

Photodynamic therapy for the treatment of trichodysplasia spinulosa in an Asian renal transplant recipient: A case report and review of literature



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Key words: immunosuppression; photodynamic therapy; polyomavirus; trichodysplasia spinulosa.

INTRODUCTION

Trichodysplasia spinulosa (TS) has been reported in immunocompromised patients and is characterized by folliculocentric papules and keratin spicules. TS has been reported to be associated with TS-associated polyomavirus, although the exact causal mechanism remains unclear.¹ Few reports exist in the current literature, with limited evidence for treatment options. We report a case of TS in a 42-year-old Chinese woman after a renal transplant, with a good response to topical methyl aminolevulinate daylight photodynamic therapy (PDT).

CASE REPORT

A 42-year-old Chinese woman with a history of end-stage renal disease secondary to chronic glomerulonephritis underwent a deceased-donor renal transplant and subsequently received prednisolone 5 mg once daily, mycophenolate mofetil 500 mg twice daily, and tacrolimus 11 mg daily as long-term immunosuppressants. She presented to the outpatient dermatology clinic with multiple skin-colored spiculated papules (Fig 1) clustered on her face, neck, and upper portion of the trunk 7 months post the transplant. Fine white hair was seen embedded among these papules. She also reported eyebrow alopecia.

Dermoscopy (third-generation DermLite 4) showed clusters of homogenous pink circles and

Abbreviations used:

PDT: photodynamic therapy
sOTR: solid organ transplant recipients
TS: trichodysplasia spinulosa

fine white hair shafts (Fig 2). Skin biopsy of a papule on the right side of the philtrum showed markedly distended follicles (Fig 3). There were a few layers of small basophilic oval germinative cells at the base of the follicles, with overlying sheets of larger eosinophilic cells containing large purplish granules, resembling inner root sheath cells. Simian virus 40 immunostaining showed nuclear positivity in some of the inner root sheath-like cells (Fig 4). The clinical-pathologic findings supported our diagnosis of TS.

The patient was started on oral valganciclovir 450 mg daily, followed by tapering of tacrolimus to 2.5 mg daily. Mycophenolate mofetil was switched to mycophenolic acid 180 mg twice daily, with no improvement. Topical tretinoin gel (adapalene) and imiquimod gel 5% applied over few weeks did not result in any response. She was subsequently prescribed topical methyl aminolevulinate daylight PDT for the lesions on her face. After 2 sessions of daylight PDT (1 week apart), there was a significant reduction of the erythematous papules and keratotic white spicules on her face (Fig 5).

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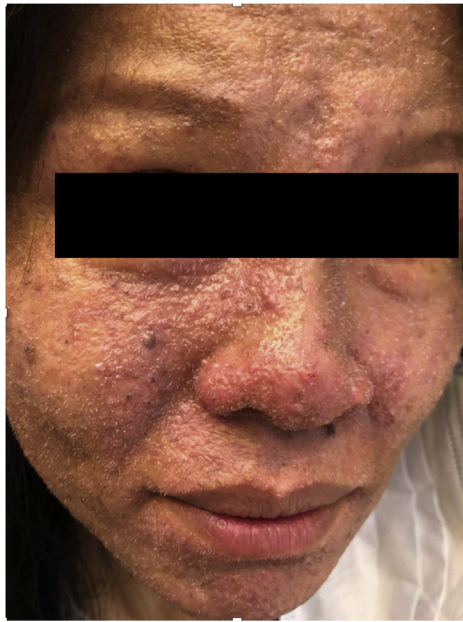


Fig 1. Facial profile showing spiculated follicular papules before PDT treatment. *PDT*, Photodynamic therapy.



Fig 2. Dermoscopy showed clusters of homogenous pink circles and fine white hair shafts.

DISCUSSION

TS was first described by Haycox et al² in 1999 as being characterized by papules that are spiculated and folliculocentric. These lesions are usually found on the face but can sometimes involve the trunk and extremities. As TS usually occurs in immunocompromised individuals, it is postulated to be related to immunosuppression, which is used in solid organ transplant recipients (sOTR).³ TS diagnosis is confirmed by typical skin findings, like those observed in our patient, as well as histologic features of enlarged trichohyalin granules and follicular inner root sheath cell proliferation. TS is postulated to be viral in etiology (typically polyomavirus), and the virus was named TS-associated polyomavirus.⁴

The absence of cases in immunocompetent individuals⁵ suggests that a robust immune system

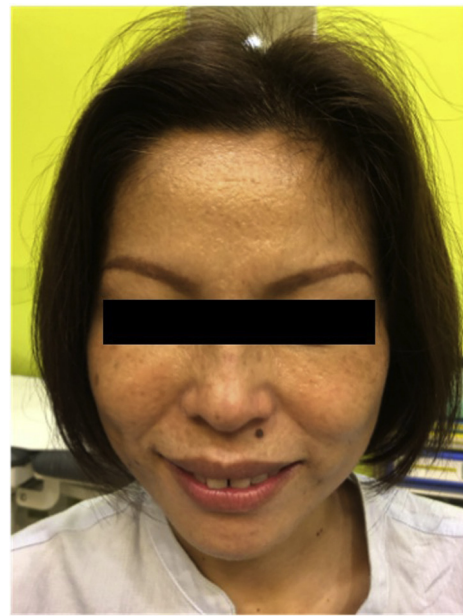


Fig 3. Facial profile showing reduction in spiculated follicular papules after PDT treatment. *PDT*, Photodynamic therapy.

prevents TS formation. Furthermore, some patients experience improvement in TS lesions after cessation of chemotherapy.⁶

We have summarized 30 cases^{2-4,6-29} reported in the literature (Table I), majority of which were described in patients undergoing sOTR, especially renal transplant recipients. The mean age of patients reported in the literature was 26 years, with an age range of 5-70 years. Majority of the TS cases reported in the literature predominantly involved the face, with a predilection for the nose and nasolabial region. The exact mechanism of the development of TS in the immunosuppressed population remains unknown. Immunosuppressive medication (mycophenolate mofetil, tacrolimus, and systemic steroids) associated with TS development are rarely seen in conditions other than sOTR or hematologic malignancies.¹⁰

Various treatments reported notably with topical cidofovir⁴ and oral valganciclovir¹⁰ have shown promising results. The treatments that have been tried include retinoids, imiquimod, antibacterials, as well as steroids. Among the treatments listed above, only topical retinoids have been reported to be effective in some patients. The exact mechanism of retinoids in TS remains unknown.

Topical methyl aminolevulinate PDT is effective for the treatment of acne vulgaris and viral warts³⁰ and is safe for use in sOTR.³¹ We postulated that the effect of PDT in TS depends on preferential uptake of photosensitive porphyrins by sebaceous glands and

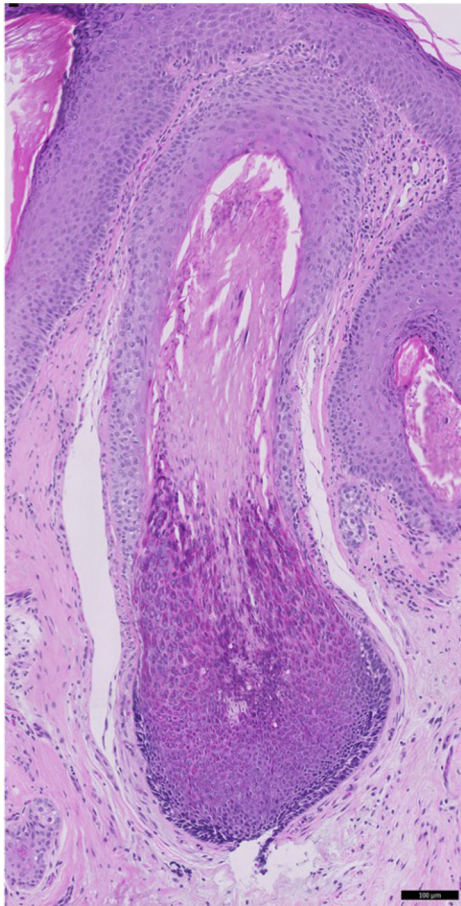


Fig 4. Histology showed a few layers of small basophilic oval germinative cells at the base of the distended hair follicles, with overlying sheets of eosinophilic cells containing large purplish granules, resembling inner root sheath cells. (Hematoxylin-eosin stain; original magnification: $\times 10$)

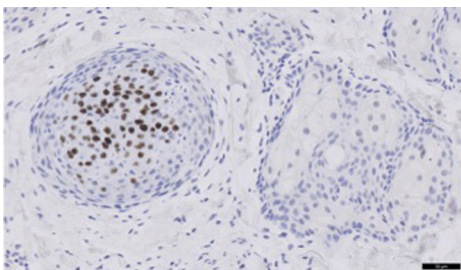


Fig 5. SV40 immunostain showed nuclear positivity in some of the inner root sheath-like cells (TSV stain; original magnification: $\times 20$). SV40, Simian virus 40; TSV, trichodysplasia spinulosa-associated polyomavirus.

their subsequent destruction, similar to that in acne vulgaris.³² We chose daylight PDT instead of conventional PDT because it is less painful, and our patient had extensive lesions on her face, neck, and limbs.

Table 1. Summary of cases reported in the literature

Case	Patient demographics	Medical history	Immunosuppressive agents	Duration of immunosuppression before onset of eruption (months)	Location of rash	Viral testing	Treatment
Benoit et al ⁷	5-year-old boy, Caucasian	Cardiac transplant	Cyclophosphamide, rituximab, intravenous immunoglobulin, tacrolimus, prednisone	12	Trunk, central portion of the face, and proximal aspect of the thighs	Done (viral cytopathic effect on histology)	No improvement with cidofovir cream 3% but significant improvement with systemic valganciclovir

Borgogna et al ⁸	7-year-old boy, Italian/Moroccan	Renal transplant x2	MMF, tacrolimus, prednisolone	24	Face, neck, back, and extremities	Done (viral DNA)	Tailing of immunosuppressants for viremia, unsure of the effect on skin
Coogle et al ⁹	11-year-old boy, Caucasian	Renal transplant	MMF, tacrolimus, prednisolone	14	Face, arms, and upper portion of the legs	Urine screen for BK PCR positive	Cidofovir cream 1% for 1 month and tailing of immunosuppression, with improvement and complete resolution in 7 months
Decrescenzo et al ¹	35-year-old man, race not mentioned	Renal transplant	Tacrolimus, MMF	6	Face, trunk, arms, and ears. Alopecia of the eyebrows and eyelashes	Not done	Slow taper of immunosuppression, with marked improvement and complete regrowth at 2 years
Haycox et al ²	44-year-old man, Caucasian	Renal-pancreatic transplant	Tacrolimus, azathioprine, prednisone	29	Nose, ears, and forehead. Alopecia of the eyebrow, eyelash, and scalp	(EMPCR, Papovaviridae family virus)	NA
Kirchhof et al ¹⁰	Woman, Caucasian	Renal transplant	Prednisone, tacrolimus, and mycophenolate mofetil	11	Face, ears, arms, legs, thighs, and back, sparing the lips. Diffuse hair loss/scalp thinning	Not done	Oral valganciclovir 900 mg BID, with 90% resolution

Continued

Table I. Cont'd

Case	Patient demographics	Medical history	Immuno-suppressive agents	Duration of immuno-suppression before onset of eruption (months)	Location of rash	Viral testing	Treatment
Laroche et al ¹¹	42-year-old woman, Caucasian	Renal transplant	Prednisone, tacrolimus, and mycophenolate mofetil	8	Face, ears, and madarosis of the eyebrows	Done but absent	No response to topical acyclovir. Satisfying response to topical retinoids
Lee et al ¹²	49-year-old woman, Caucasian	Renal transplant	Tacrolimus, mycophenolate mofetil, and prednisolone	11	Nasofacial sulcus involving the nose, forehead, cheeks, and chin	Done (PCR from biopsy-positive TSV for VP1, VP2, and VP3)	0.05% tretinoin and marked improvement with oral valganciclovir at 900 mg (given for 20 weeks)
Matthew et al ¹³	7-year-old girl, Hispanic	Pre-B ALL	Chemotherapy regime not mentioned	Not mentioned	Central portion of the face, ears, extremities, and trunk	Done (EM showed viral particles)	Topical steroids for symptomatic relief, child expired after 1 month
Osswald et al ¹⁴	68-year-old man, Caucasian	Recurrent NHL	Fludarabine, rituximab	Not mentioned	Eyebrows, glabella, nose, chin, and ears. Progressive alopecia of these areas	Done (EM showed viral particles)	Marked improvement with cidofovir cream 1%
Sadler et al ¹⁵	6-year-old boy, Caucasian	ALL (T-cell)	Cyclophosphamide, vincristine, and prednisolone	24	Trunk, face, and limbs. Alopecia over the eyebrows	Done (EM showed viral particles)	No effect with topical salicylic acid, ammonium lactate, tretinoin, and oral acitretin. Regressed with completion of chemotherapy

Sadler et al ¹⁵	8-year-old boy, Caucasian	ALL (T-cell)	Vincristine, mercaptopurine, and methotrexate	24	Face, trunk, and limbs. Mild alopecia over the eyebrows	Done (EM did not identify viral particles)	Resolved spontaneously
Sperling et al ¹⁶	13-year-old girl, race not mentioned	Renal transplant	Mycophenolate mofetil, prednisone, and tacrolimus	9	Nose, malar region, glabella, and chin. Almost total hair loss over the eyebrows and eyelashes, sparing scalp	Done (EM showed viral particles)	Minimal improvement with topical imiquimod, slow improvement with 3% topical cidofovir
van der Meijden et al ⁴	15-year-old boy, Caucasian	Heart transplant	Tacrolimus, mycophenolate mofetil, and methylprednisolone	12	Eyebrows, nose, ears, malar region, and forehead. Loss of eyebrow hair and eyelashes	Done (TSV polyomavirus amplification)	topical cidofovir BID, with gradual improvement
Wanat et al ¹⁷	57-year old woman, Caucasian	CLL	Rituximab, cyclophosphamide, and cytarabine	6	Nose, forehead, cheeks, chin, arms, thighs, chest, neck, and ears. Nonscarring alopecia and madarosis of the eyebrows	Done (Immunohistochemical analysis of polyomavirus)	Topical cimetidine, imiquimod, salicylic acid, and hydrocortisone, with limited benefit
Campbell et al ¹⁸	Not mentioned	Renal transplant	Not mentioned	Not mentioned	Not mentioned	Not done	No effect with tretinoin cream. Tazarotene gel 0.5% resulted in significant improvement

Continued

Table I. Cont'd

Case	Patient demographics	Medical history	Immuno-suppressive agents	Duration of immuno-suppression before onset of eruption (months)	Location of rash	Viral testing	Treatment
Lee et al ¹⁹	70-year-old man, Caucasian	CLL	Cyclophosphamide, fludarabine, and rituximab	48	Nose, malar area, forehead, eyelids, eyebrows, ears, trunk, thighs, legs, and arms. Scalp and eyebrow alopecia	Done (immuno-peroxidase stain for HPV negative)	No improvement with oral minocycline, 10% topical urea, or lactic acid cream 5%
Schwieger-Briel et al ²⁰	5-year-old girl, Caucasian	Cardiac transplant	Tacrolimus, MMF	9	Face (chin and nose), arms, and trunk. Eyebrow alopecia	Done (EM revealed no viral particles)	Mild improvement with topical retinoin, but systemic isotretinoin resulted in marked improvement. Patient was also started on oral valganciclovir
Wyatt et al ⁶	8-year-old boy, race not mentioned	Renal transplant	Tacrolimus, mycophenolate mofetil, and prednisone	8	Facial papules	Done (LM showed viral particles)	Severe persistent eruption
Wyatt et al ⁶	6-year-old boy, race not mentioned	ALL (B cell)	Cyclophosphamide, vincristine, prednisolone, and intrathecal methotrexate	22	Facial eruption and alopecia	Done (LM showed viral particles)	Chemotherapy was completed 3 months after the onset of eruption

Holzer et al ²¹	37-year-old woman, Caucasian	Cardiac transplant	Cyclosporine, mycophenolate mofetil, and prednisone	8	Face, upper portion of the trunk, arms, and legs. Alopecia of the face, trunk, upper extremities. Partial madarosis	Done (EM negative for viral particles)	Improvement after 5 months of systemic valganciclovir, with complete resolution at 1 year
Ali et al ²²	42-year-old woman, Caucasian	Renal transplant	MMF, tacrolimus	Not mentioned	Cheeks, forehead, and nose	Done (immunohistochemistry for SV40 positive)	Improvement with reduction of immunosuppressants and topical imiquimod
Heaphy et al ²³	34-year-old woman, race not mentioned	Renal transplant and systemic lupus erythematosus	Cyclosporine, mycophenolate mofetil, prednisone, and tacrolimus	Not mentioned	Face (nose, eyebrows, eyelashes, chin, and upper lip), ears, and body. Alopecia over the eyebrows, eyelashes, and body (except scalp)	Not mentioned	Not mentioned
Izakovic et al ²⁴	31-year old man, race not mentioned	Renal transplant	Cyclosporine and prednisone	Not mentioned	Face and extremities	Not mentioned	Not mentioned
Berk et al ²⁵	14-year-old girl, Caucasian	Lung transplant	Cyclosporine, muromonab-CD3, mycophenolate mofetil, methotrexate, prednisone, and tobramycin	36	Central portion of the face. Skin thickening and alopecia of eyebrows	Nucleated cells with cytoplasmic inclusions/granules on histology	Cryotherapy had no effect. Improvement with changing of cyclosporin to tacrolimus
Moktefi et al ²⁶	20-year-old woman, race not mentioned	Systemic lupus erythematosus	Corticosteroids, rituximab, and cyclophosphamide bolus. Then MMF replaced by azathioprine	50 since the diagnosis of systemic lupus erythematosus	Midfacial area, ears, and hands without alopecia	(TSPyV) DNA detected on lesional skin biopsy	No treatment. Patient died of cardiac arrest/pulmonary edema

Continued

Table I. Cont'd

Case	Patient demographics	Medical history	Immuno-suppressive agents	Duration of immuno-suppression before onset of eruption (months)	Location of rash	Viral testing	Treatment
Fischer et al ³	48-year-old man, African American	Renal transplant	Mycophenolic acid and tacrolimus	2-3	Central portion of the face and ears. Patchy alopecia of the eyebrows	TSPvY via PCR and sequencing in lesional skin. Also confirmed via EM	None
Chastain et al ²⁷	13-year-old woman, Caucasian	Lung transplant	Cyclosporin, mycophenolate mofetil, prednisone, methotrexate, and trimethoprim/sulfamethoxazole	36	Nose, ears, face, and proximal extremities	Attempts to detect HPV via PCR unsuccessful	Not mentioned
Burns et al ²⁸	9-year-old woman, race not mentioned	Pre-B—cell acute lymphoblastic leukemia	Mercaptopurine, methotrexate, vincristine, and dexamethasone	Not mentioned	Face, shoulders, arms, and legs, with prominent eyebrow involvement. Eyebrow alopecia	Not mentioned	Not mentioned
Shah et al ²⁹	25-year-old female, race not mentioned	Renal transplant	Mycophenolic acid, everolimus, and prednisone	Not mentioned	Nose extending onto the glabella, cheeks, and eyelids, as well as the tragi and helices of ears	Immunohistochemical staining for TS-associated polyomavirus was negative DNA PCR not done as histopathology was pathognomonic	Successfully treated with adapalene gel 0.1% and oral valganciclovir

ALL, Acute lymphoblastic leukemia; BID, twice daily; BK PCR, BK virus polymerase chain reaction; CLL, chronic lymphocytic leukemia; EM PCR, erythema multiforme polymerase chain reaction; HPV, human papilloma virus; LM, light microscopy; MMF, mycophenolate mofetil; NA, not available; NHL, non Hodgkins lymphoma; PCR, polymerase chain reaction; SV40, simian virus 40; TSPvY, trichodysplasia spinulosa polyomavirus; TSV, trichodysplasia spinulosa-associated polyomavirus; VP1, VP2, VP3, major capsid proteins.

In conclusion, we present the case of a 43-year-old Chinese woman, a renal transplant patient, with TS, who showed a good response to topical daylight PDT, which should be considered as an additional treatment option for this rare and potentially disfiguring skin condition.

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