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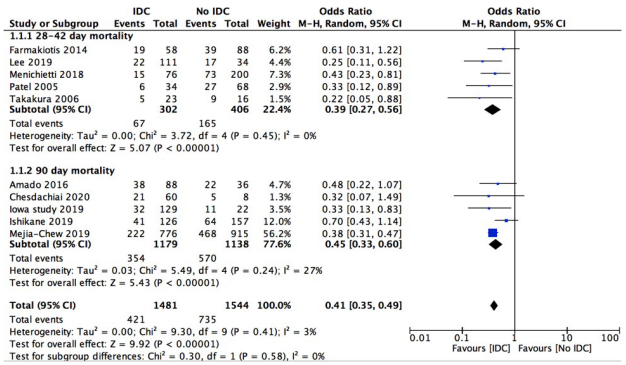
Session: P-30. Eukaryotic Diagnostics

Background: Morbidity and mortality from candidemia remain unacceptably high. While infectious disease consultation (IDC) is known to lower the mortality from *Staphylococcus aureus* bacteremia, little is known on the impact of IDC in candidemia.

Methods: We conducted a retrospective observational cohort study of candidemia patients at a large tertiary care hospital between 2015 and 2019. All patients aged ≥18 years with blood cultures positive for *Candida* species were included. We only included the first episode of candidemia. Exclusion criteria were death or transfer to the palliative care unit within 48 hours from the time cultures became positive. The crude mortality rate was compared between those with IDC and without IDC. Then, we systematically searched five publication-databases through February 2020 and performed a meta-analysis of the impact of IDC on mortality of patients with candidemia. The study protocol has been submitted to the International Prospective Register for Systematic Reviews (PROSPERO) database (ID 156939) on April 2020.

Results: A total of 151 patients at our institution met the inclusion criteria, 129 (85%) of whom received IDC. Thirty-day, and 90-day mortality rates were significantly lower in the IDC group (18% vs 50%, P = .002; 23% vs 50%, P = .0022, respectively). Our systematic literature review returned 216 reports, of which, 13 studies including ours fulfilled the inclusion criteria. Among the 13 studies with a total 3687 patients, IDC was performed in 49% of patients. Mortality numbers were available in 10 studies. Overall mortality was 38.2% with a significant difference in favor of the IDC group (28.4% and 47.6%) with a pooled relative risk of 0.41 [95% Cl 0.35-0.49]. Ophthalmology referral (61%; 790/1279 and 21%; 273/1304, P < 0.001), echocardiogram (54%; 662/1219 and 28%; 369/1296, P < 0.001), and central line removal (78%; 830/1069 and 61%; 686/1116, P < 0.02) were performed more frequently among patients receiving IDC.

Overall mortality



Conclusion: This study is the first systematic literature review and meta-analysis to evaluate the association between IDC and candidemia mortality. IDC was associated with a lower mortality and should be standard of care in all patients with candidemia.

Disclosures: Dimitrios Farmakiotis, MD, Astellas (Grant/Research Support) Paul Auwaerter, Collidion (Consultant)DiaSorin (Consultant)Johnson and Johnson (Shareholder)MicroB-Plex (Research Grant or Support)Shionogi (Consultant) Daniel Diekema, bioMerieux, Inc (Grant/Research Support)JMI Laboratories (Consultant)

750. Isavuconazole Cerebrospinal Fluid Concentration in Refractory Coccidioidal Meningitis - A Three-Patient Case Series

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Session: P-30. Eukaryotic Diagnostics

Background: Coccidioidal meningitis (CM) causes life-threatening infection with limited treatment options. Small series have reported variable treatment success with isavuconazole. An absence of published data exists on cerebrospinal fluid (CSF) penetration of this agent.

Methods: Paired serum and CSF levels were measured on three patients with refractory CM treated on salvage isavuconazole therapy.

Results: 11 CSF levels were sent on 3 patients; 7 from ventricular sources (Ommaya reservoir or external ventricular drain) and 4 from lumbar punctures at 6-44 days after treatment initiation, 2-24.6 hours after oral or intravenous dose. All levels sent from ventricular sources were undetectable < 25μg/mL despite adequate paired serum levels (mean 2.45 μg/mL, range 1.25-6.38 μg/mL; n = 7 levels). Mean lumbar CSF levels were 1.00 μg/mL (range 0.45-1.72 μg/mL; n = 4 levels) with adequate serum levels (mean 3.57 μg/mL, range 1.78-5.63 μg/mL; n = 4 levels).

Table 1. Isavuconazole serum and cerebrospinal fluid concentration measurements

Table 1. Isavuconazole serum and cerebrospinal fluid concentration measurements

Day	Route	Serum μg/mL (hours post-dose)	CSF μg/mL (hours post-dose, source)
Patient 1			
9	IV	2.6 (24.8)	--
11	IV	1.96 (2)	<0.25 (2, EVD)
12	IV	1.49 (23)	<0.25 (23, EVD)
15	IV	1.78 (24.6)	0.45 (14.5, LP)
15	IV	--	<0.25 (24.6, EVD)
25	PO	1.25 (23.5)	<0.25 (23.5, Ommaya)
25	PO	3.08 (2.3)	<0.25 (2, Ommaya)
44	PO	1.8 (22.3)	0.69 (22.9, LP)
Patient 2			
6	IV	3.02 (5.7)	<0.25 (5.8, EVD)
Patient 3			
9	PO	3.3 (23.5)	--
10	PO	6.38 (2.7)	<0.25 (2.7, Ommaya)
11	PO	5.06 (24.5)	1.15 (24.5, LP)
42	PO	5.63 (7.5)	1.72 (6.5, LP)

CSF = cerebrospinal fluid; EVD = extra-ventricular drain; LP = lumbar puncture; RBC = red blood cells

Conclusion: Isavuconazole was detected in lumbar, but not ventricular CSF in three patients treated for CM.

Disclosures: **All Authors**: No reported disclosures

751. Karius Cell-Free DNA Metagenomic Assay of Plasma Detects Pulmonary and Disseminated *Trichosporon* Infections in Patients with Hematological Malignancies

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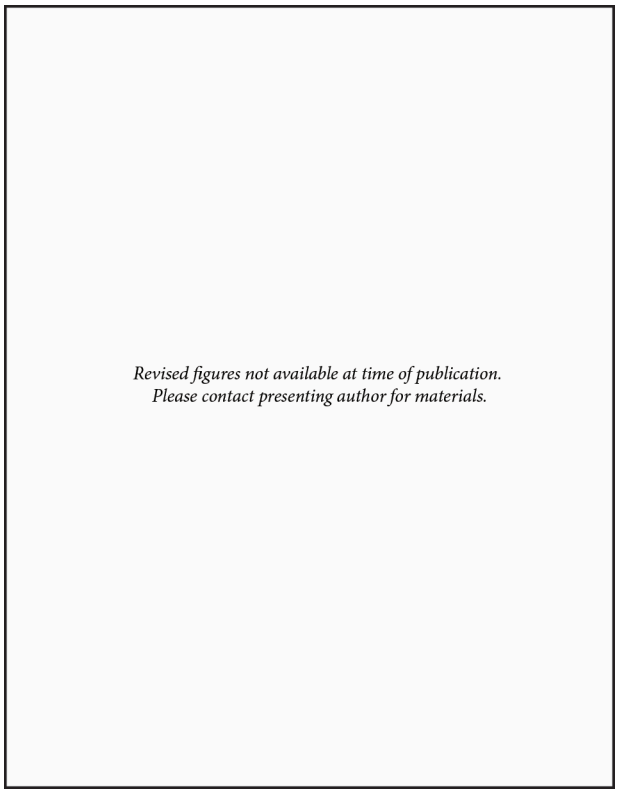
Session: P-30. Eukaryotic Diagnostics

Background: *Trichosporon* species are uncommon but emerging pathogens that cause life-threatening infections that are resistant to amphotericin B and echinocandins. Diagnosis of deeply invasive trichosporonosis is often elusive to conventional culture methods until locally advanced or disseminated disease has advanced.

CT scans Pulmonary Trichosporonosis

Revised figures not available at time of publication.
Please contact presenting author for materials.

Lung Bx of Trichosporon detected by Karius Cell-Free DNA Metagenomic Assay of Plasma



Methods: Review of cases of next-generation sequencing of microbial cell-free DNA from plasma using the Karius-based technology for establishing a diagnosis of invasive trichosporonosis

Results: We found that next-generation sequencing of microbial cell-free DNA from plasma using the Karius-based technology established a diagnosis in six pediatric and adult patients. The median age was 17 yrs (8-72 yrs) all patients had underlying acute leukemia myelogenous leukemia. Six patients had pulmonary nodules and two also had multiple cutaneous lesions with negative blood cultures. Biopsies of one pulmonary nodule and of two cutaneous lesions revealed yeast-like cells. Culture of cutaneous lesions in two patients grew *Trichosporon* sp. Karius assays performed on plasma and analyzed against a database of more than 300 species of fungi identified *Trichosporon asahii* in two cases, *Trichosporon* spp. in three, *Trichosporon faecale* in one. In all cases, the metagenomic results defined therapy for treatment of invasive trichosporonosis, which is based in antifungal triazoles. In one patient with pulmonary nodules, lung biopsy revealed mixed septate and non-septate hyphal elements that later grew *Trichosporon asahii*, *Rhizomucor pusillus*, and *Candida parapsilosis*, all of which were identified by Karius assay.

Conclusion: Invasive *Trichosporon* spp. are uncommon polyene and triazole-resistant pathogens that cause life-threatening invasive fungal disease resistant in immunocompromised patient with hematological malignancies; next-generation sequencing of fungal cell-free DNA by Karius-based technology identified all six cases of pulmonary and disseminated trichosporonosis, contributing to early detection and pathogen-directed antifungal therapy.

Disclosures: Asim A. Ahmed, MD, Karius (Employee) Joshua Wolf, MBBS, PhD, FRACP, Karius inc (Grant/Research Support)

752. Management of 20 Patients Diagnosed with Posaconazole-Induced Pseudohyperaldosteronism

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Matthew R. Davis

Session: P-30. Eukaryotic Diagnostics

Background: Posaconazole-induced pseudohyperaldosteronism (PIPH) has been associated with elevated posaconazole serum concentrations. Clinicians are faced with the difficult task of managing patients with PIPH while not compromising the efficacy of antifungal prophylaxis or treatment. Commonly, modifications to posaconazole therapy are utilized in managing PIPH including dosage reduction of posaconazole or therapeutic switch to an alternative antifungal.

Methods: We retrospectively reviewed 20 consecutive adult patients diagnosed with PIPH in this case series. Patient data including blood pressure, electrolytes, endocrine laboratory values, and posaconazole serum concentrations collected before and after therapeutic intervention.

Results: Out of 20 patients included, 17 patients (85%) underwent therapeutic modification with posaconazole dose reduction (N=11) as the most common change. Other modifications included posaconazole discontinuation (N=3), switch to an alternative antifungal (N=2), and addition of spironolactone (N=1). Clinical improvement (a decrease in systolic blood pressure and increase in serum potassium) was observed in 9 of 17 patients (52.9%).

Table 1. Management of Posaconazole-Induced Pseudohyperaldosteronism - p1

Table 1. Management of Posaconazole-Induced Pseudohyperaldosteronism

Patient	Age/Sex; Indication	Intervention (Posaconazole Dose)	Time from Intervention to Lab Draw	Syndrome	PRE	POST	Endocrine Labs	PRE	POST
1	61y M; Treatment (Empiric)	Discontinue (300mg→none)	16 weeks	K	3.6	4.6	11-deoxycortisol	810	15.1
				HCO_3	25	26	Aldosterone	0	6.4
				SBP	153	115	Renin Activity	0	3.2
				DBP	83	80	Posaconazole	3.8	-
2	26y F; Treatment (Coccidioidomycosis)	Discontinue (300mg→none)	6 weeks	K	3.5	3.6	11-deoxycortisol	33.2	0
				HCO_3	25	23	Aldosterone	0	4.9
				SBP	106	113	Renin Activity	0.2	0.5
				DBP	67	82	Posaconazole	2.5	-
3	31y M; Prophylaxis (HSCT)	Discontinue (300mg→none)	4 weeks	K	4.2	4	11-deoxycortisol	404	16.1
				HCO_3	24	24	Aldosterone	0	15.3
				SBP	124	126	Renin Activity	8.1	1.9
				DBP	85	85	Posaconazole	2.8	-
4	59y M; Treatment (Coccidioidomycosis)	Change Agent (300mg→ isavuconazole)	9 weeks	K	3.3	3.8	11-deoxycortisol	423	33.5
				HCO_3	27	26	Aldosterone	0	8.3
				SBP	130	127	Renin Activity	22.4	48.4
				DBP	79	82	Posaconazole	4.1	-
5	68y F; Prophylaxis (HSCT)	Change Agent (300mg→ isavuconazole)	N/A*	K	3.3	4.3	11-deoxycortisol	49.1	-
				HCO_3	25	25	Aldosterone	0	-
				SBP	138	127	Renin Activity	0.2	-
				DBP	93	68	Posaconazole	1.8	-
6	48y M; Treatment (Coccidioidomycosis)	Dose Reduction (300mg→200mg)	15 weeks	K	3	3.2	11-deoxycortisol	52.2	17.1
				HCO_3	28	27	Aldosterone	0	0
				SBP	145	156	Renin Activity	0.8	0
				DBP	93	73	Posaconazole	4.5	1.5
7	71 F; Prophylaxis (HSCT)	Dose Reduction (300mg→200mg)	14 weeks	K	4.4	4.2	11-deoxycortisol	80.3	60.2
				HCO_3	21	22	Aldosterone	0	9.8
				SBP	165	146	Renin Activity	0.7	4.3
				DBP	83	85	Posaconazole	4.1	1.9