



Co-organized
with:



Case presentation

Invasive Candidiasis

LEE LEE LOW

Infectious Disease Physician

Hospital Sultanah Bahiyah

Malaysia

24 years old lady

- DM type 2, diagnosed at the age of 12, poorly controlled
- Confirmed as ESKD 4 months ago, on haemodialysis via right IJC
- **Intradialytic hypotension with chills and rigor**, could not tolerate dialysis
- Capillary blood sugar : 16 -18mmol/L (not in DKA)
- Clinically, fluid overload (ankle oedema)
- SPO2 : 95% on Face Mask 5L/min
- BP 150/80, PR 100/min, Afebrile
- ECG : sinus tachycardia



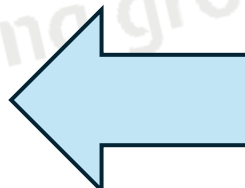
- WBC: 27, CRP: 210mg/L
- K: 3.0, Na: 132, ALT : normal
- Blood cultures from the both lumens : *yeast*
Blood culture from peripheral vein : sterile
- CXR : Cardiomegaly, fluid overload
- No other source of infection



CRBSI: YEAST

Challenges:

- Fluid overload , requiring frequent fluid extraction
 - ESKD, hypotensive during dialysis
 - CCF with poor EF
 - Hypokalaemia
-
- T Fluconazole 800mg stat and 200mg OD
 - IJC removed within 24H of the positive blood culture



**Your
comment ?**

Yeast in blood : possible candidemia

Amphotericin B

Echinocandin

Fluconazole

Candidaemia : Which Antifungal therapy

Effectiveness of echinocandins versus fluconazole for treatment of persistent candidemia: a time-dependent analysis

Prospective observational study: N=64 (echinocandin), N=132 (Fluco)

Echinocandin had positive impact on mycological eradication (AHR, 1.46; 95% CI, 1.02-2.11).

- Survival at day 30 : no significant difference between echinocandins (46.9%) and fluconazole based therapy (43.2%) (P=0.626)

Anidulafungin compared with fluconazole for treatment of candidemia and other forms of invasive candidiasis caused by *Candida albicans*: a multivariate analysis of factors associated with improved outcome

- Anidulafungin was associated with significantly faster clearance of blood cultures (log-rank $p < 0.05$)
- Median times to negative blood culture were 2 (Anid) and 5 days (Flu), respectively.
- Significantly fewer persistent infections (2.7% vs 13.1%; $p < 0.05$).
- Survival through 6 weeks did not differ between treatment groups

Candidaemia : Which Antifungal therapy

Comparative effectiveness of amphotericin B, azoles and echinocandins in the treatment of candidemia and invasive candidiasis: A systematic review and network meta-analysis

Treatment success (mycology and/or clinical response):

- Echinocandin exhibits the highest rate of success compared to amphotericin B (OR 1.41, 95% CI 1.04–1.92) and the triazoles (OR 1.82, 95% CI 1.35–2.51)
- Overall survival did not significantly differ between group

Early Stepdown From Echinocandin to Fluconazole Treatment in Candidemia: A Post Hoc Analysis of Three Cohort Studies

30-day mortality was 11.1% in the Early stepdown group and 29.8% in the non-ED group (P =0 .006).

Early stepdown had no significant impact on mortality (OR, 0.50; 95% CI, 0.16–1.53).

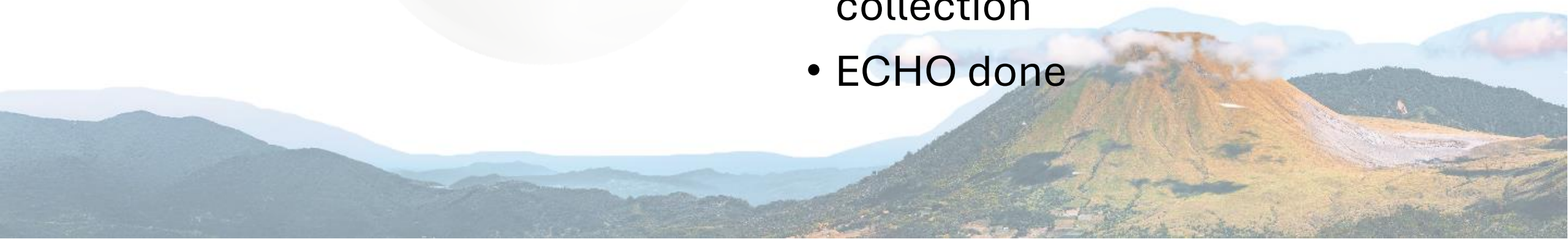
Early de-escalation is a safe strategy in patients with candidemia caused by fluconazole-susceptible strains with controlled source of bloodstream infection and hemodynamic stability

Blood culture :

C parapsilosis candidaemia

In spite of 5 days Fluconazole,
And removal of IJC

- Persistent leucocytosis, high CRP
- Hypotensive episode during dialysis (femoral catheter)
- Repeated Blood cultures : sterile
- US abdomen/Kidneys : no collection
- ECHO done

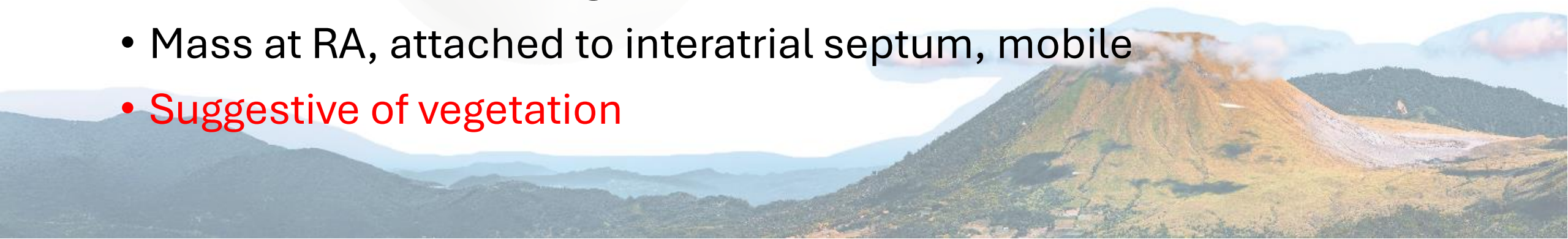


Transthoracic ECHO:

- Minimal pericardial effusion
- EF 30%
- Valves : normal
- Suspicious mass at right atrium (2cm²)

Transoesophageal echocardiogram (TOE/TEE):

- Valves : Normal, no vegetation
- Mass at RA, attached to interatrial septum, mobile
- **Suggestive of vegetation**



***C parapsilosis* mural Infective endocarditis (right atrium)**

- Choice of antifungal therapy ?
- To continue Fluconazole ?

- *C parapsilosis*

	MIC $\mu\text{g/mL}$	
Amphotericin B	0.25	S
Micafungin	2	S
Caspofungin	0.25	S
Voriconazole	0.12	S
Fluconazole	1	S

Fluid overload , requiring frequent fluid extraction
 ESKD, hypotensive during dialysis
 CCF with poor EF
 Uncontrolled DM
 Hypokalaemia

Mural infective endocarditis

Mural Endocarditis: The GAMES Registry Series

IE Registry from Spain (2008-2017)

- Mural endocarditis: 0.7% of infective endocarditis
- Associated with intravenous catheter use

Organism	Mural (MIE) N=27 (%)	Device(DIE) N=407 (%)	Valvular(VIE) N=3242 (%)	P value
Staphylococcus aureus	4(14.8)	125(30.7)	708(21.8)	<0.01
CoNS	4(14.8)	123(30.2)	515(15.9)	<0.01
Enterococcus	1(3.7)	20(4.9)	482(14.9)	<0.01
Streptococcus	7(25.9)	33(8.1)	893(27.5)	<0.01
Candida	6(22.2)	8(2.0)	39(1.2)	<0.01

- The vegetations were significantly larger in Mural IE, with a mean size of 22 mm compared to 12mm (Device IE) and 10mm (VIE) groups, respectively ($p < 0.01$).
- Mural IEs less often to had a surgical indication : 65.3% in VIE, 82.8% in DIE vs. 33.3% in MIE ($p < 0.01$)

C parapsilosis mural infective vegetation
Which antifungal agents ?

Antifungal therapy and *Candida* biofilm



- *Candida* biofilms exhibit intrinsic resistance to azoles particular fluconazole, with MIC 1000x higher than MIC obtained for planktonic populations
- Echinocandins have activity against *Candida* biofilm in vitro.
- Conventional amphotericin B has inferior biofilm activity in vitro compared with echinocandins
- Lipid amphotericin B formulations exhibit superior biofilm activity compared with conventional amphotericin B
- Both AmBs were able to reduce the biomass, with reductions between 34.64% and 89.58% for AmB-Deox, and between 43.78% and 70.72% for AmB-L
- MBEC AmB L < AmB deoxy ($P < 0.001$)

Minimum Biofilm Eradication Concentration (MBEC) is the lowest concentration, recorded in mg/L, of the drug able to reduce the biofilm cell population to at least $2 \text{ Log}_{10} \text{ CFU per cm}^2$

Ramage G et al, Antimicrob Agents Chemother 2002; 46:3634–
Ferreira JA et al. Atimicrob Agents Chemother 2009; 53:4377–84
Mora-Duarte J et al. N Engl J Med 2002; 347:2020–9.
Kuhn DM et al. Antimicrob Agents Chemother 2002; 46:1773–80.
Olabaya et al. Biofilm, 5, 2023, 100126,

Rodrigues, C.F Pathogens 2017, 6, 62.

Antifungal Therapy in Candida Infective Endocarditis: A Comparison of Echinocandins and Other Treatment Regimens in a Nationwide Cohort Study (Swedish Registry of Infective Endocarditis for 1995–2019)

Echinocandins-based regime (n = 21),
Amphotericin B-based therapy (n = 22),
Azoles (n = 8).

The proportions of treatment failure : No difference

32% (Echinocandin), 38%, (Ampho B) and 62% (Azole), respectively (P =0 .35).

Patients who received echinocandins were older and had more comorbidities.

1-year mortality : No difference

24% (Echinocandin), 19%, (Ampho B) and 60% (Azole), respectively (P =0 .18).

- 50% treatment failure among patients receiving azole as first-line therapy compared with (36%) who received an echinocandin or amphotericin B-based drug as first-line therapy ($P = 0.40$)

C. non-parapsilosis IE:

- No major difference in efficacy between echinocandin-based and amphotericin B-based regimens

Amphotericin B-based backbone therapy

- Treatment failure seen in 54% of *C. parapsilosis* IE comparing to 12.5% in *C. non-parapsilosis* IE, respectively

AmphoB based- regime: 44% discontinuation or dose reduction due to ADR vs no termination observed with echinocandins regime

Candida Infective Endocarditis: an Observational Cohort Study with a Focus on Therapy

International Collaboration on Endocarditis (ICE)-Prospective Cohort Study and ICE-Plus databases collected between 2000 and 2010.

- Echinocandin therapy was as effective as amphotericin B-based therapy
- No difference in : In hospital mortality, 42 days mortality, 1 year mortality
- A higher percentage of older patients and nosocomial infection in the echinocandin group
- 57% in Ampho B arm with AKI

Guidelines

IDSA 2016

- Lipid formulation AmphoB, 3–5 mg/kg daily
± flucytosine, 25 mg/kg 4 qid

OR

- High-dose echinocandin:
Caspofungin 150 mg daily,
Micafungin 150 mg daily,
Anidulafungin 200 mg daily
(low-quality evidence)



Step-down therapy to fluconazole for susceptible *Candida* isolates.

ECMM 2025

- Lipid ampho 3-5mg/kg/day
± flucytosine 25 mg/kg qid
- Caspo 70/50
- Anidulafungin 200/100
- Micafungin 100 ± Fluconazole 400



Step-down therapy to fluconazole, for susceptible *Candida* isolates,

C parapsilosis

- The choice of antifungal should be guided by causative *Candida* spp and the MIC
- *C. parapsilosis* isolates have a naturally occurring *fks* polymorphisms in the HS region of the *fks1* genes.
- With reduced susceptibility to echinocandins
- The European Committee on Antimicrobial Susceptibility Testing still urges caution with echinocandins for serious infections caused by *C. parapsilosis*:

The underlying reason for the higher MICs against *C. parapsilosis* (and *C. guilliermondii*) is the presence of a naturally occurring amino-acid substitution at a hot spot region of the target enzyme, known to confer resistance in other species.

C parapsilosis

This reduced susceptibility has not been associated with treatment failure in clinical practice

C parapsilosis candidaemia:

- 30 day mortality rate in the echinocandin group 9.9% versus 9.5% in the fluconazole group (OR 1.05, 95% CI 0.49–2.26).

Meta analysis (5 RCT)

- The success rates of treating *C. parapsilosis* were similar for the echinocandin group versus other Non-echinocandin antifungal treatment groups (76.5% vs 73%).
- ✓ Pan-echinocandin-resistant *Candida parapsilosis* strain been isolated following prolonged exposure to echinocandin (case reports)
- ✓ Breakthrough *Candida parapsilosis* fungemia during prolonged course of echinocandin therapy for *Candida glabrata* (MIC Mica 0.12)

- Cease Fluconazole, switch to IV micafungin 150mg od in 100ml NS
 - Symptoms resolved, able to tolerate dialysis
 - Serial blood follow up cultures x 3 : no growth
 - At week 4, switch IV micafungin to Oral fluconazole
 - Repeated ECHO at week 6
- No mass at right atrium
EF 26% , global hypokinesia



70 years old lady

- DM with ESKD, converting from CAPD to haemodialysis via right Permcatheter (tunneled catheter)
- admitted for fever, chills and rigors
- Vital signs stable, SpO₂ 99% on room air
- Antibiotics initiated as per protocol for CRBSI
- WBC 7.4, CRP 150



- blood cultures from periphery vein and catheter : yeast,
identified as *C parapsilosis*
No other organisms isolated

Permcatheter removed 4 days after positive culture

	MIC µg/mL	
Amphotericin B	1	S
Micafungin	0.5	S
Caspofungin	0.5	S
Voriconazole	0.12	S
Fluconazole	1	S

TTE

- Mass at Right atrium cavity (1.9cm²)
- No RMMA
- EF 59%

TOE

- 3.3 cm mass at right atrium extending into IVC,
- no vegetations over valves

THROMBUS

Planned for PET-CT

Copyright reserved by data providers and :

ASIA FUNGAL

WORKING GROUP

an ISHAM working group



- On Fluconazole
- Day 3 treatment and day 6 Blood cultures: no growth
- US abdomen : no collection
- Anticoagulant

PET-CT (Cardiac protocol)

- No focal increased tracer uptake within the heart
 - No intracardiac FDG avid focus lesion , in particularly right atrium
 - NOT vegetation
-
- Continue Fluconazole 2 weeks from the first negative blood culture

Approach to Candidaemia



1ST line therapy : Echinocandin

Alternative: fluconazole

(if patient is not critically ill & NOT suspecting Fluconazole resistant *Candida* spp.)

Caution if high incidence of azole-resistant *Candida* spp

Caution if site of infection : CNS, EYE, URINARY TRACT

Candida species identification and MIC

Repeat Blood culture

Removal of Central Venous catheter

as early as possible*

*Early CVC removal is associated with decreased mortality

Assessment for complications

Assessment based on risk category
(if is not applicable to all)

- Imaging for suspected foci
- ECHO
- Fundoscopy examination

De-escalation to oral azole

- Azole-susceptible *Candida* spp
- Adequate source control
- Blood culture clearance
- Haemodynamically stable

Determine duration of therapy

- 2 weeks after 1ST blood culture clearance
- Site of infection
- Adequate source control



Co-organized
with:



THANK YOU

