[redacted]yo s/p [redacted] transplant for [redacted] w/ new progressive facial rash

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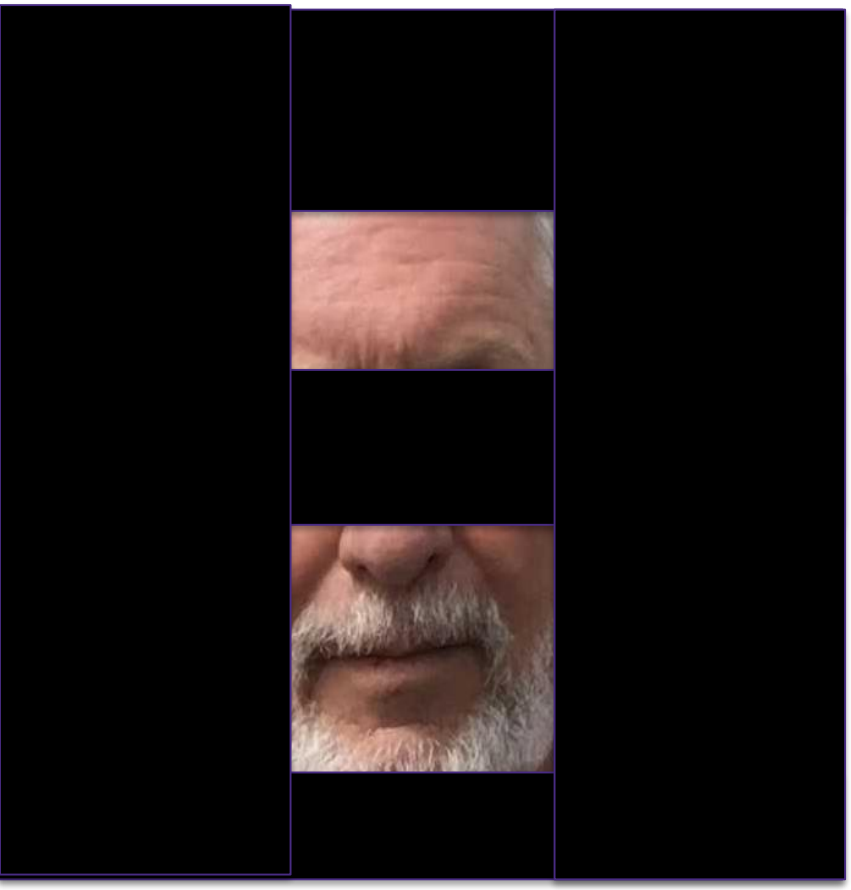
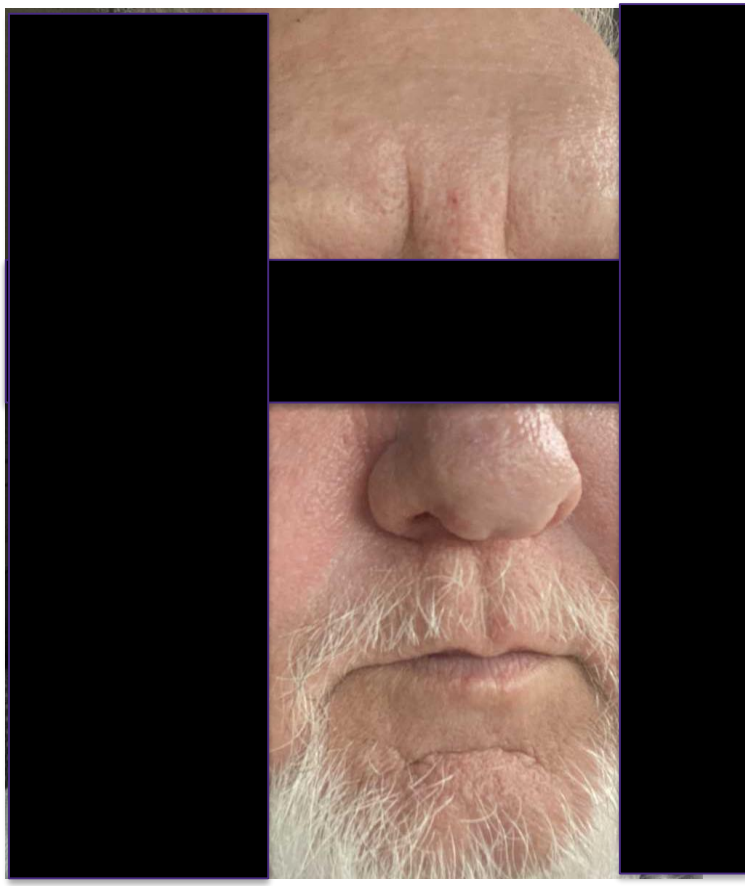
[redacted] yo s/p [redacted] transplant for [redacted] w/ new progressive facial rash

- [redacted]years s/p [redacted] for [redacted]
- Notices worsening facial edema and diagnosed with IJ DVT and started on Xarelto
- Progressive facial swelling over the next few months with new skin changes:
  - Spiky bumps and new hair loss of eyelashes, eyebrows and beard
  - Lesions are not painful
- No fevers, chills, diarrhea, nausea/vomiting etc.

[redacted] yo s/p [redacted] transplant for [redacted] w/ new progressive facial rash



6 months later…



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Transplant History:
- CMV D+/R-, EBV D+/R+
- No episodes of rejection
- Post operative course c/b prolonged rhinovirus, VAP, hyperammonemia

Social History/Relevant Exposures
- Lives in [redacted]
- Worked [redacted], now [redacted]
- No illicit drug use
- No pets
- Outdoor enthusiast

Immunosuppression:
- Tacrolimus, MPA, Prednisone

Antimicrobial prophylaxis:
- TMP/SMX, Azithromycin

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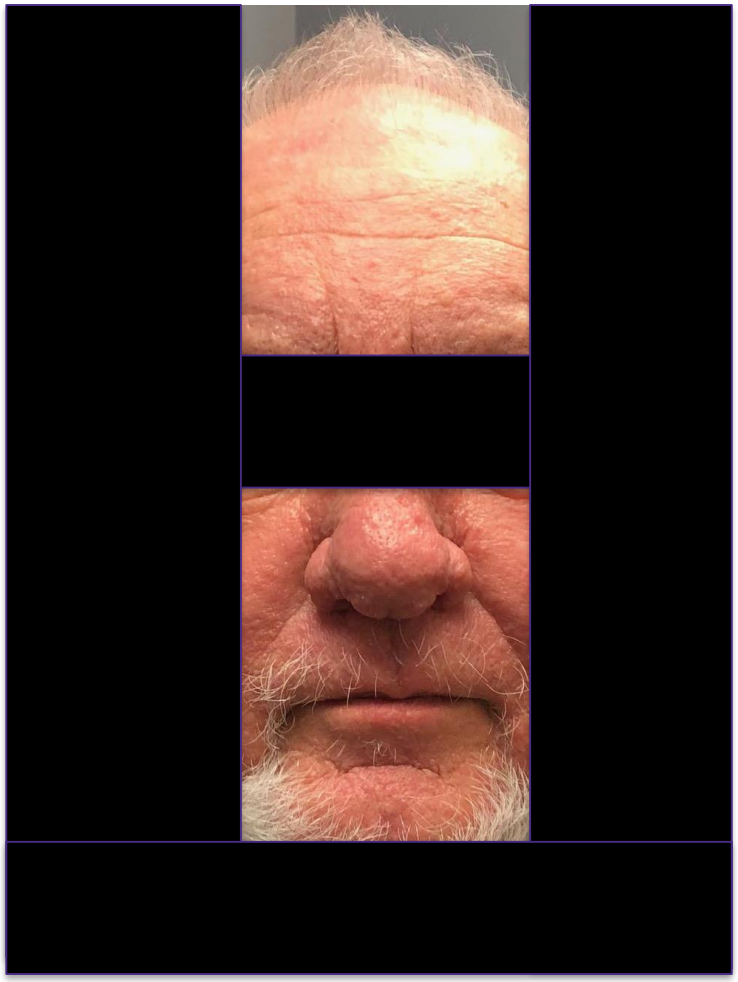
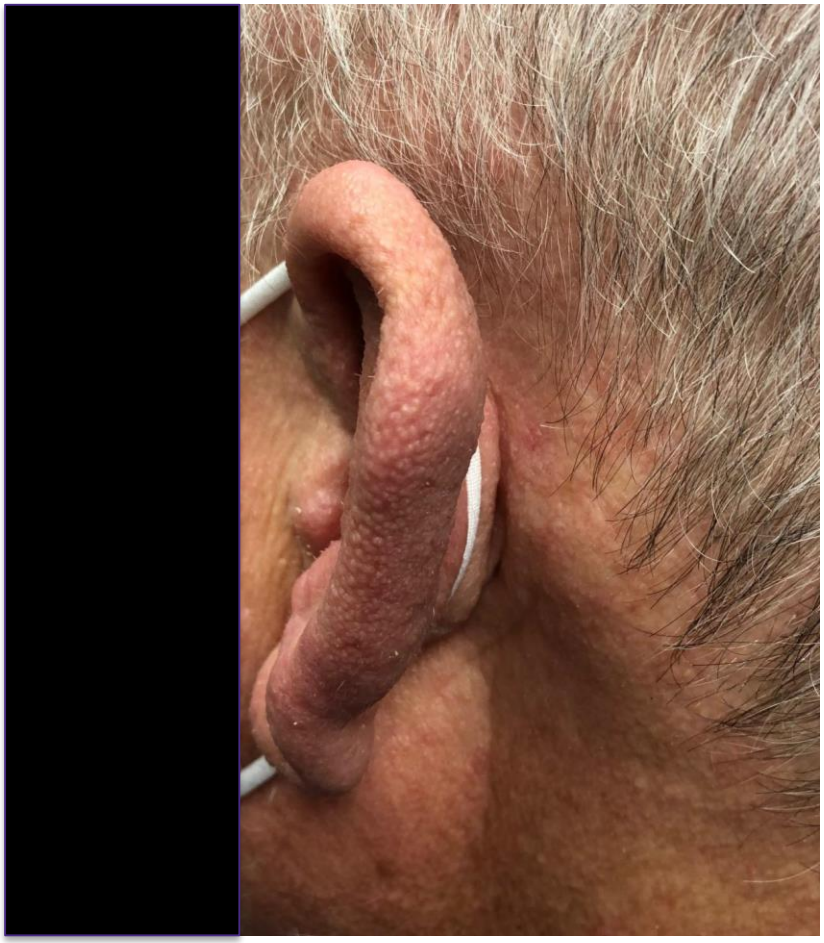
Vitals:
Afebrile.

Examination:
General: Comfortable, in no acute distress.
HEENT: No sinus tenderness, see skin exam. EOMI. Anicteric
Skin: Innumerable **non tender skin-colored papules** on the nose forehead cheeks ears, many with a **central filiform spike. No eyebrow hair or eyelashes. Beard is patchy.**
Neuro: Non focal



[redacted] yo s/p [redacted] transplant for [redacted] w/ new progressive facial rash



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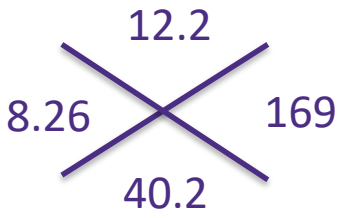
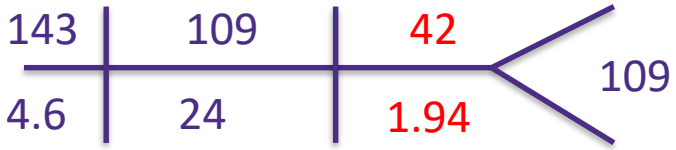
Labs:





ANC: 4830

ALC: 520

Tacrolimus 6.8 ng/ml

AST: 21 U/L

ALT: 17 U/L

Alk Phos: 52 U/L

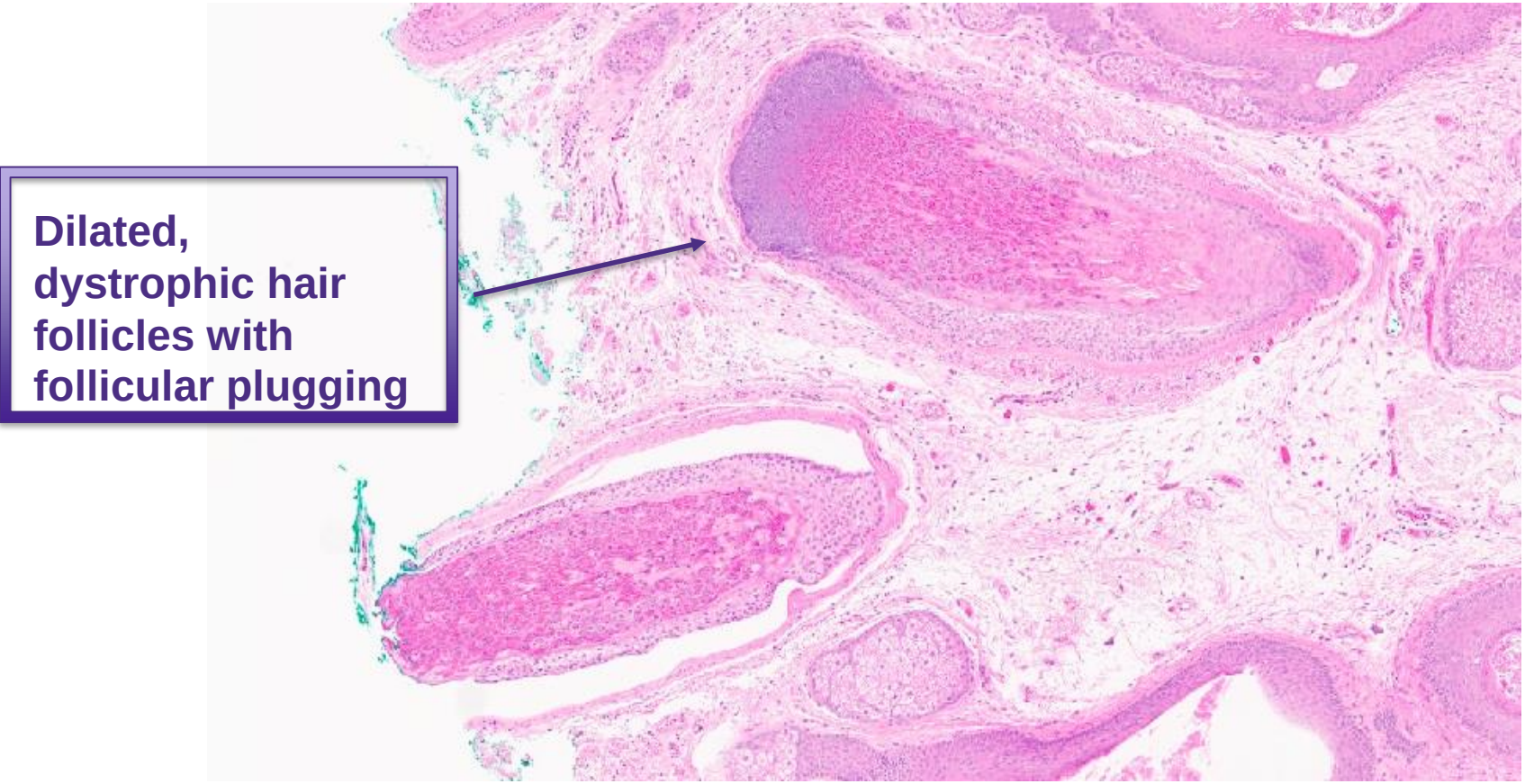
Tbili: 0.5 mg/dl

Poll Question 1:

What is the most likely etiology of this patient's rash?

- **A. Fungal**
- **B. Viral**
- **C. Parasitic**
- **D. Bacterial**
- **E. Noninfectious**

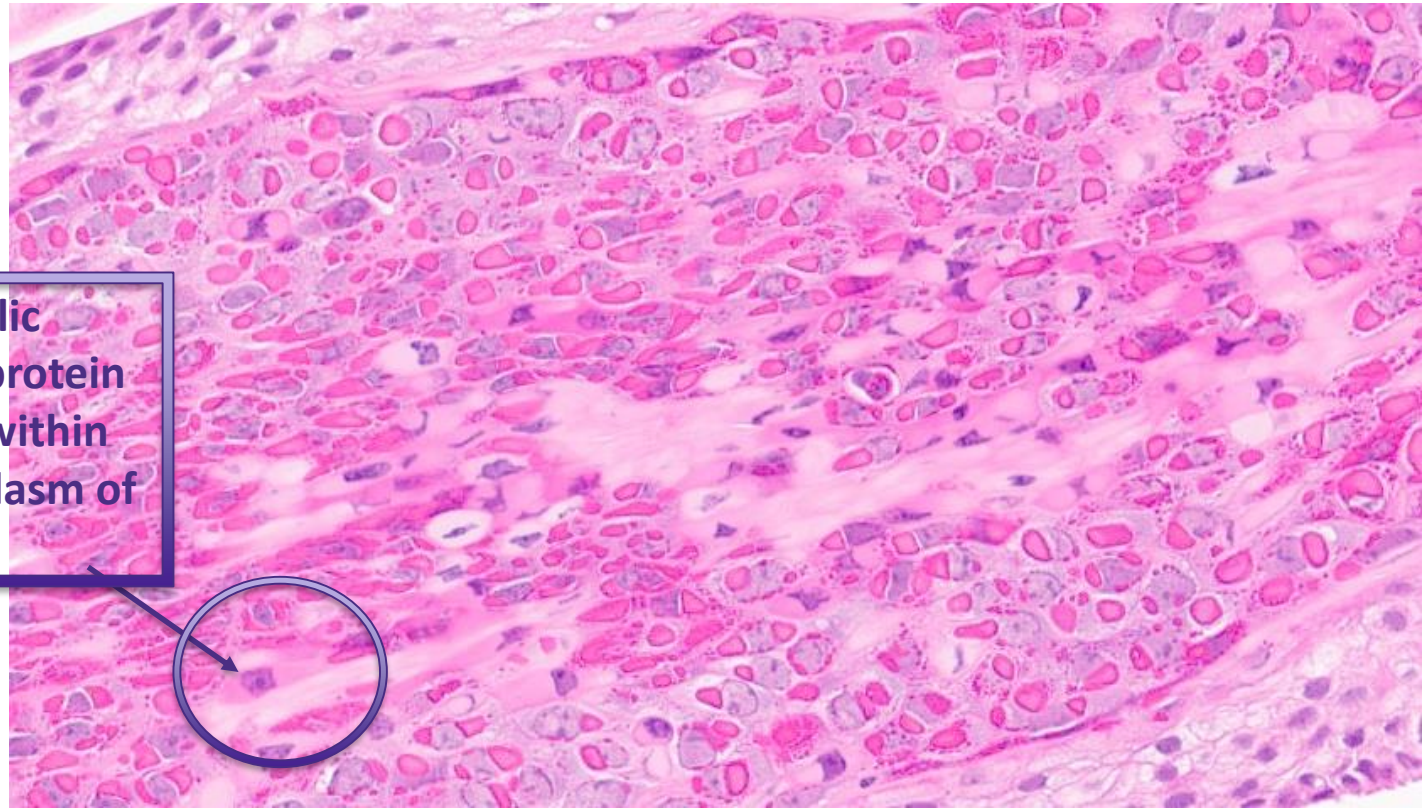
Histopathology



H&E stain, 10x magnification

Photo Credit: Mugahed Hamza, MBBS

Histopathology



H&E stain, 40x magnification

Photo Credit: Mugahed Hamza, MBBS

Poll Question 1:

What is the most likely etiology of this patient's rash?

- **A. Fungal**
- **B. Viral**
- **C. Parasitic**
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- **E. Noninfectious**

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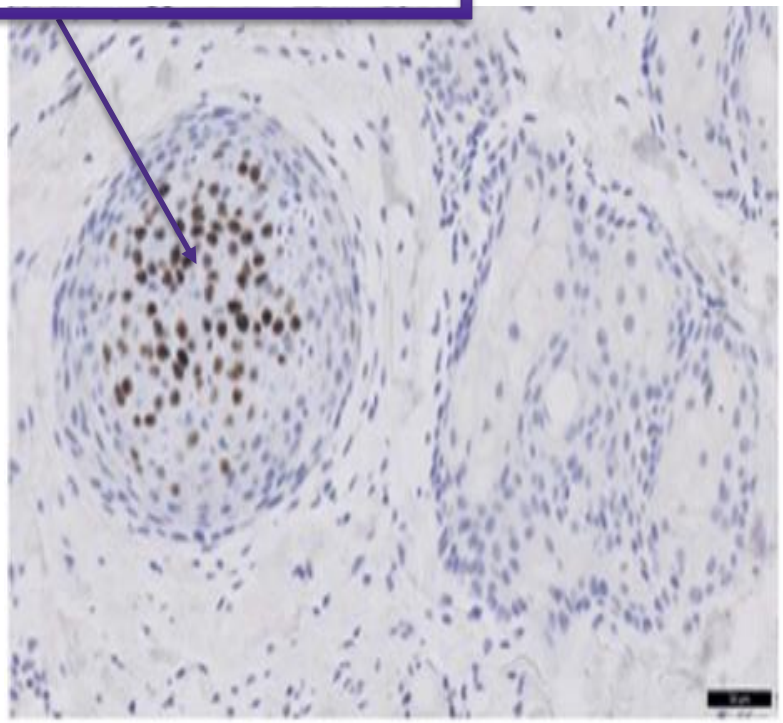
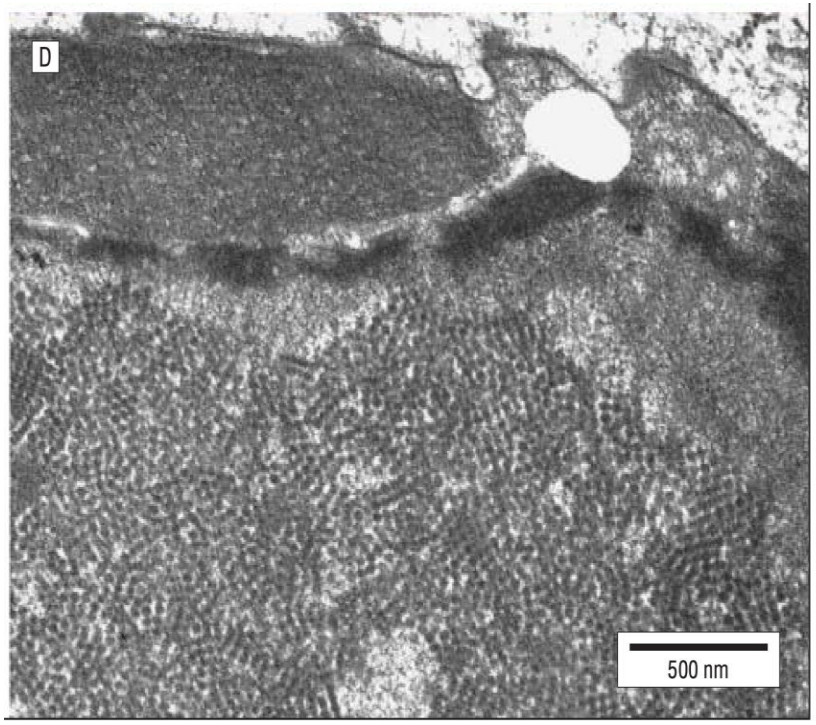
Nuclear positivity of inner root sheath cells



SV40 Immunostain, original magnification x 20



EM: “bumpy” appearance of **viral inclusions**

Image Credit: Left: PMID 33354613; Right: PMID: 32475005

Poll Question 2:

What is the most likely virus causing this patient's infection?

- **A. BK Polyomavirus (BKPyV)**
- **B. JC Polyomavirus (JCPyV)**
- **C. Merkel Cell Polyomavirus (MCPyV)**
- **D. Trichodysplasia spinulosa-associated polyomavirus (TSPyV)**
- **E. Molluscum Contagiosum**
- **F. HIV**

Trichodysplasia Spinulosa

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Trichodysplasia spinulosa

Overview and history

- **First described in 1995**
  - **“Disseminated follicular spiny hyperkeratosis”**
  - **associated with cyclosporine**
- **Formally named “ Trichodysplasia spinulosa” in 1999 after discovery of viral etiology/associated with cyclosporine in general**
- **2010 TSPyV as causative virus, renamed “Trichodysplasia spinulosa associated polyomavirus**

Polyomaviruses

- Family: Polyomaviridae
- Small (40-50nm in diameter)
- Icosahedral, Non-enveloped, DNA viruses
- Hosts: Mammals and birds
- Infection is common, disease is rare
- 15 currently known human polyomaviruses (HPyV)
  - BK Virus
  - JC Virus
  - Merkel Cell virus
  - Trichodysplasia spinulosa-associated polyomavirus (TSPyV)

1. PMID: 34662051
2. PMID: 35482045

Trichodysplasia spinulosa: Epidemiology

- Viral infection is common, clinical disease is rare
  - Seroprevalence of TSPyV between **63%—80%** of healthy and immunocompetent adult patients[1-3]
  - Approaches **90%** in kidney transplant recipients[4]

- Transmission likely early in childhood between siblings and mother/child
  - Seroprevalence is high from birth until 2 months, subsequently increases from age 3 to age 11 -> adult levels[1,3]

- Geographic distribution unknown

- No Gender predilection

1.PMID: 34662051
2. PMID: 25766994
3. PMID: 32475005
4. PMID: 21801610

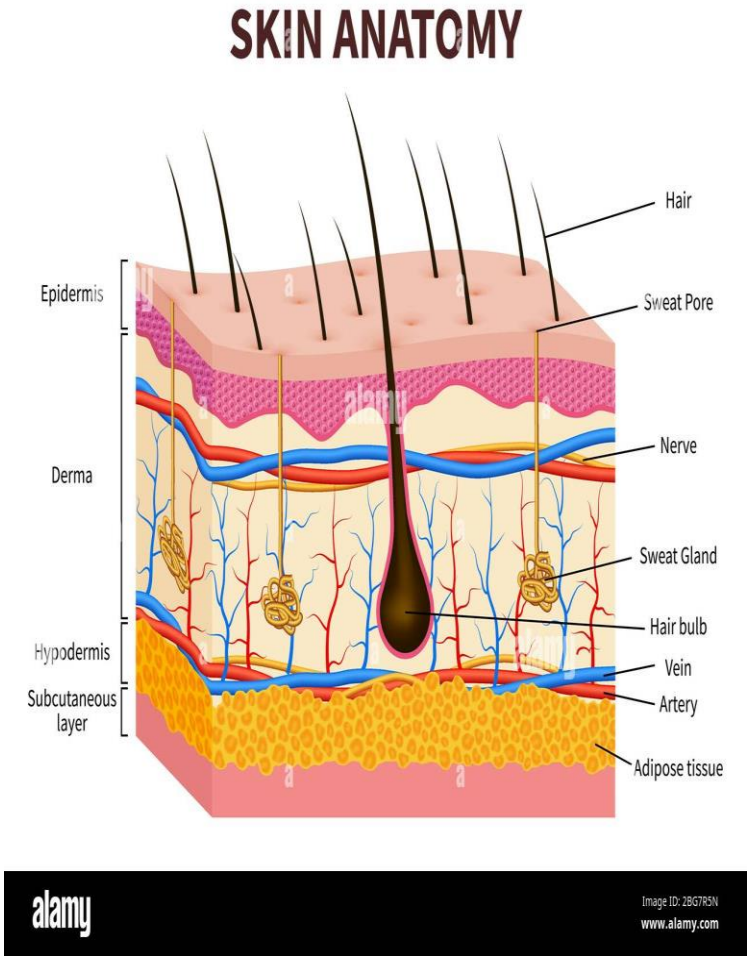
Trichodysplasia spinulosa: Epidemiology

- Disease is rare
- ~40 cases in SOT population[1] (Jose 2020)
- ~60 cases total[2] (Curman 2021)
- Risk Factors For Disease[3]
  - **Solid organ transplantation**
  - HIV
  - Immunosuppressive medications
  - **Hematolymphoid malignancy**

1.PMID: 32475005
2. PMID: 33559344
3.PMID: 34662051

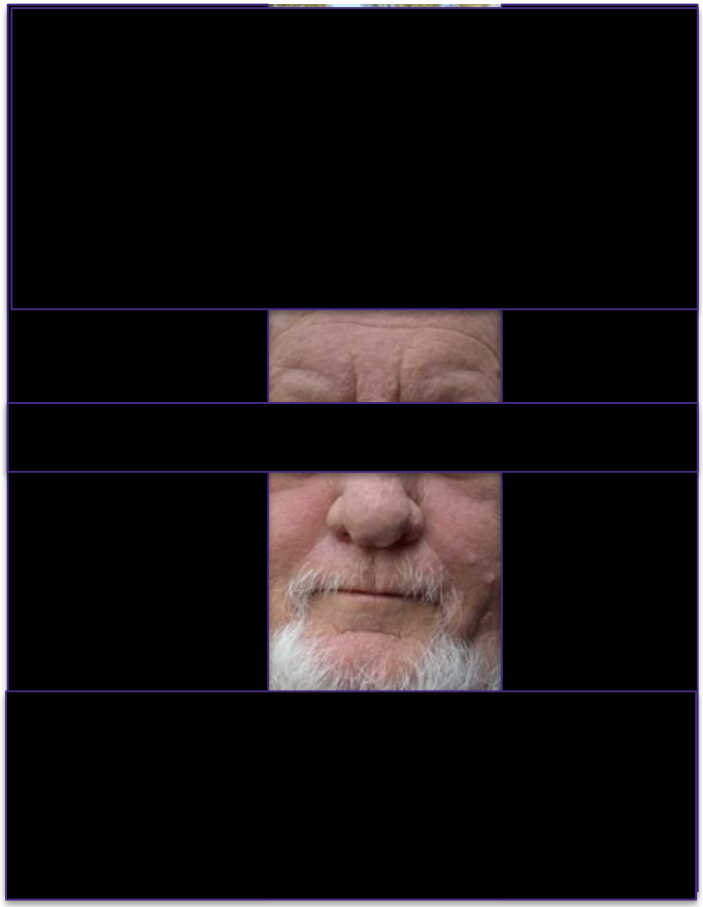
Trichodysplasia spinulosa: Pathophysiology

- Virus appears to target keratinocyte inner root sheath epithelium
- Dermal papillae absent in infected follicles which leads to (temporary) alopecia
- Proposed mechanism of disease
  - Primary exposure
  - Re exposure
  - Reactivation of latent virus
    - Latent site of reactivation unknown (possibly lymphoid tissue)



Trichodysplasia spinulosa: Clinical Presentation

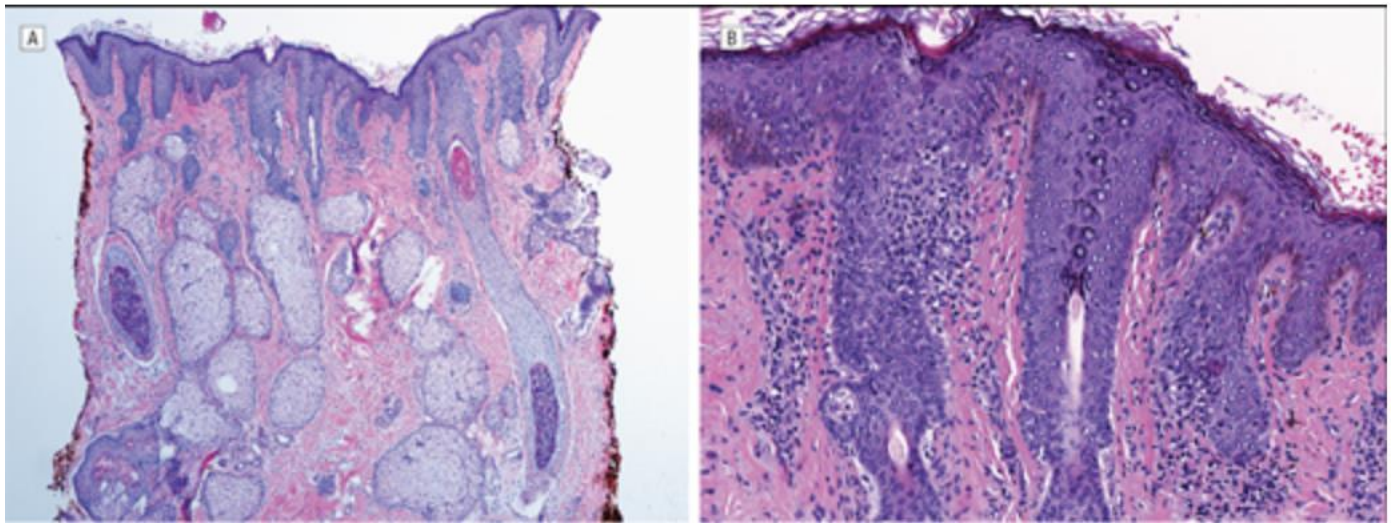
- Fleshy papules and spicules involving the face
- Rare involvement of trunk and extremities
- Non-scaring alopecia of eyebrows
- Painless
- Occasionally associated with pruritis
- Psychological distress



PMID: 33559344
PMID: 32475005

Trichodysplasia spinulosa: Diagnosis

- **Gold Standard = PCR of TSPyV in affected tissue (with typical histology + clinical presentation)**
  - **Viral load PCR** ⬆ **(**10^4–10^7 genome copies per cell)[1]
- **Histopathology**



Hematoxylin-eosin, original magnification ×40 and x100[2]

1.PMID: 23593936
2. PMID: 22351786 (Photo Credit)

Trichodysplasia spinulosa: Diagnosis

- **Transmission Electron Microscopy = intranuclear clusters of icosahedral viral inclusions with a "bumpy" appearance**

- **Serology not useful**

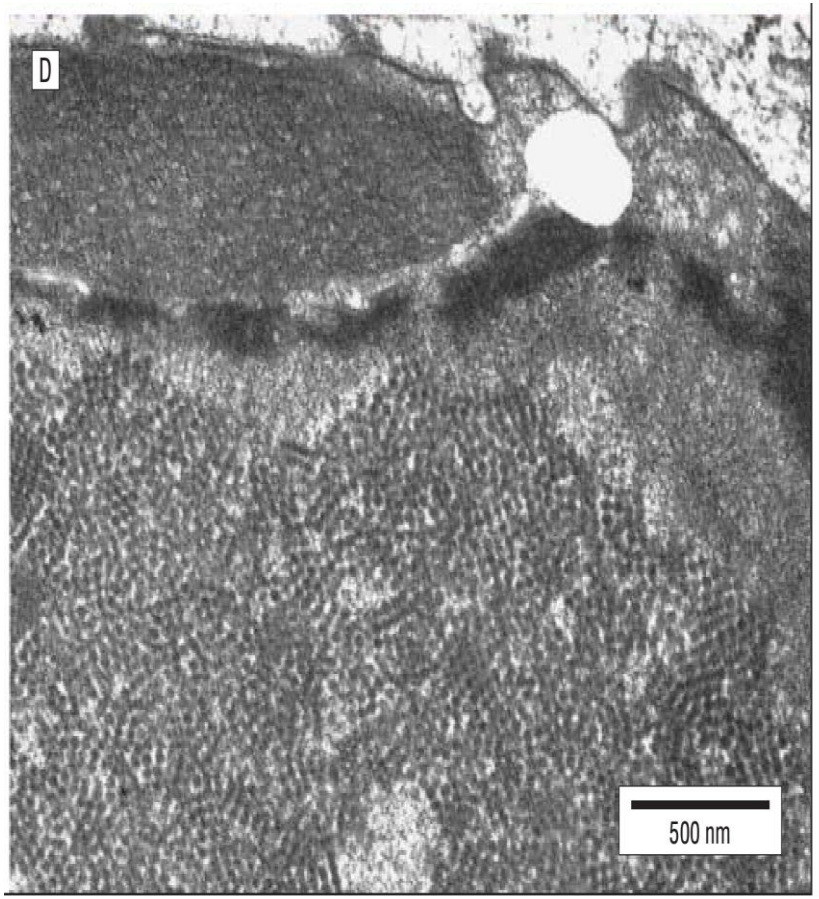


Photo Credit:
PMID: 32475005

Poll Question 3

What is the most effective treatment?

- **A. Valganciclovir**
- **B. Acyclovir**
- **C. Fluconazole**
- **D. Cidofovir**
- **E. Other**

Trichodysplasia spinulosa: Treatment

- Goal of treatment is to reduce viral load by anti-viral effect or by reduction of immunosuppression
- Data limited to case report, case series
- ”First line” treatment with reduction of immunosuppression, 3% topical cidofovir (in vitro data), Oral valganciclovir (unclear mechanism)
- Anecdotal reports of other treatments with mixed/poor results
- Optimal duration is unclear
- Spontaneous resolution can occur

PMID: 25446403
PMID: 33559344

Trichodysplasia spinulosa: Treatment

"Good" efficacy	n
Oral Valganciclovir	11
Reduced Immunosuppression	5
Cidofovir 3%**	4
Oral leflunomide	2
Manual extraction	1

n=number of treatments

Adopted from: Curman et al 2021
PMID: 33559344

Trichodysplasia spinulosa: Treatment

"No/Poor" efficacy	n
Topical retinoids	12
Topical steroids	9
Topical imiquimod	6
Topical or oral antivirals*	9
Oral retinoids	3
Topical antibiotics	3
Topical antifungals	3
Oral antibiotics	2
Oral antihistamines	2
Topical calcineurin inhibitors	2
Oral glucocorticoids	1

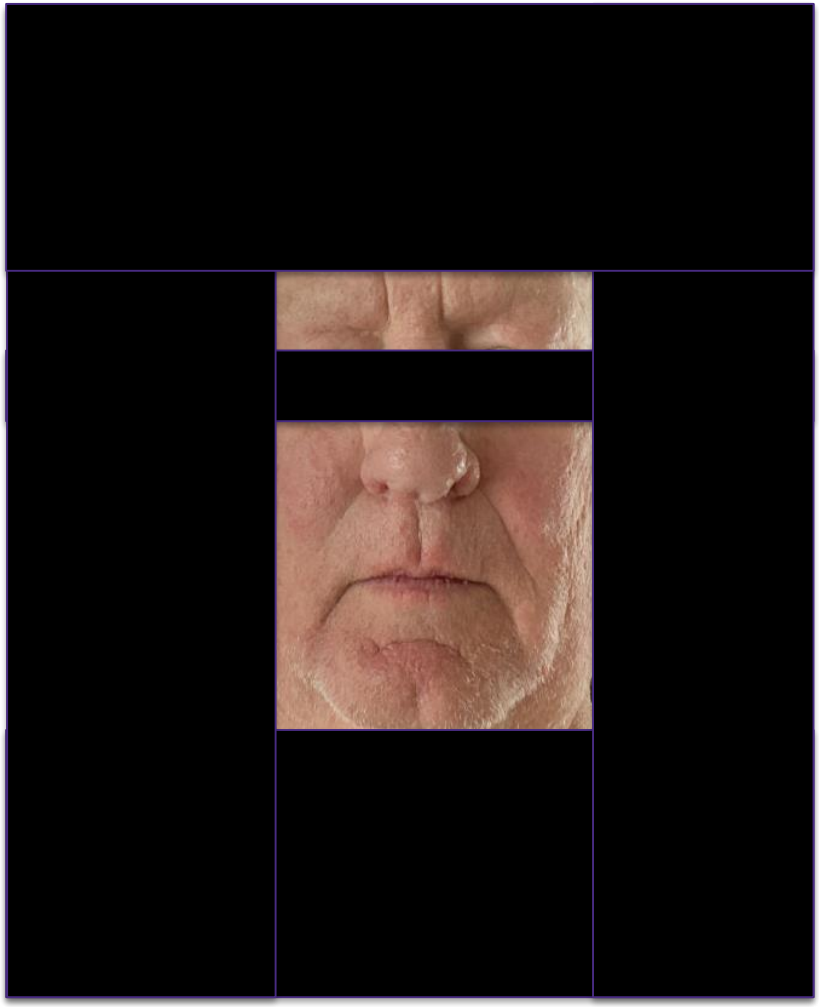
N=number of treatments; *Other than cidofovir or valganciclovir

Adopted from: Curman et al 2021;PMID 33559344

Return to case..

- Treated with
  - Topical Cidofovir 3% BID
  - Mupirocin 2% ointment PRN
  - Hydrocortisone 2.5% cream
  - Reduction of MPA
  - Added leflunomide

- Noted improvement with sunlight/outdoor exposure



Trichodysplasia spinulosa: Case reports and review of literature

Aju Jose[1] | Taimur Dad[1] | Andrew Strand[2] | Julie Y. Tse[3] | Natalia Plotnikova[4] | Helen W. Boucher[2] | Mark J. Sarnak[1] | Scott J. Gilbert[1] | Nitender Goyal[1]

- Case report and review of literature
- 29 cases of TS in SOT
  - 10 pediatric; 19 adults
- Median age of diagnosis: 37
- Time to onset of diagnosis: 11 months
- Frequently delay in diagnosis
- Most patients treated with antivirals
  - 17/19 responded well (oral valganciclovir, topical cidofovir)

PMID: 32475005

Summary/Key Points

- Trichodysplasia Spinulosa is a rare infection caused by human polyomavirus (TSPyV)
- Infection is common, clinical disease is rare and associated immunosuppression (SOT and hematological malignancy)
- Consider TS in patients who present with a fleshy, spiky rash involving the mid-face
- Treatment is not well defined but there has been reported improvement with reduction in immunosuppression, topical cidofovir 3%, and oral valganciclovir