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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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. 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 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 (adalapene) 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).

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

TS was first described by Haycox et al 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). 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.

The absence of cases in immunocompetent individuals suggests that a robust immune system prevents TS formation. Furthermore, some patients experience improvement in TS lesions after cessation of chemotherapy.

We have summarized 30 cases 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.

Various treatments reported notably with topical cidofovir and oral valganciclovir 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 warts and is safe for use in sOTR. We postulated that the effect of PDT in TS depends on preferential uptake of photosensitive porphyrins by sebaceous glands and  

![Fig 1. Facial profile showing spiculated follicular papules before PDT treatment. PDT, Photodynamic therapy.](image1)

![Fig 2. Dermoscopy showed clusters of homogenous pink circles and fine white hair shafts.](image2)

![Fig 3. Facial profile showing reduction in spiculated follicular papules after PDT treatment. PDT, Photodynamic therapy.](image3)
their subsequent destruction, similar to that in acne vulgaris. 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.

**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: ×10)

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

**Table I.** Summary of cases reported in the literature

| Case | Patient demographics | Medical history | Immunosuppressive agents | Duration of immunosuppression (months) | Location of rash | Viral testing | Treatment |
|------|----------------------|----------------|--------------------------|--------------------------------------|-----------------|---------------|-----------|
| Benoit et al | 5-year-old boy, Caucasian | Cardiac transplant | Cyclosporine, 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 |
| Authors            | Age/Gender/Race | Transplant Type                  | Immunosuppressive Regimen | Duration | Lesions                                                                 | Diagnostic Procedures/Therapy                                                                 |
|--------------------|----------------|----------------------------------|---------------------------|----------|-------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|
| Borgogna et al     | 7-year-old boy | Renal transplant x2              | MMF, tacrolimus, prednisolone | 24       | Face, neck, back, and extremities                                       | Done (viral DNA)                                                                           |
|                    | Italian/Moroccan |                                  |                           |          |                                                                         | Tailing of immunosuppressants for viremia, unsure of the effect on skin                    |
| Coogle et al       | 11-year-old boy | Renal transplant                 | MMF, tacrolimus, prednisolone | 14       | Face, arms, and upper portion of the legs                               | Urine screen for BK PCR positive                                                             |
|                    | Caucasian       |                                  |                           |          |                                                                         | Cidofovir cream 1% for 1 month and tailing of immunosuppression, with improvement and complete resolution in 7 months |
| Decrescenzo et al  | 35-year-old man | Renal transplant                 | Tacrolimus, MMF           | 6        | Face, trunk, arms, and ears. Alopecia of the eyebrows and eyelashes    | Not done                                                                                   |
|                    | race not mentioned |                                |                           |          |                                                                         | Slow taper of immunosuppression, with marked improvement and complete regrowth at 2 years |
| Haycox et al       | 44-year-old man | Renal-pancreatic transplant      | Tacrolimus, azathioprine, prednisone | 29       | Nose, ears, and forehead. Alopecia of the eyebrow, eyelash, and scalp | (EMPCR, Papovaviridae family virus)                                                        |
|                    | Caucasian       |                                  |                           |          |                                                                         | NA                                                                                          |
| Kirchhof et al     | 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
| Case | Patient demographics | Medical history | Immunosuppressive agents | Duration of immunosuppression before onset of eruption (months) | Location of rash | Viral testing | Treatment |
|------|----------------------|----------------|--------------------------|---------------------------------------------------------------|-----------------|--------------|------------|
| Laroche et al<sup>11</sup> | 42-year-old woman, Renal transplant Caucasian | | 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<sup>12</sup> | 49-year-old woman, Renal transplant Caucasian | | 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<sup>13</sup> | 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<sup>14</sup> | 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<sup>15</sup> | 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 | |
| Reference      | Age/Details                           | Diagnosis | Treatment                                                                 | Duration | Clinical Features                                                                 | Diagnosis/Result                                                                 |
|----------------|---------------------------------------|-----------|-----------------------------------------------------------------------------|----------|----------------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| Sadler et al15  | 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 al16 | 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 al15 | 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 al17   | 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 (Immuno-histochemical analysis of polyomavirus)                           | Topical cimetidine, imiquimod, salicylic acid, and hydrocortisone, with limited benefit |
| Campbell et al18 | 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 |
Table 1. Cont’d

| Case             | Patient demographics | Medical history | Immunosuppressive agents                                      | Duration of immuno-suppression before onset of eruption (months) | Location of rash                                                                 | Viral testing                                                                 | Treatment                                                                 |
|------------------|----------------------|-----------------|----------------------------------------------------------------|-----------------------------------------------------------------|------------------------------------------------------------------------------|------------------------------------------------------------------------------|----------------------------------------------------------------------------|
| Lee et al19      | 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 (immunoperoxidase stain for HPV negative)                               | No improvement with oral minocycline, 10% topical urea, or lactic acid cream 5% |
| Schwieger-Briel et al20 | 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 al6     | 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 al6     | 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             |
| Last Name et al | Age | Gender | Race | Transplant Type | Immunosuppressants | Lesions | Diagnosis | Treatment | Resolution |
|----------------|-----|--------|------|-----------------|-------------------|---------|-----------|-----------|-----------|
| Holzer et al   | 37  | 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 of the face, trunk, upper extremities. | Done (EM negative for viral particles) | Improvement after 5 months of systemic valganciclovir, with complete resolution at 1 year |
| Ali et al      | 42  | Woman  | Caucasian | Renal transplant | MMF, tacrolimus | Not mentioned | Cheeks, forehead, and nose | Done | Improvement with reduction of immunosuppressants and topical imiquimod |
| Heaphy et al   | 34  | 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 | 31  | Man    | Race not mentioned | Renal transplant | Cyclosporine and prednisone | Not mentioned | Face and extremities | Not mentioned | Not mentioned |
| Berk et al     | 14  | 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  | 20  | 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
| Case                          | Patient demographics                  | Medical history                           | Immunosuppressive agents                                                                 | Duration of immuno-suppression before onset of eruption (months) | Location of rash                                                                 | Viral testing                                                                 | Treatment                                      |
|-------------------------------|---------------------------------------|-------------------------------------------|------------------------------------------------------------------------------------------|------------------------------------------------------------------|--------------------------------------------------------------------------------|--------------------------------------------------------------------------------|------------------------------------------------|
| Fischer et al<sup>3</sup>      | 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          | TSPyV via PCR and sequencing in lesional skin. Also confirmed via EM       | None                                          |
| Chastain et al<sup>27</sup>    | 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<sup>28</sup>       | 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<sup>29</sup>        | 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; TSPyV, 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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