

# Widespread Hyperkeratotic Papules in a Transplant Recipient

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A 4-year-old girl with a history of cardiac transplantation 1 year prior for dilated cardiomyopathy presented to the dermatology consultation service with widespread hyperkeratotic papules of 2 months' duration. The eruption initially had appeared on the face with subsequent involvement of the trunk and extremities. Her immunosuppressive medications included oral tacrolimus and mycophenolate mofetil. No over-the-counter or prescription treatments had been used for the eruption; the patient's mother had been manually extracting the spicules from the nose, cheeks, and forehead with tweezers. The lesions were asymptomatic with only mild follicular erythema. Physical examination revealed multiple folliculocentric keratinous spicules on the nose, cheeks, forehead (top), trunk (bottom), arms, and legs.



## WHAT'S YOUR DIAGNOSIS?

- filiform warts
- keratosis pilaris
- lichen spinulosus
- millia
- trichodysplasia spinulosa

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The authors report no conflict of interest.

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## THE DIAGNOSIS: Trichodysplasia Spinulosa

Trichodysplasia spinulosa has been described in case reports over the last several decades, with its causative virus trichodysplasia spinulosa-associated polyomavirus (TSPyV) identified in 2010 by van der Meijden et al.<sup>1</sup> Trichodysplasia spinulosa-associated polyomavirus is a small, nonenveloped, double-stranded DNA virus in the *Polyomaviridae* family, among several other known cutaneous polyomaviruses including Merkel cell polyomavirus, human polyomavirus (HPyV) 6, HPyV7, HPyV10, and possibly HPyV13.<sup>2</sup> The primary target of TSPyV is follicular keratinocytes, and it is believed to cause trichodysplasia spinulosa by primary infection rather than by reactivation. Trichodysplasia spinulosa presents in immunosuppressed patients as a folliculocentric eruption of papules with keratinous spines on the face, often with concurrent alopecia, eventually spreading to the trunk and extremities.<sup>3</sup> The diagnosis often is clinical, but a biopsy may be performed for histopathologic confirmation. Alternatively, lesional spicules can be painlessly collected manually and submitted for viral polymerase chain reaction (PCR).<sup>4</sup> The diagnosis of trichodysplasia spinulosa can be difficult due to similarities with other more common conditions such as keratosis pilaris, milia, filiform warts, or lichen spinulosus.

Similar to trichodysplasia spinulosa, keratosis pilaris also presents with folliculocentric and often erythematous papules.<sup>5</sup> Keratosis pilaris most frequently affects the posterior upper arms and thighs but also may affect the cheeks, as seen in trichodysplasia spinulosa. Differentiation between the 2 diagnoses can be made on a clinical basis, as keratosis pilaris lacks the characteristic keratinous spines and often spares the central face and nose, locations that commonly are affected in trichodysplasia spinulosa.<sup>3</sup>

Milia typically appear as white to yellow papules, often on the cheeks, eyelids, nose, and chin.<sup>6</sup> Given their predilection for the face, milia can appear similarly to trichodysplasia spinulosa. Differentiation can be made clinically, as milia typically are not as numerous as the spiculed papules seen in trichodysplasia spinulosa. Morphologically, milia will present as smooth, dome-shaped papules as opposed to the keratinous spicules seen in trichodysplasia spinulosa. The diagnosis of milia can be confirmed by incision and removal of the white chalky keratin core, a feature absent in trichodysplasia spinulosa.

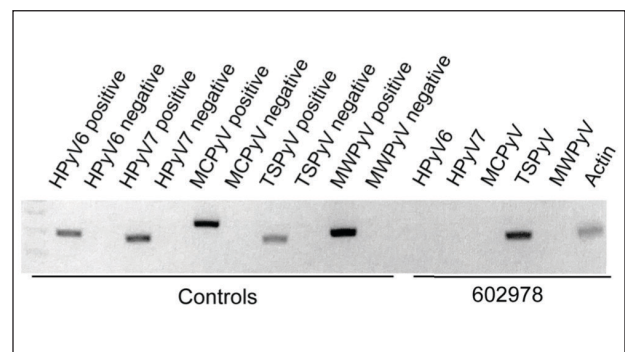
Filiform warts are benign epidermal proliferations caused by human papillomavirus infection that manifest as flesh-colored, verrucous, hyperkeratotic papules.<sup>7</sup> They can appear on virtually any skin surface, including the face, and thus may be mistaken for trichodysplasia

spinulosa. Close inspection usually will reveal tiny black dots that represent thrombosed capillaries, a feature lacking in trichodysplasia spinulosa. In long-standing lesions or immunocompromised patients, confluent verrucous plaques may develop.<sup>8</sup> Diagnosis of filiform warts can be confirmed with biopsy, which will demonstrate a compact stratum corneum, coarse hypergranulosis, and papillomatosis curving inward, while biopsy of a trichodysplasia spinulosa lesion would show polyomavirus infection of the hair follicle and characteristic eosinophilic inclusion bodies.<sup>9</sup>

Lichen spinulosus may appear as multiple folliculocentric scaly papules with hairlike horny spines.<sup>10</sup> Lichen spinulosus differs from trichodysplasia spinulosa in that it commonly appears on the neck, abdomen, trochanteric region, arms, elbows, or knees. Lichen spinulosus also classically appears as a concrete cluster of papules, often localized to a certain region, in contrast to trichodysplasia spinulosa, which will be widespread, often spreading over time. Finally, clinical history may help differentiate the 2 entities. Lichen spinulosus most often appears in children and adolescents and often has an indolent course, typically resolving during puberty, while trichodysplasia spinulosa is seen in immunocompromised patients.

In our patient, the dermatology team made a diagnosis of trichodysplasia spinulosa based on the characteristic clinical presentation, which was confirmed after approximately 10 lesional spicules were removed by tissue forceps and submitted for PCR analysis showing TSPyV (Figure). Two other cases utilized spicule PCR analysis for confirmation of TSPyV.<sup>11,12</sup> This technique may represent a viable option for diagnostic confirmation in pediatric cases.

Although some articles have examined the molecular and biologic features of trichodysplasia spinulosa,



Spicule polymerase chain reaction results showed the presence of trichodysplasia spinulosa-associated polyomavirus (TSPyV).

literature on clinical presentation and management is limited to isolated case reports with no comprehensive studies to establish a standardized treatment. Of these reports, oral valganciclovir 900 mg daily, topical retinoids, cidofovir cream 1% to 3%, and decreasing or altering the immunosuppressive regimen all have been noted to provide clinical improvement.<sup>13,14</sup> Other therapies including leflunomide and routine manual extraction of spicules also have shown effectiveness in the treatment of trichodysplasia spinulosa.<sup>15</sup>

In our patient, treatment included decreasing immunosuppression, as she was getting recurrent sinus and upper respiratory infections. Mycophenolate mofetil was discontinued, and the patient was continued solely on tacrolimus therapy. She demonstrated notable improvement after 3 months, with approximately 50% clearance of the eruption. A mutual decision was made at that visit to initiate therapy with compounded cidofovir cream 1% daily to the lesions until the next follow-up visit. Unfortunately, the patient did not return for her scheduled dermatology visits and was lost to long-term follow-up.

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