

West Coast Transplant Infectious Disease Case

Nico Campalans, MD

UW Infectious Disease Fellow, PGY-4

History of Presenting Illness

A [REDACTED] [REDACTED] with a history of acute respiratory distress syndrome (ARDS) vs. rapidly progressive undiagnosed interstitial lung disease (ILD) underwent bilateral orthotopic lung transplant (2025) and presents to ED with **several days of profound fatigue 11 months after transplant.**

Past Medical History

- ARDS vs. rapidly progressive ILD (explant pathology with organizing diffuse alveolar damage)
- Atrial fibrillation status-post left atrial appendage clipping
- Hypertension
- Eczema

Social History



Resides in the Pacific Northwest on rural property. Moldy bathroom in basement.



Retired [REDACTED] Avid-gardener pre-transplant, has not gardened since.



[REDACTED] previously ran a small cattle operation, but has no current pets or livestock exposure.



No sick contacts or TB risk factors. Negative QuantiFERON gold prior to transplant.

Timeline

2025 - Bilateral orthotopic lung transplant (CMV D-/R+, EBV D+/R+) + LAA clipping due to intra-operative AF w/ RVR

Pre-transplant micro

Recipient sputum: Rare
Geotrichum spp.

Donor respiratory cultures:
H. influenzae, *S. epidermidis*,
C. albicans

Post-transplant micro

BAL: *Aspergillus versicolor*

Sacral ulcers: HSV-1/2 +

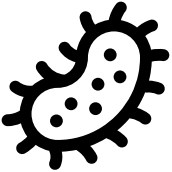
ulcer: HSV-2+

Immunosuppression:

- Induction with methylprednisolone + basiliximab
- Transitioned to MMF 100mg BID, prednisone 20mg PO QD, tacrolimus

Antimicrobials:

- Inhaled ambisome & tobramycin per protocol
- Cefepime + linezolid for donor respiratory cultures
- Isavuconazole for *A. versicolor* isolated on early post-transplant bronchoalveolar lavage (BAL)
- Acyclovir → valganciclovir for HSV-2 lesions + CMV ppx



Timeline

2 months post-transplant

- Meets with outpatient ID – sacral & penile lesions resolved
- Remains on isavuconazole for *A. versicolor*, stopped 1 month later after 3 months of treatment

6 months post-transplant

- New *A. fumigatus* pulmonary infection diagnosed after new cough, chest CT showing R lung nodules and ground glass opacities (GGOs). Resumed treatment with isavuconazole

9 months post-transplant

- Obtained end of therapy CT which showed resolved nodules and GGOs. New small bilateral pleural effusions and moderate pericardial effusion present. Surveillance bronchoscopy cultures were negative, and isavuconazole stopped.

11 months post-transplant

- Presents to hospital following days of worsening fatigue

On arrival

BP 129/88, HR 101, Temp 96.5 °F, RR 24, SpO2: 97 % on RA

General: Ill-appearing

Cardiovascular: Regular rate and rhythm, **distant heart tones**, no murmurs, rubs, gallops, **jugular venous distention**. No lower extremity edema.

Pulmonary: Normal work of breathing, decreased breath sounds at bilateral bases.

Neuro: Patient alert and oriented to person, place, and time. No focal neurological deficits.

Skin: no lesions

125	88	106	121
5.6	20	3.5	

11	11	388
	35	

	0.4	
565		948
	163	

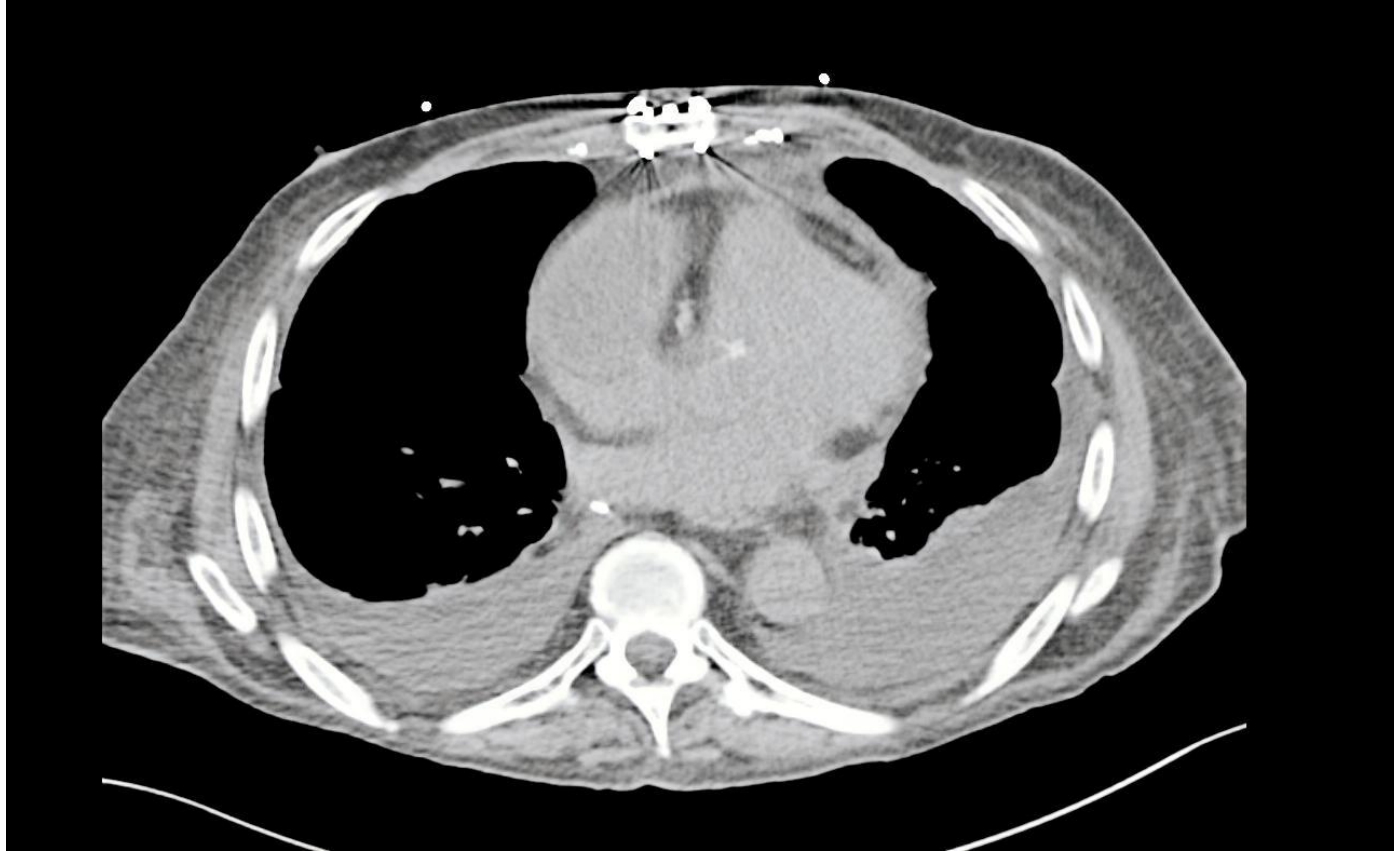
Troponin **455.4ng/L**

BNP **1767 pg/mL**

CK-MB 5.4ng/mL

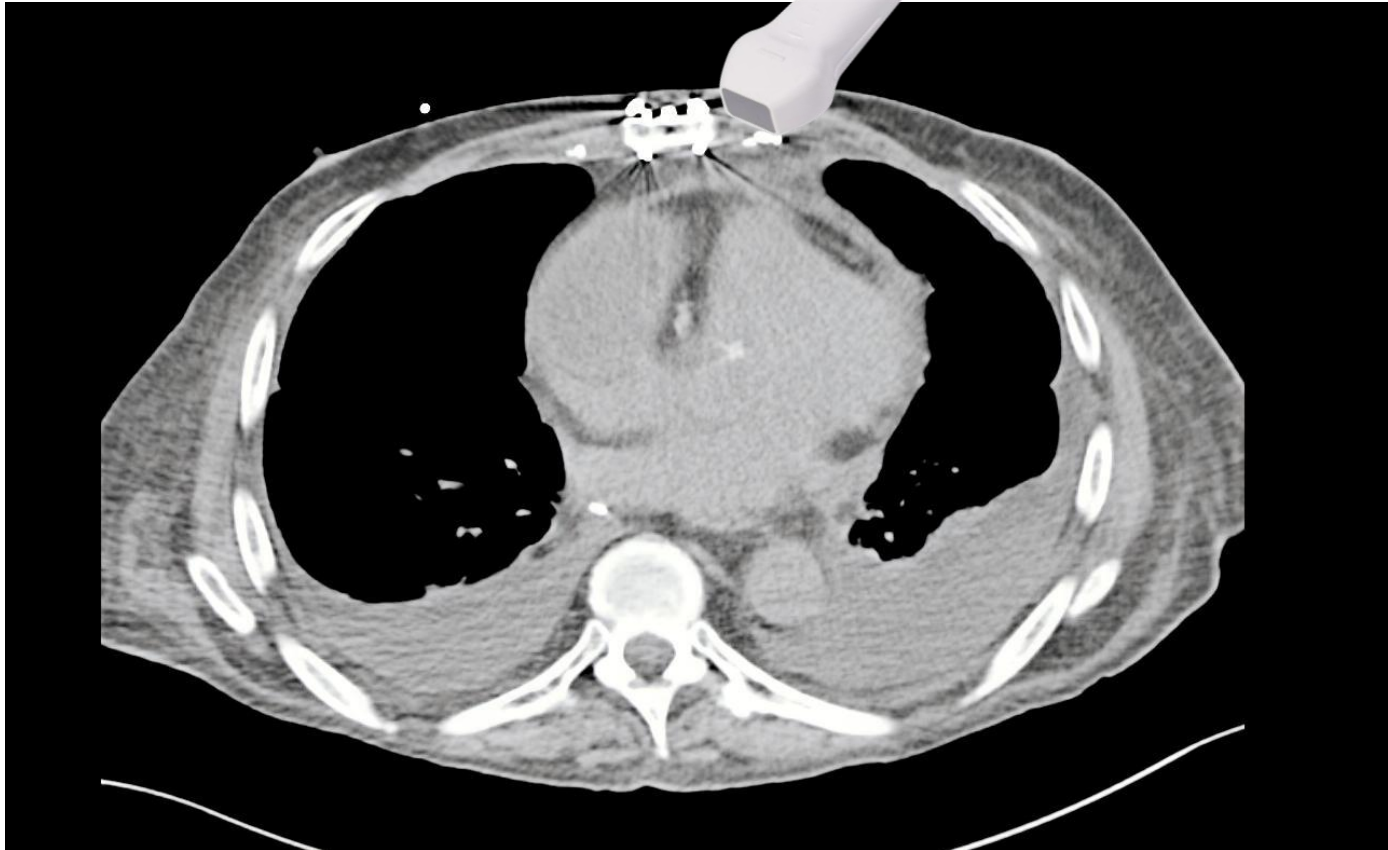
Tacrolimus level: **24.9 ng/mL**

CT Chest without Contrast



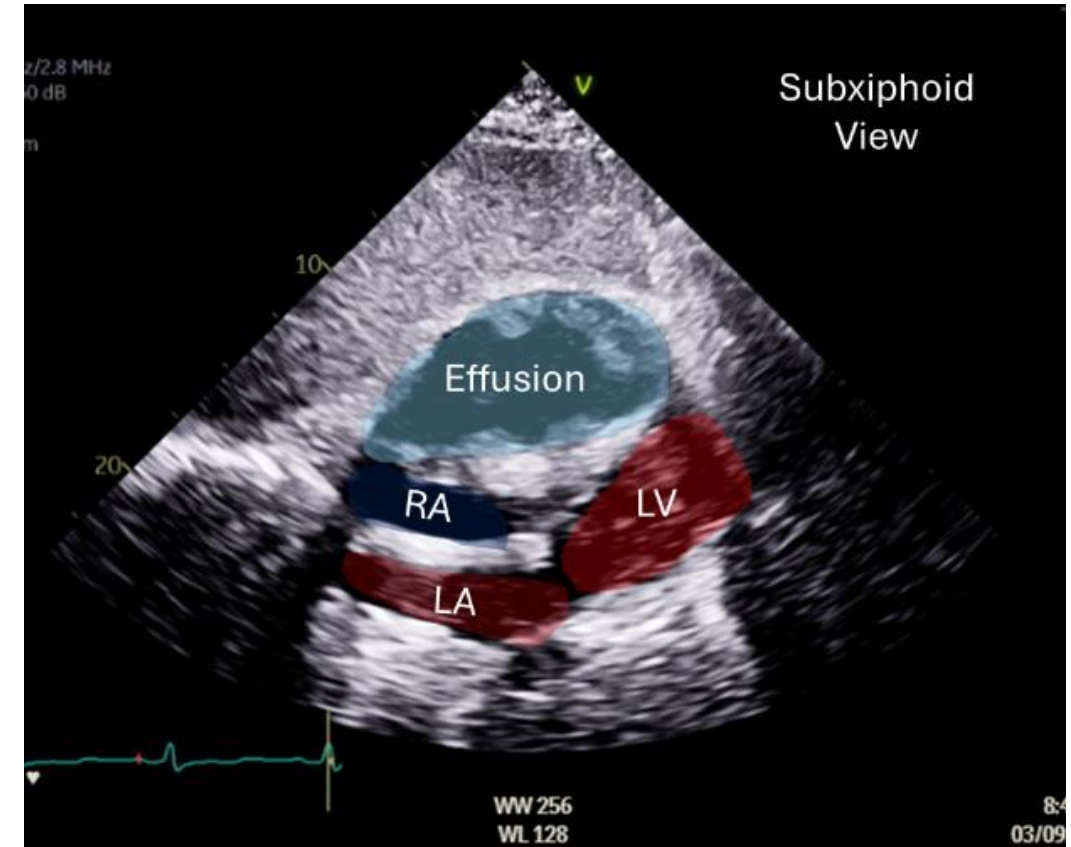
Large 10 x 6 x 9 cm right inferolateral encapsulated pericardial fluid collection, moderate bilateral pleural effusions

CT Chest without Contrast



Large 10 x 6 x 9cm right inferolateral encapsulated pericardial fluid collection, moderate bilateral pleural effusions

TTE



Large loculated anterior effusion measuring approximately 4.5cm compressing RV. RV small and collapsed.

Recap:

A [REDACTED] with a history of ARDS vs. rapidly progressive ILD s/p bilateral orthotopic lung transplant c/b pulmonary aspergillosis presents to the ED with several days of profound fatigue, found to have loculated pericardial effusion with radiographic concern for cardiac tamponade.

Differential Diagnosis for Pericarditis

Common infectious etiologies:

Viral - Enterovirus (coxsackieviridae and echoviridae), Epstein-Barr virus (EBV), and cytomegalovirus (CMV).

Bacterial - *Mycobacterium tuberculosis*, particularly in subacute and chronic presentations.

Rare bacterial causes:

Coxiella burnetii, *Borellia burgdorferi*, *Pneumococcus*, *Streptococcus* species, *Staphylococcus* species, *Haemophilus* species, *Chlamydia* species, *Mycoplasma* species, *Legionella* species

Pericarditis

Noninfectious:

Acute myocardial infarction
Rheumatologic (e.g. SLE, scleroderma, RA)
Drug-induced (e.g. procainamide, hydralazine).
Neoplastic

Possible fungal etiologies given recent isavuconazole course:

Candida species, *Aspergillus* species, *Fusarium* species, *Scedosporium* species, *Lomentospora prolificans*, Mucormycoses

How would you empirically treat?

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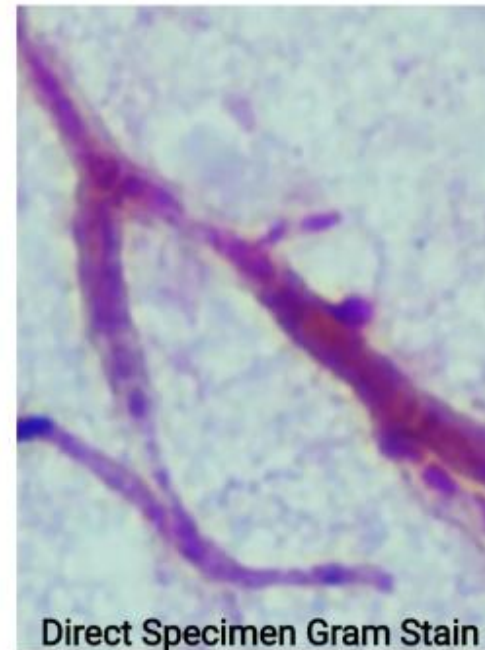
- A) Vanc, cefepime
- B) Vanc, cefepime, amphotericin
- C) Vanc, cefepime, amphotericin, and azole
- D) No antibiotics
- E) Steroids

Diagnostic Procedures & Results:

- Blood Cultures: negative on 2 sets
- Cryptococcus serum antigen: negative
- Coccidioides Ab: negative
- Left Pleural Fluid Culture: negative
- CMV Blood PCR: Negative
- Pericardial CMV PCR: Negative
- AFB Pericardial Fluid Culture: negative
- Pericardial Galactomannan: 0.642 optical density index
- **Pericardiotomy Tissue Culture:** 10 colonies of mould
- **Pericardial Fluid Culture:** >30 colonies *Verruconis gallopava*
- **Pericardial Fluid Bacterial/Fungal PCR:** *Verruconis gallopava*
- **Right Pleural Fluid Bacterial Culture:** 1 colony presumptive *Verruconis* species, PCR positive for *A. fumigatus*

Diagnosis

- Acute angle branching hyphae, cylindrical conidia seen on stain and KOH prep
- Dematiaceous mold isolated 3 days later identified as *Verruconis gallopava*



(Image courtesy of Lori Bourassa, PhD, MPH)



MRI Brain with contrast

- Left parietal occipital ring-enhancing and diffusion restricting lesion
- Additional focus of left parietal subcutaneous cortical diffusion

What antifungal regimen might you choose?

A [REDACTED] with a history of ARDS vs. rapidly progressive ILD s/p bilateral orthotopic lung transplant c/b pulmonary aspergillosis presents to the ED with several days of profound fatigue, found to have disseminated *V. gallopava* infection (pulmonary, pericardial, CNS).

- A) Isavuconazole
- B) Amphotericin B + flucytosine
- C) Voriconazole + Amphotericin B
- D) Posaconazole + Amphotericin B

Treatment

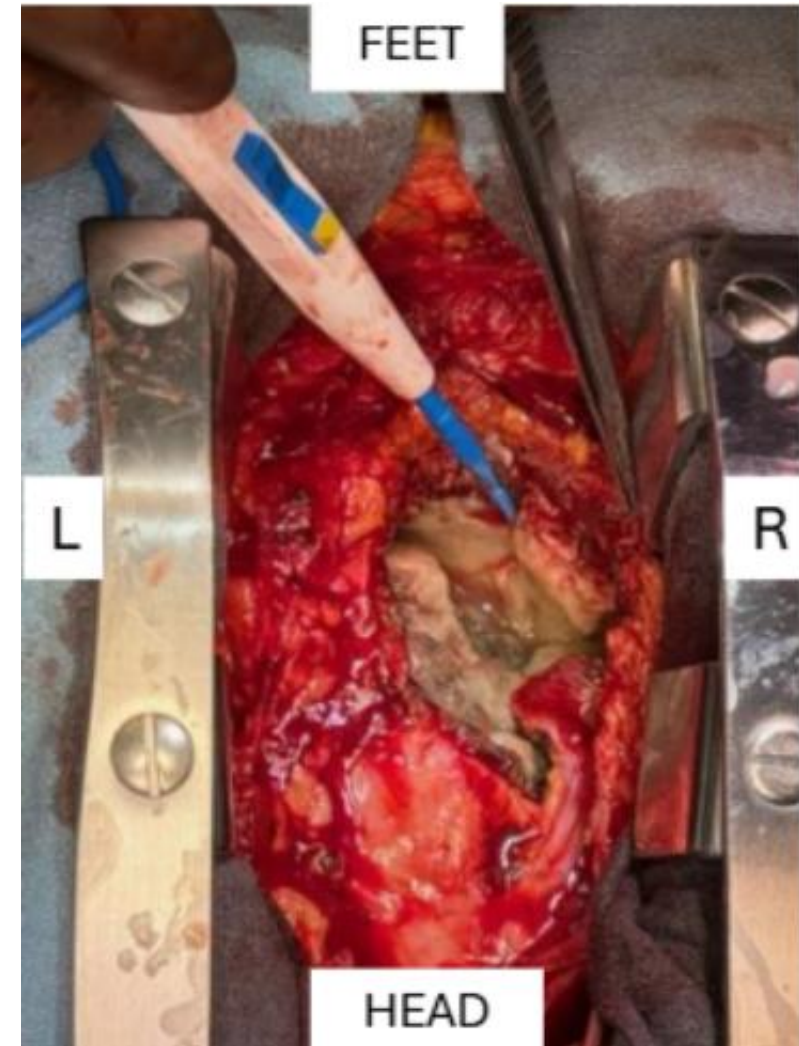
Started on **liposomal amphotericin B** and **posaconazole** based on reports of favorable activity

Neurosurgery evaluated, **deferred debridement**

Pericardial debridement and decortication of **thick fungal rind**. **LAA clip retained** due to surgical constraints.

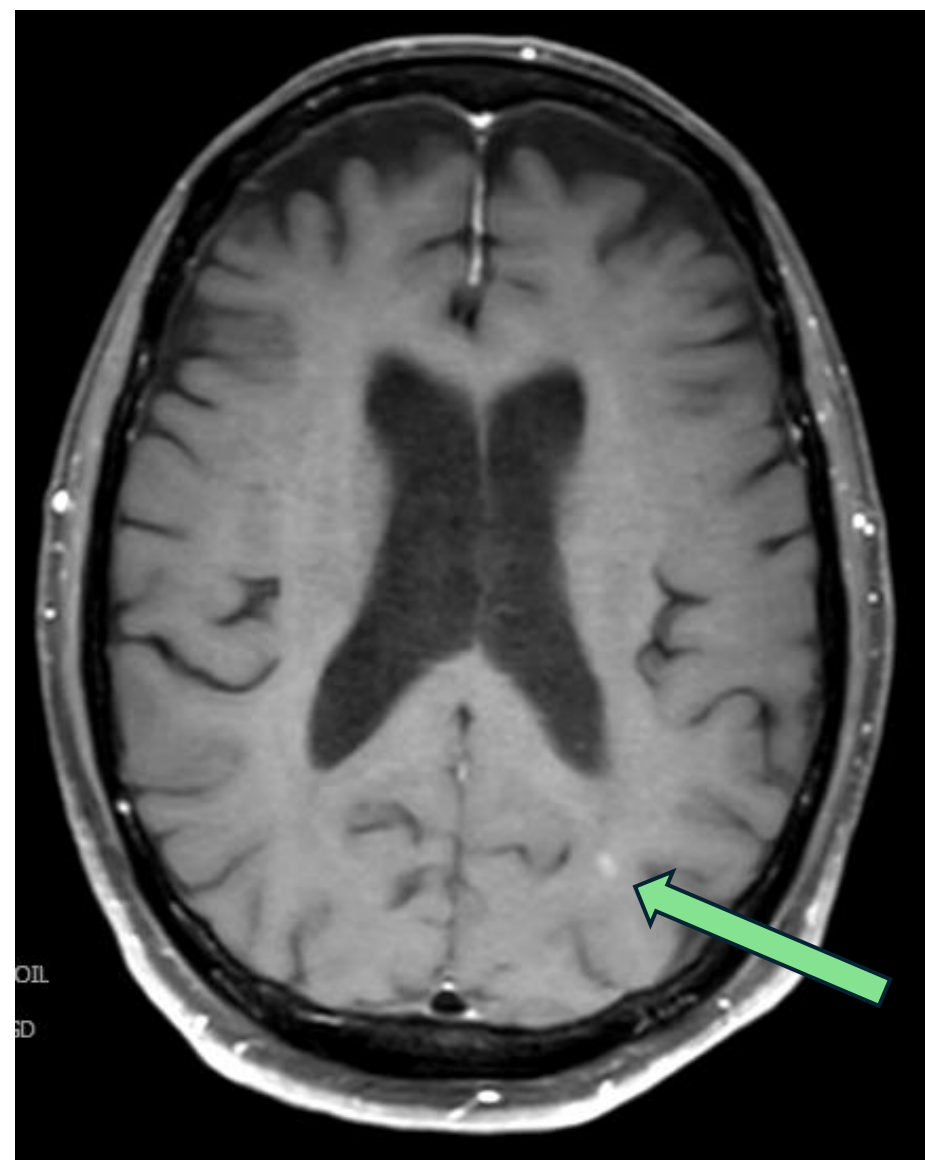
Decortication of thick R pleural rind for trapped lung

Discharged home on **micafungin** and **posaconazole**. Remains home and stable on therapy!





Start of therapy



4 weeks into therapy

Verruconis gallopava

Thermophilic dematiaceous mold,
uncommon cause of **phaeohyphomycosis**

Known by many names

- *Diplorhinotrichum gallopavum*
- *Scolecobasidium gallopava*
- *Dactylaria gallopava*
- *Ochroconis gallopava*

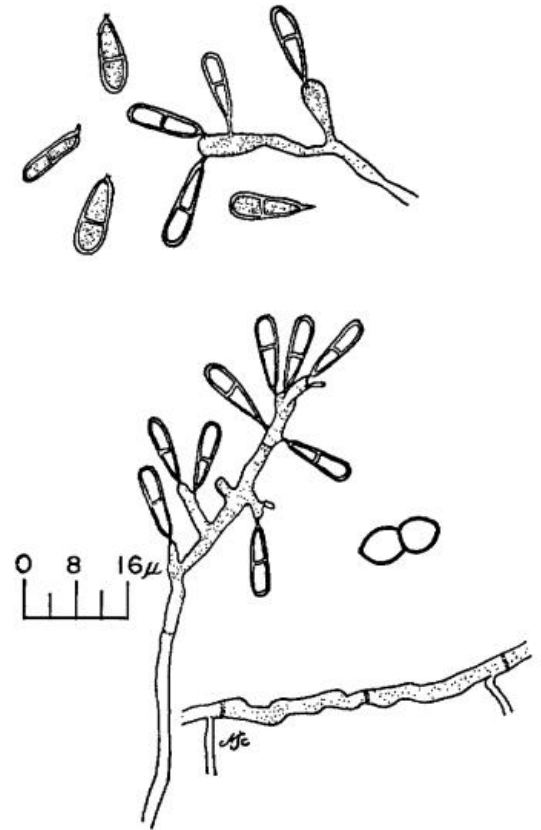
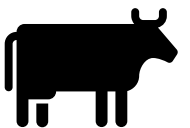
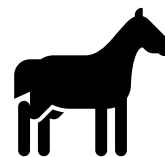


Fig. 2.— Camera lucida drawings. *Diplorhinotrichum gallopavum*.

First described in 1964 in?





Meleagris gallopavo

Verruconis gallopava

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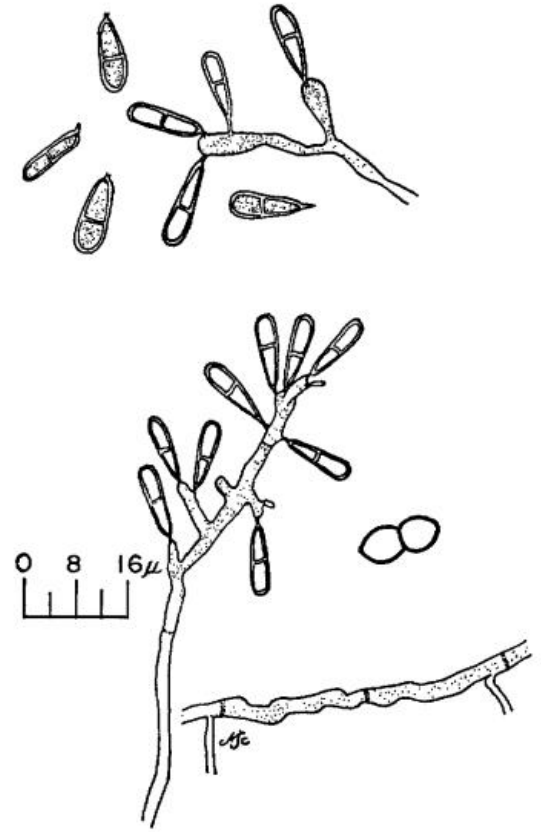


Fig. 2.— Camera lucida drawings. *Diplorhinotrichum gallopavum*.

**First described in 1964 in young turkey poult
following an outbreak of avian encephalitis –
600/4,000 birds of a flock developed symptoms
with 67% case morality rate**

Verruconis gallopava

We have isolated *D. gallopava* from geothermal habitats and from self-heated coal waste piles (Table 1). The 393 samples examined represented a wide range of pH values (<2 to >10). The fungus was isolated from thirty-one samples, all acidic (pH 2.1 to 5.9), suggesting that this is its preferential habitat in nature.

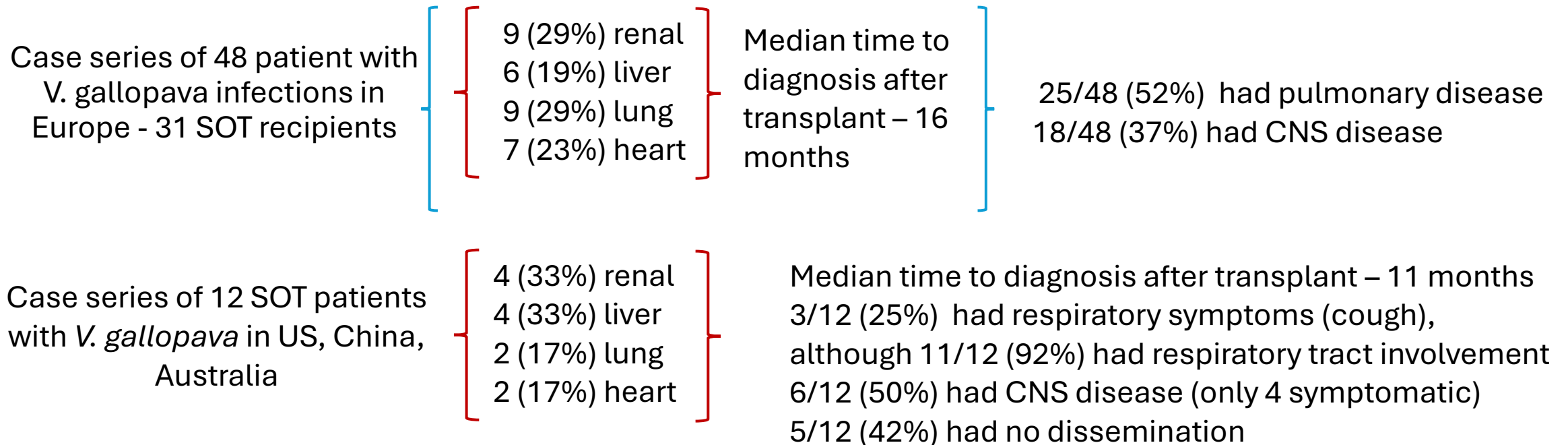
Table 1 Sample Sites which yielded *Dactylaria gallopava**

Sample site	Temperature†	pH‡
Thermal soil, Roaring Mountain, YNP§	42–43° C	4.5
Thermal soil, Solfatara Plateau, YNP	38.5–49.5	4.0
Thermal soil, Rush Lake Meadow, YNP	57.8–61.5	4.3
Thermal soil, Sylvan Springs, YNP	29	2.1
Hot spring effluent, Nymph Creek, YNP	50	2.8
Hot spring effluent, Sylvan Springs, YNP	48	2.9
Hot spring effluent, Ebro Springs, YNP	43	2.9
Hot spring effluent, Cyanidium Creek, YNP	46	3.0
Coal waste pile, Sonman, Pennsylvania	36–68	5.9
Coal waste pile, Mather, Pennsylvania	35–71	3.5

***Verruconis gallopava* infections in solid organ transplant (SOT) recipients**

Presentation ranges from cutaneous to pulmonary to disseminated infection with predilection for central nervous system

Alemtuzumab induction associated with infection within first 6 months after transplant



Verruconis gallopava and pericardial disease

- One case of *V. gallopava* infection in a patient with steroid-dependent autoimmune hemolytic anemia
- Identified after diagnostic bronchoscopy for RLL mass-like consolidation
- Started on posaconazole although developed new pericardial effusion after 3 weeks.
- Diagnostic pericardiocentesis negative for infection.
- Ultimately received 9 months of posaconazole with radiographic resolution of effusion and nodule.



Empiric Therapy

<i>V. gallopava</i> (n = 18)	MIC or MEC (mg/L)		
	Range	50%	90%
Amphotericin B	0.125-4	0.25	0.5
Flucytosine	0.5-64	4	32
Fluconazole	0.4-64	64	>64
Itraconazole	0.0016-4	0.125	0.5
Voriconazole	0.5-2	1	2
Posaconazole	<0.016-4	0.031	0.125
Caspofungin	0.25-1	0.5	1
Anidulafungin	0.016-0.125	0.031	0.063

Halliday et al. report isavuconazole MIC 4 - >8mg/L (n=5)

What regimen might you choose?

- A) Isavuconazole
- B) Amphotericin B + flucytosine
- C) Voriconazole + Amphotericin B
- D) Posaconazole + Amphotericin B

Antifungal Therapy in SOT recipients with *V. gallopava*

Antifungal Therapy	Lung involvement without CNS disease (n=25)	CNS disease (n=18)
Ampho B	1 (4%)	2 (11%)
Azoles	11 (44%)	2 (11%)
Ampho B + Azoles	11 (44%)	7 (39%)
Ampho B + Flucytosine + azoles	0 (0%)	6 (33%)

*Pooled from 48 patient case series with 31 SOT recipients

Antifungal Therapy	Lung involvement without CNS disease (n=6)	Lung involvement + CNS disease (n=6)
Ampho B	1 (17%)	2 (33%)
Azoles	2 (33%)	0
Ampho B + Azoles	3 (50%)	2 (33%)
Ampho B + Flucytosine + azoles	0	2 (33%)

Fluconazole
Itraconazole
Voriconazole

Surgical Management of Disease

- Overall described case survival with *V. gallopava* is 43.8%
 - Decreases to 22% with CNS disease
- Survival with brain abscess improves with complete surgical debridement (38%) compared to limited resection or aspiration (14%) across all phaeohyphomycoses
- Epicardial LAA clip retained in our patient – unclear if this should be implicated as source. No hardware associated cases described, although would likely favor explantation of implicated hardware when feasible

Olorofim and *Verruconis gallopava*

- Fungal dihydroorotate dehydrogenase inhibitor
- Oral formulation
- Olorofim accessible through eIND shows *in vitro* activity, possible salvage agent. No *in vivo* cases described.
- Single arm, open-label, phase-2b study. 203 patients with invasive fungal disease or pulmonary aspergillosis treated with olorofim
 - 25% of patients SOT recipients
 - 27% successful global response at 84 days
 - 63% successful clinical response at 54 days

Organism	Antifungal agent	Number isolates tested	MIC or MEC (mg/L)				
			Range	Modal	Geometric mean	MIC ₅₀ or MEC ₅₀	MIC ₉₀ or MEC ₉₀
<i>Verruconis gallopava</i>	Olorofim	10	0.008–0.125	0.008	0.02	0.015	0.06
	Amphotericin B	10	0.5–2	1	1	1	2
	Anidulafungin	10	0.06–0.125	0.125	0.105	0.125	0.25
	Isavuconazole	5	4–>8	>8			
	Posaconazole	10	0.125–0.25	0.25	0.216	0.25	0.25
	Voriconazole	10	0.5–4	2	1.414	2	2

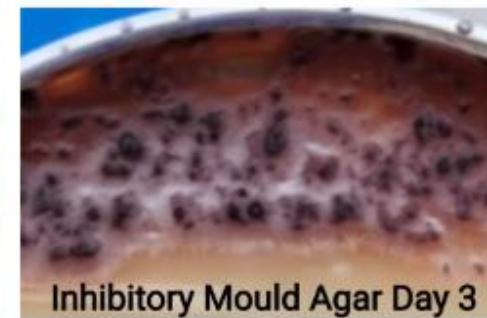
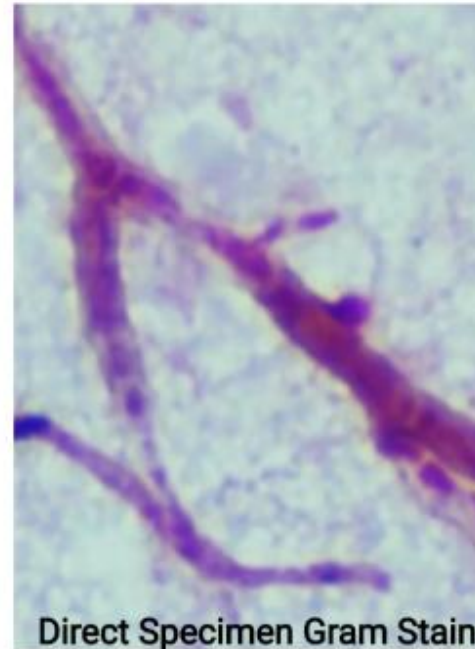
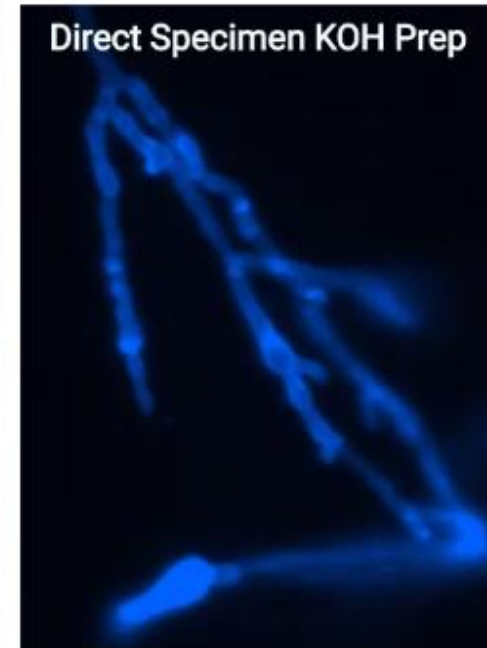
Summary points

***Verruconis gallopava* is a neurotropic dematiaceous mold that causes phaeo hyphomycoses in immunocompromised hosts**

The differential of breakthrough fungal infections in solid organ transplant recipients on isavuconazole is broad

Empiric antifungal therapy can be tailored to sites of involvement and should ultimately be guided by susceptibility testing

A multidisciplinary approach is critical to achieve a rapid diagnosis and surgical source control along with adjunctive antifungal therapy



(Image courtesy of Lori Bourassa, PhD, MPH)

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