Widespread Keratotic Spiky Follicular Papules Associated With Hyperpigmentation: Answer

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ANSWER

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Trichodysplasia spinulosa associated with chemotherapy-induced pigmentation.

DISCUSSION

Virus-associated trichodysplasia spinulosa was first described as a distinct entity in 1999 by Haycox et al.[1] They described a solid organ-transplant patient on immunosuppressive therapy who developed follicular keratotic spiky papules predominantly over the forehead, nose, and ears associated with alopecia. Histopathologically, anagen follicles exhibited abnormal maturation with excessive proliferation of dystrophic inner root sheath (IRS). Papovaviridae-like viral particles were detected by electron microscopy within the IRS cells. The authors postulated that this entity represents a folliculocentric viral infection in immunosuppressed individuals. Similar cases in the same clinical setting were reported under the term pilomatrix dysplasia and cyclosporine-induced follicular dystrophy.[2,3]

Later, many cases have been reported using the term tricodysplasia spinulosa (TDS), not only in immunosuppressed solid organ transplant patients but also in patients with different hematologic malignancies receiving chemotherapy. Viral particles morphologically similar to polyomavirus were detected in these cases.[4–8] However, it was not until 2010, when a specific polyomavirus was isolated by polymerase chain reaction from the follicular spicules of a patient with TDS. The virus was given the name trichodysplasia spinulosa-associated polyomavirus (TSPyV or TSV).[9]

Certain antigens in the TSPyV, particularly large tumor antigen, induce cell-cycle progression through inhibiting retinoblastoma proteins (pRB) causing unchecked proliferation of IRS cells, which in turn act as a reservoir for viral DNA. The terminal differentiation product of these cells explains the accumulation of cells containing trichohyalin granule with lack of hair shafts and subsequent formation of the follicular spicules.[10]

Typically, lesions of TDS involve mainly the central face and are associated with variable amounts of alopecia involving the eyebrows, eyelashes, and other hair-bearing parts of the face. Subsequent loss of scalp and body hair has also been reported.[1] In addition to the cardinal histopathological feature of expanded dystrophic IRS cells with irregular variable-sized trichohyaline granules, lesions of TDS show follicular dilatation with keratotic plugging of the infundibula and absent normal hair shafts. Acantholysis and apoptotic cells were also seen among the IRS cells.[1] The keratotic spikes were found to be composed of compact orthokeratosis admixed with IRS cells that may contain central small, poorly formed hair shafts.[6,8]

None of the reported cases showed associated pigmentation as in our case. We have noticed that necrotic keratinocytes within the epidermis and dermal melanophages were seen only in biopsies taken from lesions with a background of pigmentation. We assume that the associated pigmentation is mostly chemotherapy-related drug-induced pigmentation because one of the drugs received by the patient was methotrexate, which is known in causing pigmentary side effects.[11,12]

The treatment of TDS generally comprises reduction of immunosuppression and the use of various antiviral therapies such as cidofovir,[13] valganciclovir,[14] or oral valacyclovir.[15] Spontaneous remission has also been reported with improvement in the immune status.[3,16]

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The authors declare no conflicts of interest.

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REFERENCES

1. Haycox CL, Kim S, Fleckman P, et al. Trichodysplasia spinulosa: a newly described folliculocentric viral infection in an immunocompromised host. *J Investig Dermatol Symp Proc.* 1999;4:268–271.
2. Chastain MA, Millikan LE. Pilomatrix dysplasia in an immunosuppressed patient. *J Am Acad Dermatol.* 2000;43:118–122.
3. Heaphy MR Jr, Shamma HN, Hickmann M, et al. Cyclosporine-induced folliculodystrophy. *J Am Acad Dermatol.* 2004;50:310–315.
4. Wyatt AJ, Sachs DL, Shia J, et al. Virus-associated trichodysplasia spinulosa. *Am J Surg Pathol.* 2005;29:241–246.
5. Sadler GM, Halbert AR, Smith N, et al. Trichodysplasia spinulosa associated with chemotherapy for acute lymphocytic leukaemia. *Australas J Dermatol.* 2007;48:110–114.

6. Lee JS, Frederiksen P, Kossard S. Progressive trichodysplasia spinulosa in a patient with chronic lymphocytic leukaemia in remission. *Australas J Dermatol.* 2008;49:57–60.
7. Osswald SS, Kulick KB, Tomaszewski MM, et al. Viral-associated trichodysplasia in a patient with lymphoma: a case report and review. *J Cutan Pathol.* 2007;34:721–725.
8. Sperling LC, Tomaszewski MM, Thomas DA. Viral-associated trichodysplasia in patients who are immunocompromised. *J Am Acad Dermatol.* 2004;50:318–322.
9. van der Meijden E, Janssens RW, Lauber C, et al. Discovery of a new human polyomavirus associated with trichodysplasia spinulosa in an immunocompromized patient. *PLoS Pathog.* 2010;6: e1001024.
10. Kazem S, van der Meijden E, Wang RC, et al. Polyomavirus-associated trichodysplasia spinulosa involves hyperproliferation, pRB phosphorylation and upregulation of p16 and p21. *PLoS One.* 2014;9:e108947.
11. Ikawa Y, Nishimura R, Araki R, et al. Nonallergic cutaneous pigmentation is commonly observed after methotrexate administration. *J Oncol Pharm Pract.* 2019;25:769–771.
12. Toussirot E, Wendling D. Methotrexate-induced hyperpigmentation in a rheumatoid arthritis patient. *Clin Exp Rheumatol.* 1999;17:751.
13. Wanat KA, Holler PD, Dentchev T, et al. Viral-associated trichodysplasia: characterization of a novel polyomavirus infection with therapeutic insights. *Arch Dermatol.* 2012;148:219–223.
14. Benoit T, Bacelieri R, Morrell DS, et al. Viral-associated trichodysplasia of immunosuppression: report of a pediatric patient with response to oral valganciclovir. *Arch Dermatol.* 2010;146:871–874.
15. Elaba ZHS, Andrea A. Trichyodysplasia spinulosa in a lung transplant patient. Poster presented at: American Society of Dermatopathology 47th Annual Meeting, 7–10 October 2010. Atlanta, GA.
16. Izakovic JBS, Büchner SA, Düggelin M, et al. Hair-like hyper-keratoses in patients with kidney transplants: a new cyclosporin side-effect. *Hautarzt.* 1995;46:841–846.