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[CME INTRO PAGE – please make changes to text which is updated monthly using track changes]

American Journal of Transplantation Images in Transplantation – Continuing Medical Education (CME)

Each month, the *American Journal of Transplantation* will feature Images in Transplantation, a journal-based CME activity, chosen to educate participants on current developments in the science and imaging of transplantation. Participants can earn 1 *AMA PRA Category 1 Credit*™ per article at their own pace.

This month's feature article is titled: "An eruption of numerous spiny papules in a pediatric transplant patient."

Accreditation and Designation Statement

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Statement of Need

Transplant patients are immunosuppressed to prevent graft rejection, which can cause a wide range of opportunistic infections. Physicians must maintain graft viability while providing early recognition and treatment of atypical or rare infections.

Purpose of Activity

This activity was designed to educate physicians to accurately and promptly recognize and safely treat a rare cutaneous eruption associated with trichodysplasia spinulosa virus.

Identification of Practice Gap

Virus-associated trichodysplasia spinulosa (VATS) is a rare skin eruption that occurs in the setting of immunosuppression, putting transplant patients at particularly increased risk. Not all physicians are well versed in the diagnosis and treatment of VATS due to its rarity. This knowledge gap may lead to diagnostic delays, nonoptimal treatment regimens, and poor outcomes. This activity will illustrate the diagnostic characteristics and therapeutic approaches to treating VATS patients in an effort to mend this knowledge gap.

Learning Objectives

Upon completion of this educational activity, participants will be able to:

- Recognize this rare entity characterized by a cutaneous eruption of folliculocentric papules and keratin spicules on the central face and ears, with concomitant alopecia of the eyebrows and eyelashes.
- Identify the underlying pathogen.
- Treat this entity appropriately.

Target Audience

This activity has been designed to meet the educational needs of physicians and surgeons in the field of transplantation.

[NOTE: use text above unless something else is provided]

Disclosures

No commercial support has been accepted related to the development or publication of this activity. John Wiley & Sons, Inc. has reviewed all disclosures and resolved or managed all identified conflicts of interest, as applicable.

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[CME ACTIVITY – please start on new page, following this heading]

An eruption of numerous spiny papules in a pediatric transplant patient

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Case Report

An eight-year-old African American female presented to the dermatology clinic with a three-month history of numerous, tiny, asymptomatic, white folliculocentric papules and spicules on the face, with concomitant alopecia of the eyebrows and eyelashes (Figure 1). The patient had a past medical history of congenital renal dysplasia and was 18 months status following renal transplant. The patient had a history of antibody-mediated rejection four months posttransplant, which was treated with intravenous methylprednisolone and rituximab. Her current immunosuppressive medications included oral tacrolimus, mycophenolate mofetil, and prednisolone. No adjustments had been made to this regimen for seven months prior to

presentation. Laboratory testing revealed a negative serum BK virus PCR. A 3 mm punch biopsy of the left ear revealed a dilated follicular canal, underlying cyst formation with a granular layer, and keratinous material and inflammatory debris in the lumen. The surrounding dermis showed fibrosis, dilated vessels, and sparse perifollicular inflammatory cell infiltrate. Abnormal eosinophilic inclusions were noted surrounding the inner root sheath of a hair follicle (Figure 2). After appropriate treatment, the patient showed improvement of the perifollicular papules, facial spicules, and eyelash and eyebrow regrowth (Figure 3).

Questions

1. Given the clinical and histopathological presentation, what is the most likely diagnosis for this patient?
    a. Alopecia areata
    b. Atypical fungal infection, specifically blastomycosis
    c. Chronic eczematous dermatitis
    d. Virus-associated trichodysplasia spinulosa
    e. Viral warts

2. What is the causative pathogen associated with this cutaneous eruption?
    a. BK polyoma virus
    b. Human immunodeficiency virus
    c. Human papillomavirus
    d. JC polyoma virus
    e. Trichodysplasia spinulosa–associated polyomavirus

3. What additional studies could be useful in making the diagnosis if clinically not apparent?
    a. Electron microscopy
    b. Immunohistochemical staining
    c. Liver function tests
    d. PCR for BK virus
    e. Renal ultrasound

4. What is the safest next step for this patient given her dermatologic findings and recent transplant management history?

    a. Intravenous cidofovir
    b. Oral itraconazole
    c. Reduction in immunosuppressive regimen
    d. Topical 1% cidofovir
    e. Topical valaciclovir

Figure Legend

Figure 1: Eight-year-old child status following renal transplant with numerous tiny white folliculocentric papules and spicules on the face, with concomitant alopecia of the eyebrows and eyelashes.

Figure 2: Dermatopathology of a hair follicle at 100x magnification showing abnormal cytoplasmic eosinophilic inclusions (arrow) in the inner root sheath.

Figure 3: Eight-month follow-up visit showing improvement of the folliculocentric papules and spicules on the face with associated postinflammatory hyperpigmentation and regrowth of the eyebrows and eyelashes.

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[ANSWERS – please start on new page, following this heading. NOTE: ONLINE ONLY CONTENT]

1. Given the clinical and histopathological presentation, what is the most likely diagnosis for this patient?

    a. Alopecia areata
    b. Atypical fungal infection, specifically blastomycosis
    c. Chronic eczematous dermatitis
    d. Virus-associated trichodysplasia spinulosa

e. Viral warts

The correct answer is a. Virus-associated trichodysplasia spinulosa (VATS) is characterized by folliculocentric papules and keratin spicules on the central face and ears, with concomitant alopecia of the eyebrows and eyelashes[1]. Viral warts present as verrucous lesions and blastomycosis presents as pustules that evolve into ulcerated lesions. Neither present with alopecia or share this pathology. Similarly, blastomycosis would present with systemic signs and show broad-based budding yeast on pathology. A chronic eczematous dermatitis is typically defined by erythema, scale, and lichenification with spongiotic epidermis. Alopecia areata would be atypical on such an immunosuppressive regimen due to its autoimmune nature and the pathology does not include a follicular bulbar lymphocytic infiltrate.

2. What is the causative pathogen associated with this cutaneous eruption?
    a. BK polyoma virus
    b. Human immunodeficiency virus
    c. Human papillomavirus
    d. JC polyoma virus
    e. Trichodysplasia spinulosa–associated polyomavirus

The correct answer is e. VATS is a rare cutaneous eruption that results from trichodysplasia spinulosa polyomavirus (TSPyV) infection in immunosuppressed patients[1]. VATS prevalence is roughly equal between adults and children[2]. TSPyV is a ubiquitous virus, with early asymptomatic infection and eruption after immunosuppression[3]. Human papillomavirus causes viral warts, which do not share this pathology or present with alopecia. BK polyoma virus, human immunodeficiency virus, and JC polyoma virus are all associated with immunocompromised hosts; however, none cause this characteristic skin eruption.

3. What additional studies could be useful in making the diagnosis if clinically not apparent?
    a. Electron microscopy
    b. Immunohistochemical staining
    c. Liver function tests
    d. PCR for BK virus
    e. Renal ultrasound

The correct answer is a. Electron microscopy shows intranuclear viral particles within keratinocytes of hair follicles and can be helpful in diagnosis, although this may not be necessary due to the distinct clinical presentation[1,3,4]. TSPyV proliferates in the inner root sheath of hair follicles, resulting in abnormally increased cytoplasmic collections of eosinophilic keratin protein (trichohyalin) on histology[1]. These collections were apparent in our patient (Figure 2), and these, along with the characteristic history and presentation, are adequate evidence for diagnosis. TSPyV PCR can confirm viremia, but given this test's lack of availability, BK viral loads have been suggested as a surrogate marker for TSPyV viral load[4]. However, this patient was negative for BK virus PCR in the case presentation. Immunohistochemical stain, liver function tests, and renal ultrasound would provide no utility in diagnosis of VATS.

4. What is the safest next step for this patient given her dermatologic findings and recent transplant management history?
    a. Intravenous cidofovir
    b. Oral itraconazole
    c. Reduction in immunosuppressive regimen
    d. Topical 1% cidofovir
    e. Topical valaciclovir

The correct answer is d. Generally, treatment of VATS consists of reducing immunosuppressive medications as well as antiviral medications[4,5]. However, reduction in immunosuppression may cause recurrence of graft rejection in this patient. Oral itraconazole is a viable treatment option for blastomycosis; however, it plays no role in the treatment of VATS. Several reports in pediatric patients have described successful treatment of VATS with compounded topical 1% or 3% cidofovir, which is both a safe and effective option[4]. This patient was started on topical cidofovir 1% cream twice a day and showed significant improvement in pruritus and clinical appearance after two months and sustained response for six months (Figure 3) with initial crusting in the weeks prior to healing. There is one report of a patient treated with intravenous (IV) cidofovir initially, followed by topical cidofovir, which accelerated clearance of the lesions; however, in this child, it is difficult to justify IV medication when a safe topical alternative exists[5]. Finally, topical valaciclovir may be used if topical cidofovir is unavailable, but has slower onset.

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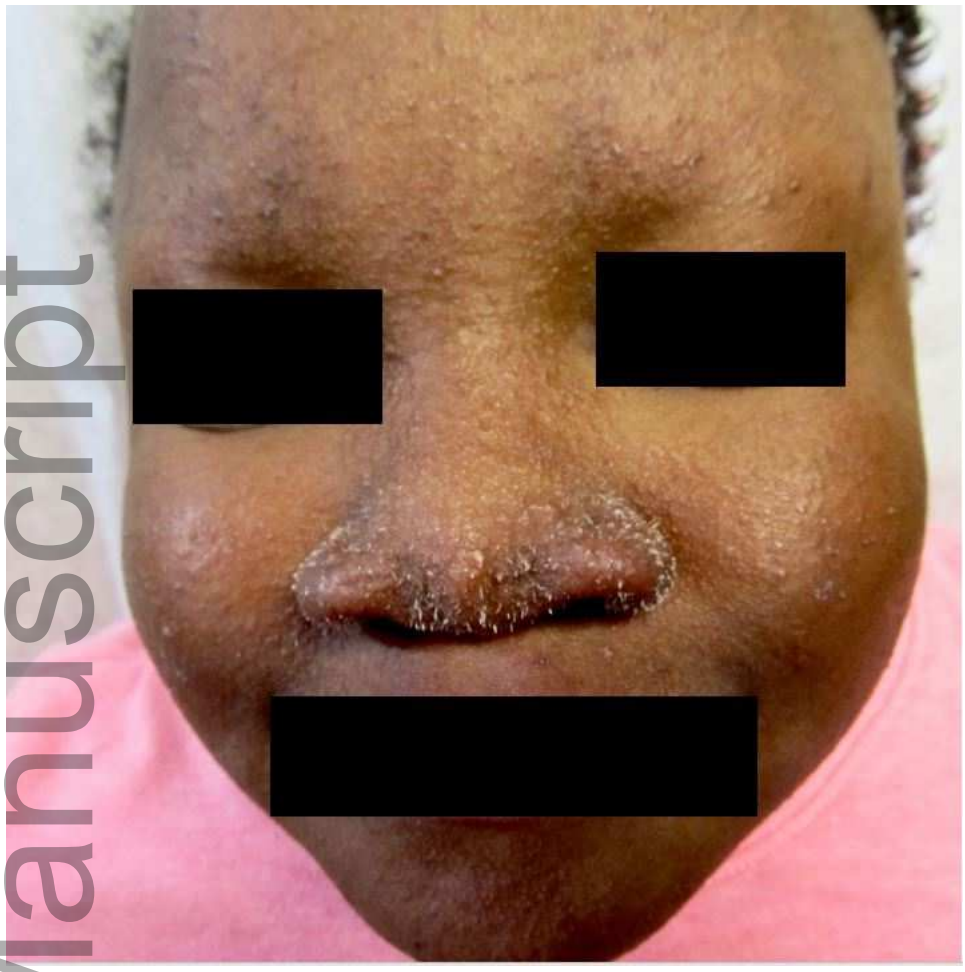

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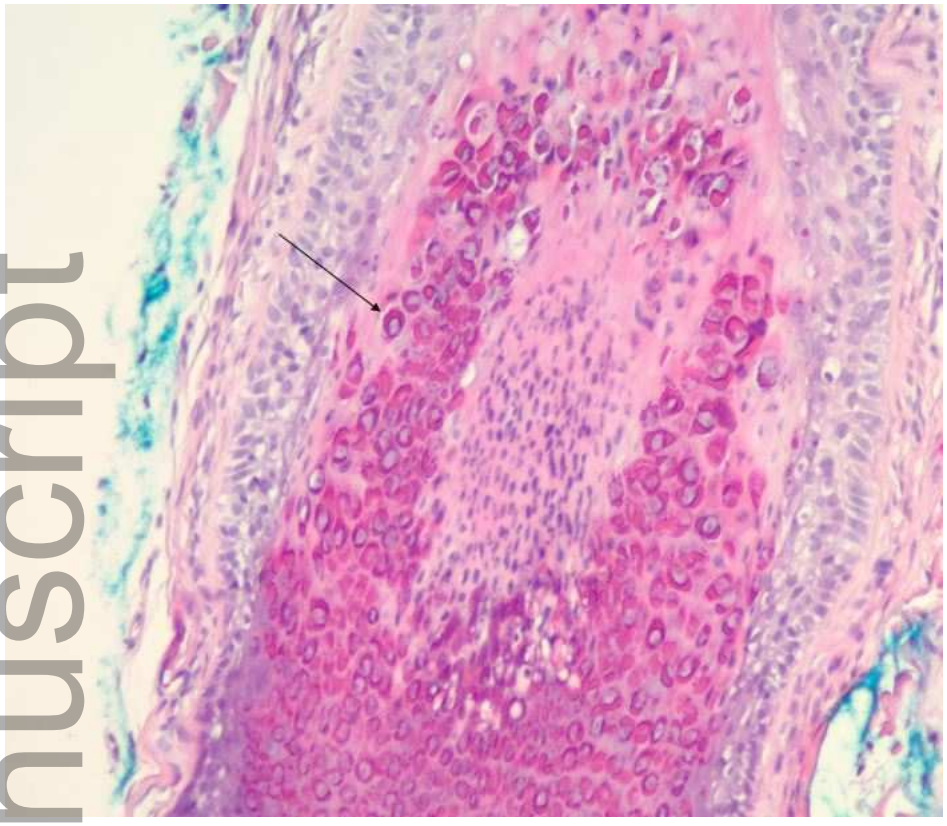

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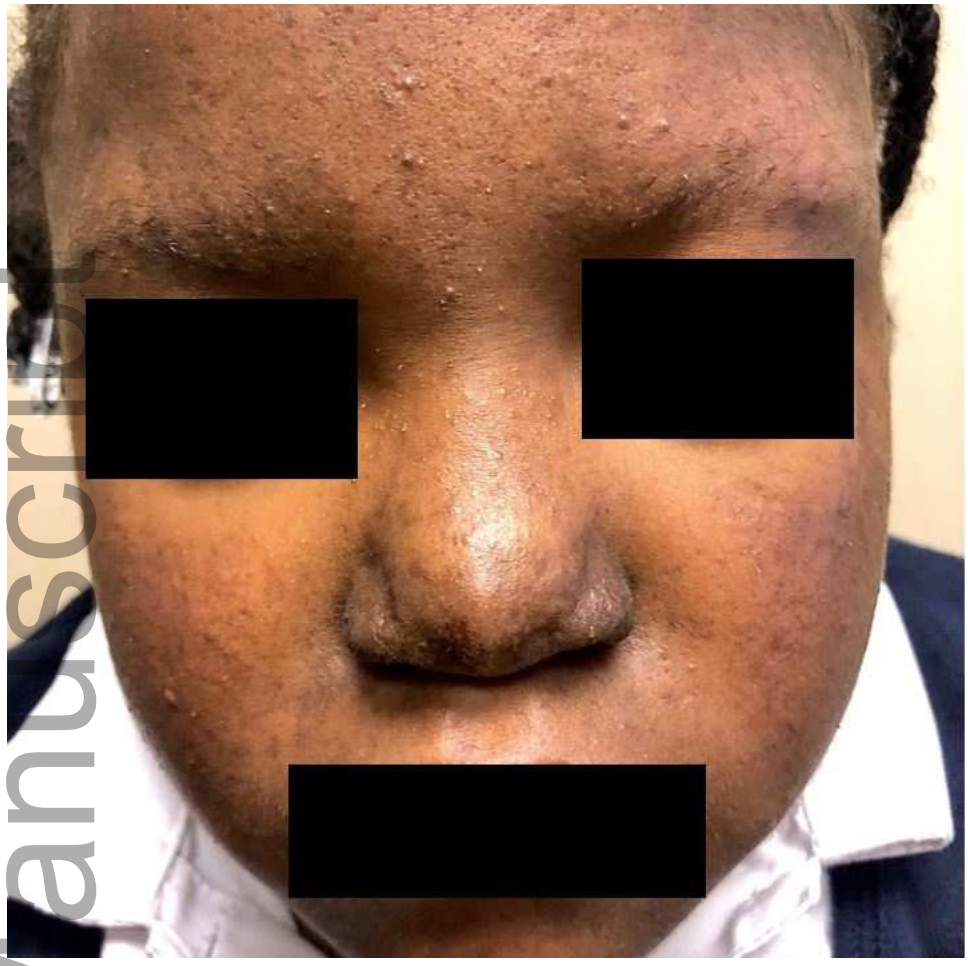

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