Fever, Neutropenia, and a Rash

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CASE PRESENTATION

16 year old male admitted for chemotherapy

4 days of fever, chills, and cough

Past medical history:
- Pre-B cell ALL with CNS relapse
- Bactrim and fluconazole prophylaxis
- ADHD
- Osteomyelitis of left second metatarsal

Family history: Brother with Hepatitis C

Exposures: Hepatitis A

Lines: Infusaport in place 36 days

Failed to improve despite empiric vancomycin, cefepime, and caspofungin

PHYSICAL EXAM

GEN	Ill-appearing
HEENT	Mild scleral icterus, alopecia
CV	Tachycardic, II/VI systolic murmur
RESP	Mildly increased work of breathing
GI	Mild RUQ tenderness
MSK	Moves all extremities well
DERM	Scattered 2mm blanching red macules/papules on upper chest and shoulders + non-blanching macules/petechiae on lower extremities and left palm

CV: cardiovascular, DERM: dermatology, GEN: general, GI: gastrointestinal, HEENT: head, eyes, ear, nose, and throat, HSM: hepatosplenomegaly, MSK: musculoskeletal, RESP: respiratory, RUQ: right upper quadrant

LABS/IMAGING

	Result	Reference
WBC	0.05	4.5-13 x 10^3 per µL
Hgb	6.5	13-16 g/dL
Hct	17.9	37- 49 %
Plt	7	140-440 x 10^3 per µL

Hct: hemotocrit, Hgb: hemoglobin, Plt: platelets, WBC: white blood count

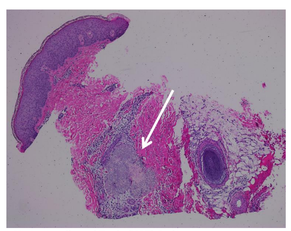
	Result	Reference
Total Bilirubin	2.6	0.2-1.3 mg/dL
Conj Bilirubin	0	0-0.3 mg/dL
Unconj Bilirubin	2.0	0-1.1 mg/dL
AST	24	15-46 U/L
ALT	55	13-69 U/L

ALT: alanine aminotransferase, AST: aspartate aminotransferase, Conj: conjugated, Uncong: unconjugated

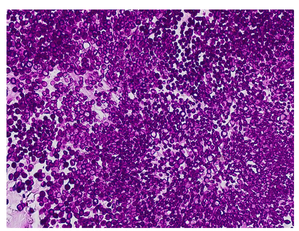
Negative Labs:
- Daily blood cultures
- Fungal blood cultures
- Mycobacterial blood culture
- Hepatitis panel
- CMV serum PCR
- Enterovirus serum PCR
- Respiratory pathogen panel

Negative Imaging:
- Chest x-ray
- CT chest, abdomen, pelvis
- Transthoracic echocardiogram

SKIN BIOPSY



Haemotoxalin and Eosin (H&E) Stain



Periodic Acid Schiff (PAS) stain

Pathology:
- Dermal fungus (yeast) with minimal inflammatory reaction
- Morphology most consistent with *Candida* species

Tissue Culture:
- *Candida dubliniensis*

Antifungal	MIC
5-Fluorocytosine	<0.06
Amphotericin B	0.25
Anidulafungin	0.12
Caspofungin	0.06
Fluconazole	<0.12
Itraconazole	<0.016
Micafungin	0.016
Posaconazole	<0.008
Voriconazole	<0.008

MIC: mean inhibitory concentration

CLINICAL COURSE

Escalated to amphotericin B pending tissue culture speciation and susceptibilities

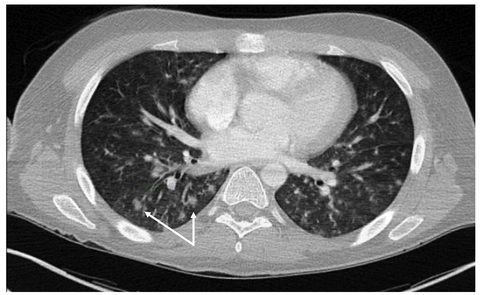
Persistent fever with respiratory decline

Infusaport removed

Transesophageal echocardiogram negative for vegetations

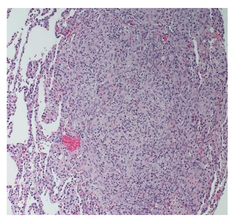
Repeat CT abdomen, pelvis, and sinuses negative

REPEAT CHEST CT



Numerous nodules measuring 1-8 mm in bilateral lungs with no internal cavitations or calcifications

VATS & LUNG BIOPSY



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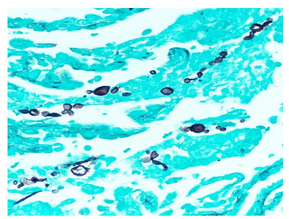

Grocott's Methanamine Silver (GMS) stain

Pathology:
- Organizing pneumonia
- Yeast and pseudohyphae
- *Candida* species similar to skin biopsy

OUTCOMES

De-escalated to caspofungin

Echinocandin continued through Chimeric Antigen Receptor (CAR) T-cell therapy

Candida resolved, remains on antifungal prophylaxis

CANDIDA DUBLINIENSIS

First described in oral candidiasis of AIDS patients

Now associated with invasive disease

Phenotypically similar to *Candida albicans*

Most isolates pan-susceptible

CONCLUSIONS

Widespread fluconazole prophylaxis → antifungal resistance

Increasing number of infections with non-albicans *Candida* species

Neutropenic patients at high risk for invasive disease

Blood and fungal cultures only 50% sensitive in diagnosing invasive candidiasis

Cultures less sensitive with deep organ involvement in absence of prolonged candidemia

Delayed treatment → increased morbidity/mortality

When fever persists with negative cultures, search for cryptogenic foci of infection

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