyrin and remote history of a blistering rash on his hands also supported the diagnosis of acquired PCT in the setting of the known associated risk factors of hepatitis C and end stage renal disease [8,9].

Given the unusual photo-distributed nature of the patient's cGVHD lesions and the long latency period between his organ transplantions and cGVHD manifestations, we postulated that PCT acted as a photosensitizing co-stimulant for the development of sclerodermoid cGVHD in this patient. Although a sclerodermoid form of PCT exists [2], the severity of this patient's clinical presentation and the biopsy findings are consistent with sclerodermoid cGVHD. The patient was successfully treated for sclerodermoid cGVHD by increasing his immunosuppressive regimen, resulting in improvement at subsequent examination.

This is a unique patient with a history of PCT who presented with delayed sclerodermoid cGVHD following solid organ transplant. Though the patient had a known history of PCT, it was critical to consider other diseases also associated with sclerodermoid lesions. This led to his second and critical diagnosis of cGVHD, for which he was treated with subsequent improvement. Further studies are needed to investigate the interplay between these two clinically distinct entities.

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