CASE REPORT

Widespread keratosis pilaris–like eruption in an immunocompromised child

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INTRODUCTION

Trichodysplasia spinulosa (TS) is a folliculocentric disorder seen in immunosuppressed patients that is highly associated with a human polyomavirus. The disorder is characterized by eruptions of folliculocentric papules with keratotic spicules that can be asymptomatic to pruritic. Lesions classically involve the nose, eyebrows, and ears but are also seen to a lesser extent on the trunk and extremities. Variable degrees of nonscarring alopecia and madarosis are known complications. The differential diagnosis of TS can be broad, including keratosis pilaris and related disorders, lichen spinulosus, sarcoidosis, rosacea, and perforating disorders. Clinico-histopathologic correlation is essential, and a biopsy can help establish a diagnosis.

In addition to the central facial distribution typical of trichodysplasia spinulosa, we present a case that exhibits trunk and extremity involvement clinically reminiscent of keratosis pilaris.

CASE REPORT

A 7-year-old boy with relapsed high-risk pre-B acute lymphoblastic leukemia presented with a 6-month history of a widespread follicular keratotic eruption. The eruption started as flesh-colored pinpoint papules on his cheeks during his first round of chemotherapy with vincristine, mercaptopurine, and methotrexate. He subsequently had numerous similar papules on the rest of the face, back of the neck, trunk, buttocks, and all extremities including dorsal hands and feet (Fig 1). The eruption was only mildly pruritic. Previous treatments included topical hydrocortisone and oral prednisone with no benefit. Skin examination found a widespread keratosis pilaris–like eruption with follicular spicules on the nasal tip and eyebrow reminiscent of ulerythema ophryogenes.

Skin biopsies from the trunk and extremities showed follicular infundibular plugging with dystrophy and expansion of the inner root sheath by cells with pale cytoplasm, mild nuclear enlargement, and smudged chromatin. Large, irregular eosinophilic trichohyalin granules were noted (Fig 2). TS polyomavirus (TSPyV) infection was confirmed by immunochemistry (IHC) using antibodies reactive against TSPyV viral capsid antigen 1 (Fig 2). A focal leukemic infiltrate was also noted on skin biopsy; however, leukemia cutis was not detectable on repeat skin biopsies 4 weeks later.

The eruption initially improved with no specific treatment during the chemotherapy induction phase. It has then flared multiple times with the chemotherapy; flares seem to occur more often after methotrexate. The patient’s parents chose not to treat this condition because it was mostly asymptomatic and not bothersome.

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DISCUSSION

TS was initially described by Izakovic et al\(^1\) in 1995 and viewed as a potential side effect of cyclosporine; however, as more reports of these lesions developing in noncyclosporin cases surfaced, investigation turned to other causes. Because lesions of TS are nearly always seen in immunosuppression, a viral etiology was proposed. By using transmission electron microscopy, Haycox et al\(^2\) were able to identify the presence of intranuclear viral particles typical of the Polyomaviridae family in 1999. In 2010 van der Meijden et al\(^3\) identified a new polyomavirus from plucked keratotic spicules and named it *trichodysplasia spinulosa*–associated polyomavirus.\(^3\) Other investigators were able to show that TS specimens contained high viral loads of TSPyV DNA and that the TSPyV viral protein 1 (VP1) was expressed in TS specimens localized to inner root sheath cells, where trichohyalin proteins were being overexpressed.\(^4\)

The seroprevalence for TSPyV is about 70% to 90% in the general population. Infections are usually acquired during early childhood from a familial source with lifelong latency and periodic shedding of virions. Although viral DNA for TSPyV has been found in feces, urine, and blood, it is believed that the upper respiratory tract and secretions are major routes for transmission.\(^5\)

The manifestations of clinical disease have been reported in the setting of immunosuppression, typically in association with solid organ transplantation or hematolymphoid malignancies. On a review of 20 cases, the eruption occurred at least 6 months after solid organ transplant and at least 2 years after leukemia or lymphoma diagnosis; children and adults were equally affected.\(^6\)

Clinical manifestations of TS are attributed to lytic reactivation of TSPyV and the expression of early viral proteins including the viral large T antigen (LT). TSPyV LT has been found to inhibit the

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**Fig 1.** TS with classic central facial spicules (A) and widespread keratosis pilaris–like eruption on the extremities (B) and trunk (C).

**Fig 2.** TS skin biopsy from the trunk. Inner root sheath cells exhibit large, irregular eosinophilic trichohyalin granules. (A, Hematoxylin-eosin stain; original magnification: ×200. B, TSPyV viral capsid antigen 1 immunohistochemistry; original magnification: ×100.)
retinoblastoma family of tumor suppressor proteins and to induce cell cycle progression in host cells. Thus, TSPyV LT expression can lead to hyperproliferation of infected inner root sheath cells.

TS presenting as a widespread keratosis pilaris–like eruption has not been well documented. The differential diagnosis for the presented case was broad, including keratosis pilaris, keratosis pilaris atrophicans faciei, lichen spinulosus, sarcoidosis, rosacea, and perforating disorders. The acute presentation and central facial distribution helped differentiate TS from other entities. Drug-induced keratosis pilaris–like eruption is an important differential diagnosis in the same patient population often afflicted with TS. Keratosis pilaris–like eruptions have been linked to multiple targeted cancer agents including BRAF, tyrosine kinase, and EGFR inhibitors. It is important for physicians working with patients that are immunosuppressed or have hematologic malignancies to recognize TS as a dermatologic manifestation that reflects failure of immune surveillance.

Histology findings show dilated follicles with an expansion of the inner root sheath cells that also contain large perinuclear eosinophilic trichohyalin granules. Routine hematoxylin-eosin staining is generally sufficient to establish a pathology diagnosis, but additional studies including scanning electron microscopy, IHC, or polymerase chain reaction can be used to confirm a viral etiology. We showed the importance and ease of use for IHC staining as described previously. Corroborating data provided from IHC has been used in several TS cases with success and IHC is more practical than performing polymerase chain reaction assays or electron microscopy. Despite the rare occurrence of TS, the sensitivity and specificity of IHC appear high. Positive, negative control tissues and cell pellet arrays were used to validate the sensitivity and specificity of the TSV-VP1 antibody staining.

Currently, there is no established treatment for TS. Reported therapies include spicule extraction, topical cidofovir up to 5% concentration (often difficult to acquire given expense), oral valganciclovir, oral and topical retinoids, leflunomide, topical steroids, tacrolimus, antibiotics, imiquimod, and oral minocycline. These therapies have been limited to case reports and case series, and improvement is seen in reduction in immunosuppression and improvement of underlying immune function.

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REFERENCES

1. Izakovic J, Büchner SA, Düggelin M, Guggenheim R, Itin PH. [Hair-like hyperkeratoses in patients with kidney transplants. A new cyclosporin side-effect]. Hautarzt. 1995;46(12):841-846.
2. Haycox CL, Kim S, Fleckman P, et al. Trichodyplasia spinulosa–a newly described folliculocentric viral infection in an immunocompromised host. J Invest Dermatol Symp Proc. 1999;4(3):268-271.
3. Van der Meijden E, Janssens RWA, Lauber C, Bavinck JNB, Gorbalenya AE, Feltkamp MCW. Discovery of a new human polyomavirus associated with trichodysplasia spinulosa in an immunocompromized patient. PLoS Pathog. 2010;6(7):1-10.
4. Kazem S, van der Meijden E, Kooijman S, et al. Trichodyplasia spinulosa is characterized by active polyomavirus infection. J Clin Virol. 2012;53(3):225-230.
5. Pedergnana V, Martel-Jantin C, Nicol JTJ, et al. Trichodyplasia spinulosa polyomavirus infection occurs during early childhood with intrafamilial transmission, especially from mother to child. J Invest Dermatol. 2017;137(5):1181-1183.
6. Matthews MR, Wang RC, Reddick RL, et al. Viral-associated trichodyplasia spinulosa: a case with electron microscopic and molecular detection of the trichodyplasia spinulosa-associated human polyomavirus. J Cutan Pathol. 2011;38(5):420-431.
7. Kazem S, Van Der Meijden E, Wang RC, et al. Polyomavirus-associated trichodyplasia spinulosa involves hyperproliferation, pRB phosphorylation and upregulation of p16 and p21. PLoS One. 2014;9(10):1-7.
8. Macdonald JB, Macdonald B, Golitz LE, et al. Cutaneous adverse effects of targeted therapies: part II: inhibitors of intracellular molecular signaling pathways. J Am Acad Dermatol. 2015;72(2):221-236.
9. Toptan T, Yousem SA, Ho J, et al. Survey for human polyomaviruses in cancer. JCI Insight. 2016;1(2):e85562.
10. Wanat KA, Holler PD, Dentchev T, et al. Viral-associated trichodyplasia. Characterization of a novel polyomavirus infection with therapeutic insights. Arch Dermatol. 2012;148(2):219-223.