

BRIEF ARTICLES

Indurated and Puckered Skin on the Lateral Thighs

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INTRODUCTION

Chronic graft-versus-host disease (cGVHD) is an immune-mediated reaction and a major complication following allogeneic hematopoietic stem cell transplantation (HSCT). Cutaneous manifestations are the most common and often the first sign of GVHD. The clinical presentation can vary widely with pruritus, rash, pain, dyspigmentation and fibrotic or sclerodermatous lesions.¹ cGVHD can lead to long-term complications such as cosmetic and functional disorders. Moreover, persistent cutaneous lesions can also have a significant impact on morbidity and quality of life.² Here we describe a case of a delayed presentation of sclerodermatous cGVHD.

CASE PRESENTATION

A Caucasian man in his 60s presented with asymptomatic, bilateral indurated areas on his lateral thighs. He had a past medical history of leukemia, previously treated with full body radiation and bone marrow transplantation more than 20 years ago. A few years ago, the patient first noticed that he had small hard spots about the size of a silver dollar in symmetrical locations on the

lateral side of both upper thighs. Over the subsequent years, he became concerned that the spots were growing and expanding distally, but remained otherwise asymptomatic. He denied any history of trauma or surgery in the area. Physical examination revealed bilateral puckered skin changes and linear depressions which were more prevalent on the right lateral thigh (Figure, 1 and 2). A punch biopsy was performed on the right lateral thigh.

Figure 1. Sclerodermatous cGVHD. The right thigh of the patient with puckered skin and linear depressions.



Histological assessment revealed fascial thickening and extensive dermal sclerosis. There was general loss of the peri-adnexal

fat. The pathologist also noted that there was minimal inflammation (Figure, 3 and 4). Given the clinical context, a diagnosis of sclerodermatous chronic cutaneous graft-versus-host disease was made. The patient was notified and expressed concern about the rapidly expanding hardened areas. We discussed the available treatment options including oral corticosteroids and immunosuppressants. The patient decided to observe and notify us if it became worse or symptomatic.

Figure 2. Sclerodermatous cGVHD. The left thigh of the patient with less evident puckering.



Figure 3. Epidermal thinning with pan-dermal sclerosis (H&E, 2x)

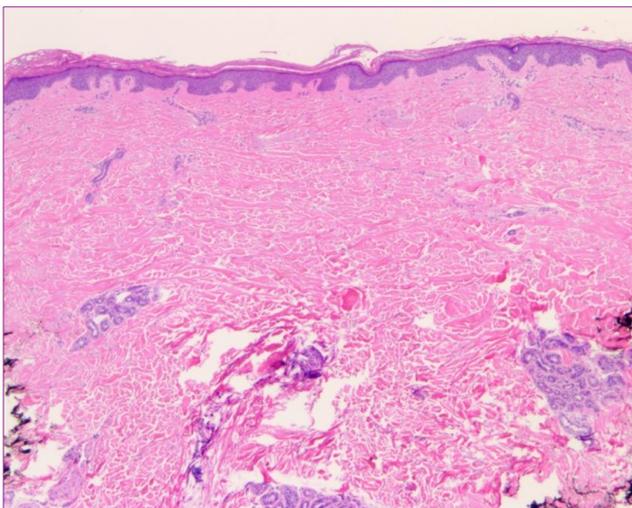
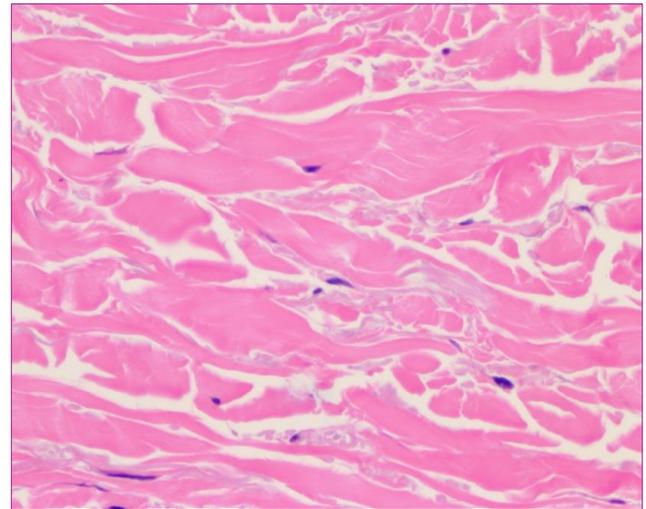


Figure 4. Thickened, homogenized collagen bundles (H&E, 20x)



DISCUSSION

Cutaneous manifestations are the most common and are often the presenting sign of graft-versus-host disease (GVHD).³ Sclerodermatous GVHD is a rare form of chronic GVHD with a prevalence of approximately 3% in patients receiving allogeneic bone marrow transplantation.⁴ Sclerodermatous GVHD may be generalized or localized. Shuman et al⁵ described the generalized disease as following a biphasic course, with a generalized erythematous rash preceding poikiloderma with sclerotic hidebound skin. Dermal induration with no previous lichenoid phase was described in those with localized disease. Similar to Peñas et al⁶, we believe that sclerodermatous disease occurred independently of a lichenoid phase in this patient.

Sclerodermatous GVHD has been characterized by cutaneous features such as sclerosis, atrophy, contractures, ulceration, hair loss and nail changes (dystrophy, atrophy and koilonychia).³ Sclerotic eruptions can be characterized by

fibrosis, which may be superficial and localized, resembling lichen sclerosis and morphea, or deep and disseminated, mimicking systemic scleroderma. In a case series of 10 patients, White et al⁴ described features of dermal nodules, atrophic white plaques, hyperpigmentation and tethered skin with dimpling. However, a feature that was common among all of the patients was indurated plaques. Of note, 90% of the patients had plaques on the arms and legs. Additional symptoms such as joint limitations and contractures may develop and should be monitored to allow for early intervention.

Because the sclerodermatous form of chronic GVHD is rare, there is no gold standard for treatment, and little information exists regarding successful treatment. Thirty-two patients with sclerodermatous GVHD were treated with retinoids as an adjunct to standard immunosuppressive therapy such as corticosteroids and ciclosporin. Etretinate 1 mg/kg daily was added to the treatment regimen. 74% of patients had some clinical improvement, including 2 with near clearance.⁷ Treatment of sclerodermatous GVHD with ultraviolet A1 (340– 400 nm) without psoralen with standard immunosuppression was shown to achieve a complete response in 3 of 5 patients and a partial response in 2 patients.⁸ However, relapse is common with this therapy and maintenance treatment is needed. In a series of 12 patients with sclerodermatous GVHD alone or with concomitant lichenoid change, all responded favorably to extracorporeal photopheresis. Nine of 12 patients achieved a complete response while 3 made a partial response.⁹ Finally, the British Society for Bone Marrow Transplantation recommends physiotherapy and massage of potent topical steroids and calcineurin inhibitors to soften the skin.¹⁰

Sclerodermatous GVHD must be differentiated from other disorders known to be associated with bone marrow

transplantation, such as eosinophilic fasciitis (EF). While the initial phases may be indistinguishable from early sclerodermatous skin changes, the irregular, woody peau d'orange texture of EF is distinct from the morphea-like plaques or atrophic and shiny surface seen in those with sclerodermatous GVHD.¹¹ Furthermore, Sclerodermatous GVHD may be differentiated from morphea based on the absence of early erythematous lesions as well as a yellow-white sclerotic plaque with erythematous borders, or the aptly named "lilac-ring".¹²

CONCLUSION

This case illustrates a rare variant of chronic GVHD with a delayed presentation. Little information exists in the literature regarding prognosis and treatment and therefore highlights the need for additional studies in cutaneous GVHD.

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