Trichodysplasia Spinulosa in the Setting of Colon Cancer

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PRACTICE **POINTS**

- Rashes have a life span and can evolve with time.
- If apparent straightforward conditions do not appear to respond to standard therapy, start to think outside the box for underlying potential causes.

Trichodysplasia spinulosa (TS) is a rare skin condition seen in immunosuppressed patients that is characterized by folliculocentric papules with central spiny spicules mainly on the face. We report the case of an 82-year-old woman with a history of treated non-Hodgkin lymphoma and a recent diagnosis of stage IV colon cancer. She presented with clinical and histopathologic findings consistent with TS occurring prior to starting immunosuppressive therapy for colon cancer. We conclude that this case of TS may either be secondary to the prior immunosuppressive treatment for the non-Hodgkin lymphoma or that it may represent a paraneoplastic condition warranting appropriate cancer screenings in affected patients.

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Case Report

An 82-year-old woman presented to the clinic with a rash on the face that had been present for a few months. She denied any treatment or prior occurrence. Her medical history was remarkable for non-Hodgkin lymphoma that had been successfully treated with chemotherapy 4 years prior. Additionally, she recently had been diagnosed with stage IV colon cancer. She reported that surgery had been scheduled and she would start adjuvant chemotherapy soon after.

On physical examination she exhibited perioral and perinasal erythematous papules with sparing of the vermilion border. A diagnosis of perioral dermatitis was made, and she was started on topical metronidazole. At 1-month follow-up, her condition had slightly worsened and she was subsequently started on doxycycline. When she returned to the clinic again the following month, physical examination revealed agminated folliculocentric papules with central spicules on the face, nose, ears, upper extremities (Figure 1), and trunk. The differential diagnosis included multiple minute digitate hyperkeratosis, spiculosis of multiple myeloma, and trichodysplasia spinulosa (TS).

A punch biopsy of 2 separate papules on the face and upper extremity revealed dilated follicles with enlarged trichohyalin granules and dyskeratosis (Figure 2), consistent with TS. Additional testing such as electron microscopy or polymerase chain reaction was not performed to keep the patient's medical costs down; also, the strong clinical and histopathologic evidence did not warrant further testing.

The plan was to start split-face treatment with topical acyclovir and a topical retinoid to see which agent was more effective, but the patient declined until her chemotherapy regimen had concluded. Unfortunately, the patient died 3 months later due to colon cancer.

Comment

History and Presentation—Trichodysplasia spinulosa was first recognized as hairlike hyperkeratosis.[1] The name by which it is currently known was later championed by Haycox et al.[2] They reported a case of a 44-year-old man who underwent a combined renal-pancreas transplant and while taking immunosuppressive medication developed erythematous papules with follicular spinous processes and progressive alopecia.[2] Other synonymous terms used for this condition include *pilomatrix dysplasia, cyclosporine-induced folliculodystrophy, virus-associated trichodysplasia,*[3] and *follicular dystrophy of immunosuppression*.[4] Trichodysplasia spinulosa can

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The authors report no conflict of interest.

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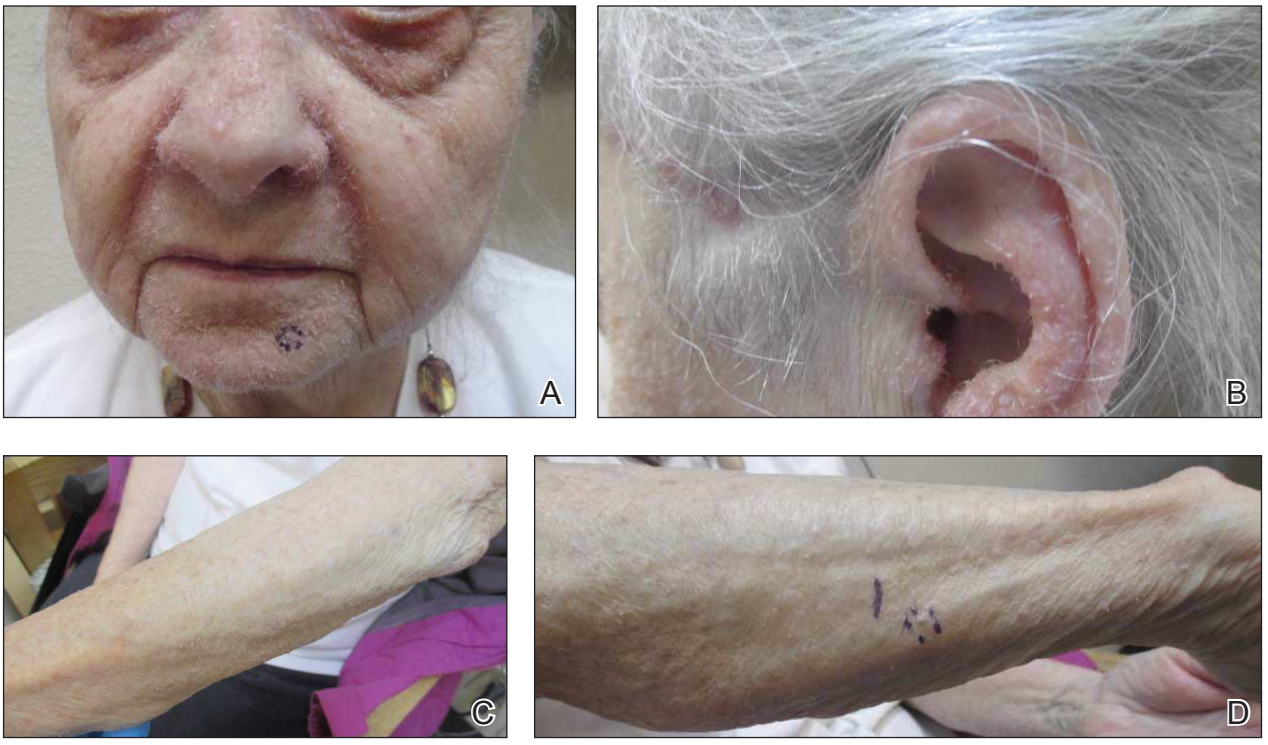

FIGURE 1. Trichodysplasia spinulosa with agminated folliculocentric papules with central spicules on the central face (A), ear (B), and bilateral upper extremities (C and D).

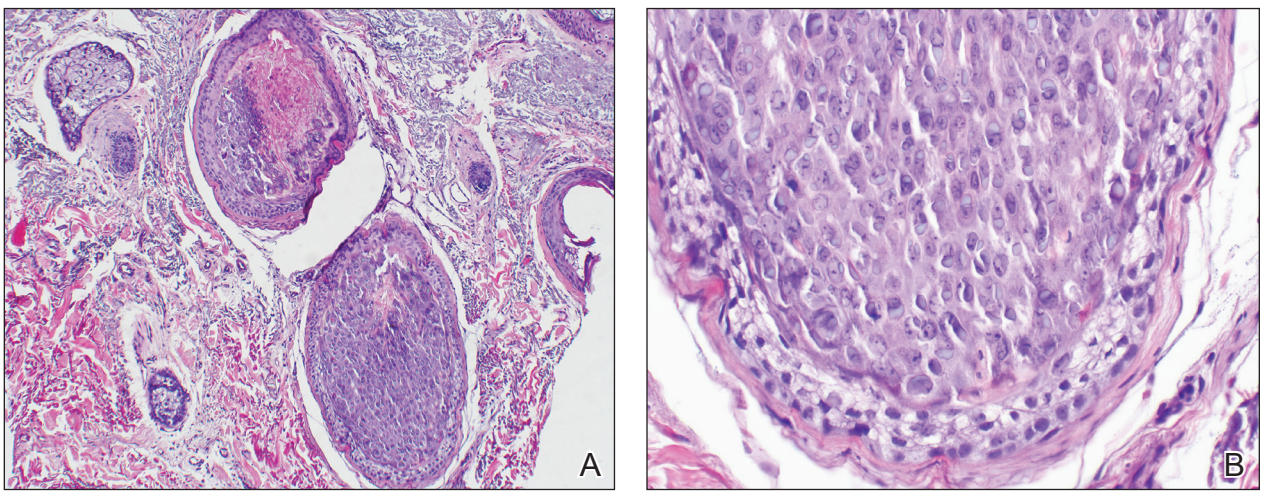

FIGURE 2. Distended hair bulb, expansion of the inner root sheath, and dyskeratosis (A)(H&E, original magnification ×10). Enlarged trichohyalin granules also were noted on higher power (B)(H&E, original magnification ×40).

affect both adult and pediatric immunocompromised patients, including organ transplant recipients on immunosuppressants and cancer patients on chemotherapy.[3] The condition also has been reported to precede the recurrence of lymphoma.[5]

Etiology—The connection of TS with a viral etiology was first demonstrated in 1999, and subsequently it was confirmed to be a polyomavirus.[2] The family name of Polyomaviridae possesses a Greek derivation with *poly-* meaning many and *-oma* meaning cancer.[3] This name was given after the polyomavirus induced multiple tumors in mice.[3,6] This viral family consists of multiple naked viruses with a surrounding icosahedral capsid containing 3 structural proteins known as VP1, VP2, and VP3. Their life cycle is characterized by early and late phases with respective early and late protein formation.[3]

Polyomavirus infections maintain an asymptomatic and latent course in immunocompetent patients.[7] The prevalence and manifestation of these viruses change when the host's immune system is altered. The first identified JC virus and BK virus of the same family have been found at increased frequencies in blood and lymphoid tissue during host immunosuppression.[6] Moreover, the Merkel cell polyomavirus detected in Merkel cell carcinoma is well documented in the dermatologic literature.[6,8]

A specific polyomavirus has been implicated in the majority of TS cases and has subsequently received the name of *TS polyomavirus.*[9] As a polyomavirus, it similarly produces capsid antigens and large/small T antigens. Among the viral protein antigens produced, the large tumor or LT antigen represents one of the most potent viral proteins. It has been postulated to inhibit the retinoblastoma family of proteins, leading to increased inner root sheath cells that allow for further viral replication.[9,10]

The disease presents with folliculocentric papules localized mainly on the central face and ears, which grow central keratin spines or spicules that can become 1 to 3 mm in length. Coinciding alopecia and madarosis also may be present.[9]

Diagnosis—Histologic examination reveals abnormal follicular maturation and distension. Additionally, increased proliferation and amount of trichohyalin is seen within the inner root sheath cells. Further testing via viral culture, polymerase chain reaction, electron microscopy, or immunohistochemical stains can confirm the diagnosis. Such testing may not be warranted in all cases given that classic clinical findings coupled with routine histopathology staining can provide enough evidence.[10,11]

Management—Currently, a universal successful treatment for TS does not exist. There have been anecdotal successes reported with topical medications such as cidofovir ointment 1%, acyclovir combined with 2-deoxy-D-glucose and epigallocatechin, corticosteroids, topical tacrolimus, topical retinoids, and imiquimod. Additionally, success has been seen with oral minocycline, oral retinoids, valacyclovir, and valganciclovir, with the latter showing the best results. Patients also have shown improvement after modifying their immunosuppressive treatment regimen.[10,12]

Conclusion

Given the previously published case of TS preceding the recurrence of lymphoma,[5] we notified our patient's oncologist of this potential risk. Her history of lymphoma and immunosuppressive treatment 4 years prior may represent the etiology of the cutaneous presentation; however, the TS with concurrent colon cancer presented prior to starting immunosuppressive therapy, suggesting that it also may have been a paraneoplastic process and not just a sign of immunosuppression. Therefore, we recommend that patients who present with TS should be evaluated for underlying malignancy if not already diagnosed.

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