Trichodysplasia spinulosa successfully treated with adapalene 0.1% gel and oral valganciclovir in a renal transplant recipient

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INTRODUCTION

Trichodysplasia spinulosa (TS) is a rare condition primarily affecting recipients of solid organ transplants who are receiving immunosuppressive medication.[1,2] Although reducing immunosuppression is often recommended, there is no criterion standard for treatment. We present a case of TS in a kidney transplant recipient that was successfully treated with adapalene 0.1% gel and oral valganciclovir.

Abbreviations used:

TLR: Toll-like receptor
TS: trichodysplasia spinulosa

CASE REPORT

A 25-year-old woman presented to the dermatology clinic with pruritic facial lesions progressively increasing in extent over a 6-month period. Treatment with oral antibiotics for presumed perioral dermatitis 2 months before presentation had failed. Her past medical history was significant for mesangial IgG glomerulonephritis causing end-stage renal disease, ultimately requiring living donor kidney transplant 9 years prior. She developed a late acute antibody-mediated rejection leading to right-sided allograft nephrectomy and, thereafter, initiation of hemodialysis (1 month before presentation to the dermatology clinic). Although the patient was receiving active immunosuppression (mycophenolic acid, everolimus, and prednisone) at the time of rash onset, these medications were discontinued at the time of allograft explant, with the exception of prednisone 5 mg daily. There was patient-reported transient improvement in the rash a few days after nephrectomy, but it was followed by subsequent progression and worsening, thus prompting the referral to the dermatology clinic.

Skin examination was notable for numerous coalescing skin-colored to erythematous papules with follicular white spicules diffusely on the nose, extending onto the glabella, cheeks, and eyelids, as well as the tragi and helices of ears (Fig 1). Two 3-mm punch biopsies of the bilateral nasal ala were performed. Histologic examination showed expansion of dystrophic follicular inner root sheath cells and the presence of enlarged trichohyalin cytoplasmic granules with centrally necrotic debris, supporting a diagnosis of TS. Immunohistochemical staining results for TS-associated polyomavirus were negative; however, the histopathology was pathognomonic. DNA polymerase chain reaction and gene sequencing were not performed.

The patient was initially treated with adapalene 0.1% gel nightly, resulting in moderate improvement in the rash in less than 2 weeks. She was referred to an infectious disease specialist, who started oral valganciclovir 450 mg 3 days per week after hemodialysis. At her follow-up visit, 7 weeks after initial presentation, the patient was noted to have significant resolution of her lesions on a combination regimen of topical retinoid and oral antiviral therapy

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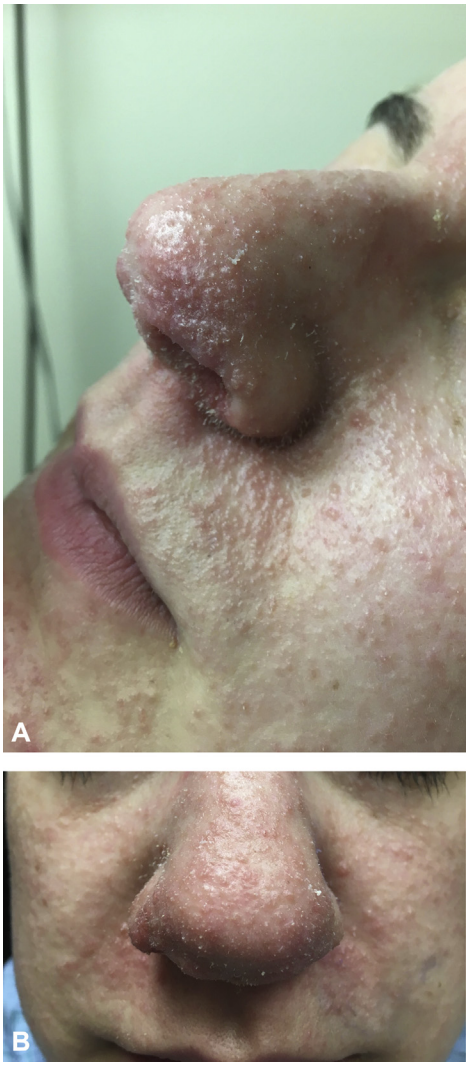

Fig 1. Initial clinical presentation. Skin-colored to erythematous papules with follicular white spicules are seen diffusely, on the (**A**) nose and (**B**) bilateral cheeks.

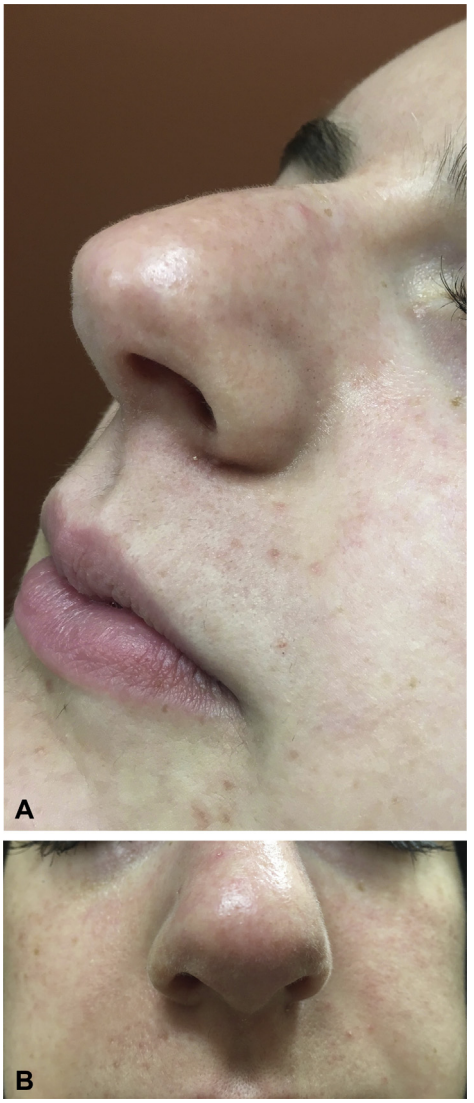

Fig 2. Resolution of rash after 7 weeks of treatment. Previously involved areas including the (**A**) nose and (**B**) cheeks were nearly resolved.

(Fig 2). Of note, the dose of valganciclovir was decreased to 450 mg twice weekly due to decreasing white blood cell count. She underwent living donor kidney transplant 3 months later with thymoglobulin induction and continued receiving valganciclovir, with close monitoring for recurrence. Five months after her second kidney transplant, the patient is receiving active immunosuppression, yet her skin remains clear.

DISCUSSION

TS is a rare condition primarily found in recipients of solid organ transplants (notably renal transplants) receiving immunosuppressive medication or patients undergoing chemotherapy for hematologic malignancies.[1,2] The central face and ears are classically involved, with characteristic folliculocentric, keratotic white spicules, which result from the accumulation of trichohyalin in the inner root sheath of affected hair follicles.[3] A novel polyomavirus—now known as *TS-associated polyomavirus* —was identified in association with the condition in 1999, although viral particles have not been detected in all cases.[2]

There is no criterion-standard treatment for TS. Dosage reduction of immunosuppressive agents is typically recommended, and resolution of the lesions has occurred with this alone.[4] Our patient reported that her skin lesions transiently improved for a few days after nephrectomy (and, therefore, with the reduction of immunosuppression), although they ultimately worsened for inexplicable

reasons. It could be speculated that her skin lesions arose in the setting of the acute antibody-mediated rejection of her allograft, and, thus, the nephrectomy resulted in transient improvement. In other cases, clinical improvement has been reported with antiviral therapy such as topical cidofovir and oral valganciclovir, which may suggest viral reactivation as a significant contributor to the development of TS. However, reducing immunosuppression is often not feasible in organ transplant recipients, and oral valganciclovir can cause further bone marrow suppression.[4,5] Therapy with vitamin A derivatives has been implemented with mixed results.[3] This could be attributed to the demonstrated activation of Toll-like receptor (TLR) 2 and TLR4 as part of the innate immune response against polyomaviruses and the opposing downregulation of TLR-2 by vitamin A derivatives.[3,6]

Our case is particularly unique given the progression of the rash despite efforts to minimize immunosuppression, further highlighting the unknown mechanism and exact role of polyomavirus in the genesis of TS. Furthermore, the notable improvement in the rash with topical adapalene 0.1% gel monotherapy preceding the systemic antiviral therapy lends support to reconsideration of the potential of vitamin A derivatives to treat this rare condition, especially in patients without detectable polyomavirus.

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