Evaluating the Impact of the 2016 Candidemia Guidelines on the Incidence of Ocular Complications of Candidemia

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Introduction

The incidence of bloodstream infections with *Candida* species has risen over the last several decades. Candidemia is known to cause disseminated infectious complications including endogenous fungal endophthalmitis which can result in devastating outcomes including vision loss. Due to declining rates of ocular infection, the recommendation for screening eye exams for all candidemic patients has been challenged.[1-3] In December 2015, the IDSA guidelines were updated to recommend echinocandins, which are known to have poor ocular penetration,[4] as initial therapy for candidemia in neutropenic and non-neutropenic patients . We sought to examine whether patients who received empiric echinocandin therapy developed higher rates of ophthalmic complications of candidemia.

Methods

We identified the patients in our healthcare system who had blood cultures positive for *Candida* species and a completed ophthalmology consult between January 1, 2014 and April 30, 2019. We reviewed the antifungals received prior to eye examination and the findings on these exams before and after the updated IDSA guidelines were released in late 2015. Chi squared analysis and Fisher's exact test were used to assess whether patients who received eye-penetrating antifungals had higher rates of positive eye exams in comparison to patients who received echinocandins.

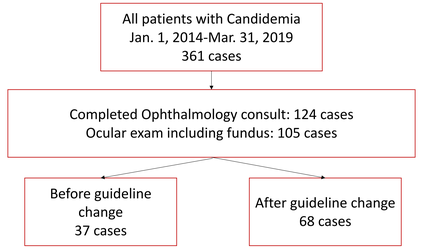


Figure 1. Cases were identified in our health systems EMR based on identified *Candida* species in blood culture. Cases with completed ophthalmology consult including fundus exam were included in analysis.

Clinical Data	Laboratory Data	Eye exam findings
• Immunocompromised status • Recent antibiotic exposure • Presence of an indwelling catheter • Incisional gastrointestinal surgery within the last six months • Parenteral alimentation • Active intravenous drug use • Concomitant bacteremia • Need for dialysis following a positive blood culture • Type of antifungal received prior to eye exam	• WBC count • ANC • eGFR • Duration of candidemia • Total number of positive cultures • Candida species • Evidence of vegetation on echo	• Non-specific findings • Chorioretinitis • Endophthalmitis

Table 1. Clinical and laboratory data were extracted in chart review. Ocular exam findings were recorded as documented by the examining ophthalmologist.

Results

Ocular Findings	All	2016 ISDA Guideline		P-value
		Before N=47	After N=77	
Eye exam, N (%)	105 (84.7)	37 (78.7)	68 (88.3)	0.15
Non-specific fundus lesion	12 (9.7)	5 (10.6)	7 (9.1)	0.78
Chorioretinitis	5 (4.0)	1 (2.1)	4 (5.2)	0.40
Endophthalmitis	1 (0.8)	1 (2.1)	0 (0.0)	0.38
Vitreal abscess	N/A	N/A	N/A	
Type of ocular finding				
Specific	6 (4.8)	2 (4.3)	4 (5.2)	0.94
Non-specific	12 (9.7)	5 (10.6)	7 (9.1)	

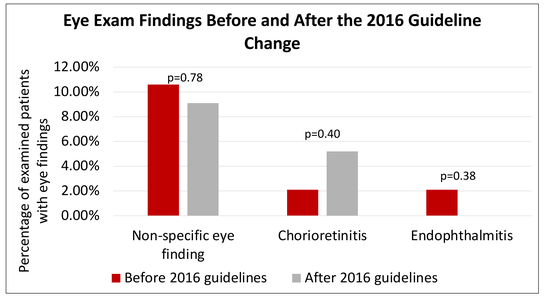
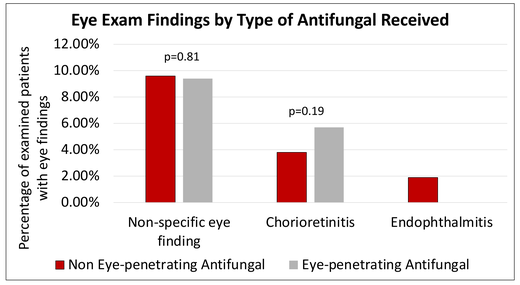
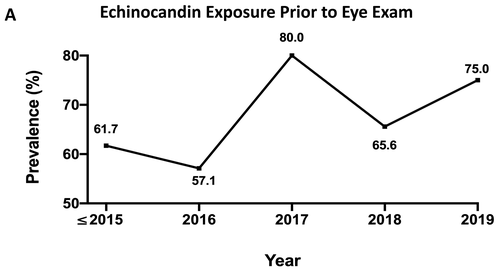


Table 2 and Figure 2. Comparison of eye findings in patients examined in the time before the guideline update (January 1, 2014-December 31, 2015) and after the guideline update (January 1, 2016-March 31, 2019).



Ocular Findings	Eye Penetrating antifungal		P-value
	No (N = 52)	Yes (N = 53)	
Any ocular finding, N(%)	10 (19.2)	8 (15.1)	0.57
Non-specific fundus lesion	5 (49.6)	5 (9.4)	0.81
Chorioretinitis [a]	2 (3.8)	3 (5.7)	0.19
Endophthalmitis	1 (1.9)	0 (0.0)	0.50
Vitreal abscess	0	0	N/A
Type of ocular finding			
Specific [a]	3 (5.8)	3 (5.7)	0.81
Non-specific [a]	7 (13.5)	5 (9.4)	

Table 3 and Figure 3. Comparison of ocular exam findings between patients who received eye-penetrating antifungals (azoles, amphotericin) and those who received antifungals with poor ocular penetration (echinocandins). [a] P value calculated using Fisher's exact test.



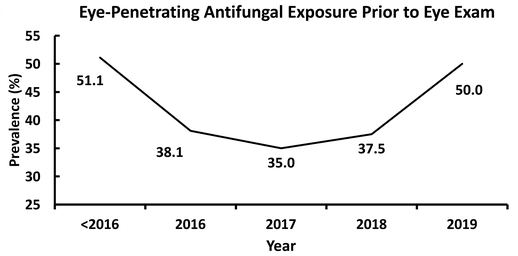


Figure 4A. Year to year prescribing trends for echinocandins, trend p value =0.39. **Figure 4B**. Year to year prescribing trends for eye-penetrating antifungals, trend p value =0.27.

Clinical Characteristics of Patients with Ocular Findings

Characteristics	Ocular finding		P-value
	No (N = 87)	Yes (N = 18)	
Clinical characteristics			
Diabetes, N (%)	25 (28.7)	6 (33.3)	0.70
Hypertension, N (%)	35 (40.2)	5 (27.8)	0.32
Immunocompromised, N (%) [a]	20 (23.3)	2 (11.1)	0.25
Antibiotics use, last 3 months, N (%)	69 (79.3)	15 (83.3)	0.70
Indwelling IV catheter, N (%)	66 (75.9)	14 (77.8)	0.86
GI surgery, last 6 months, N (%)	28 (32.2)	5 (27.8)	0.71
Receiving TPN, N (%) [a]	16 (18.6)	3 (17.6)	0.93
Active intravenous drug abuse, N (%) [a]	8 (9.2)	3 (16.7)	0.35
Concomitant bacteremia, N (%)	25 (28.7)	8 (44.4)	0.19
RRRT after candidemia, N (%)	16 (18.4)	5 (27.8)	0.36
Death during admission, N (%)	10 (11.5)	4 (22.2)	0.22
Ocular penetrating antifungal received, N (%)	45 (51.7)	8 (44.4)	0.57
After 2016 guideline	57 (65.5)	11 (61.1)	0.72
Duration of candidemia in days, median (IQR)	3.1 (1.4, 5.5)	2.1 (0.8, 2.9)	0.10
Number of positive cultures, median (IQR)	1.5 (1.0, 2.8)	1.6 (1.0, 3.5)	0.74

Table 4. There were no clinical or laboratory characteristics that were associated with a positive eye exam throughout the study period (January 1,2014-March 31, 2019). [a] P value calculated using Fisher's exact test.

Conclusions

There were no differences in demographic, clinical, or laboratory characteristics of our patients before or after the publication of the 2016 *Candida* guidelines. The overall prevalence of chorioretinitis and endophthalmitis was low (4% and 0.8%, respectively). Our study did not demonstrate a significant difference in ocular complications of candidemia following the recommendation of echinocandins as first line systemic therapy in neutropenic and non-neutropenic patients. There was not a significant difference in positive eye exams between patients who received eye-penetrating antifungals when compared to patients who did not. Importantly, there has not yet been a significant change in antifungal prescribing practices at our institution since the publication of the updated guidelines. Our data do not demonstrate any clinical characteristics that were associated with eye findings.

As a retrospective, single-center analysis our study is limited in size and scope. Future directions will include a review of all candidemic patients in our study window to identify patients with completed eye exams who may not have been captured in our initial chart abstraction using completed ophthalmology consults. Additionally, we intend to extend our IRB through June 2020 to further evaluate the trend in prescribing practices towards empiric echinocandin therapy and to investigate whether a change in empiric therapy is associated with an increased risk of eye findings. Ultimately, we aim to build a statistical model that can inform best practices for screening eye exams in patients with candidemia.

References

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