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T2MR: A New Tool for Anti-Fungal Stewardshi

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269. Epidemiology and Outcomes of Invasive Aspergillosis (IA) Among Pediatric Immunocompromised Patients: A 12-Year, Single-Center Experience

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Background. IA remains a leading cause of morbidity and mortality in immunocompromised children, and our understanding regarding epidemiology and outcomes of IA are limited and based on adult studies.

Methods. We conducted a retrospective evaluation of cases of proven or probable IA according to the 2008 EORTC/MSG criteria cared for at Boston Children's Hospital from 2007 to 2019. We collected data including demographics, clinical characteristics, diagnosis modality, antifungal treatment, and survival. Survival curves over one year were estimated using the Kaplan-Meier method and univariate and multivariate Cox modeling was used to evaluate for risk factors for mortality.

Results. 67 patient cases were identified, 20 (30%) with proven IA and 47 (70%) with probable IA. The mean age at diagnosis was 11.9 years (6 months-28 years). Underlying conditions included hematopoietic-cell transplantation (HCT) in 45%, cancer in 21%, and solid-organ transplantation in 18%. Pulmonary IA was the most common (70.1%) presentation. Diagnostic modalities included positive microbiology alone (18%), fungal PCR alone (1.5%), galactomannan alone (28%), and multiple modalities for the remaining cases (52.5%). 44.8% of patients were neutropenic at diagnosis and 78.5% of patients with malignancies were receiving chemotherapy. Immunosuppressive drugs included glucocorticoids in 34.3%, calcineurin inhibitors in 31.3%, and IMDH inhibitors in 25.3%. Voriconazole was the most common treatment used (72%). Twenty-two (33%) deaths occurred in the cohort attributable to IA (6 of which underwent autopsies and 4 had histopathological confirmation) Most deaths occurred in the BMT patients (15 patients, 45% of deaths). The 6 week mortality was 18% while the 12 week mortality was 25.4%. No antifungal or immunosuppressive regimen had a statistically significant impact on mortality.

Conclusion. We demonstrate in our >10-year retrospective cohort analysis of immunocompromised hosts that IA is associated with 49% all-cause mortality with particular impact on the BMT population. No protective nor harmful association was also noted with a particular antifungal or immunosuppressive regimen.

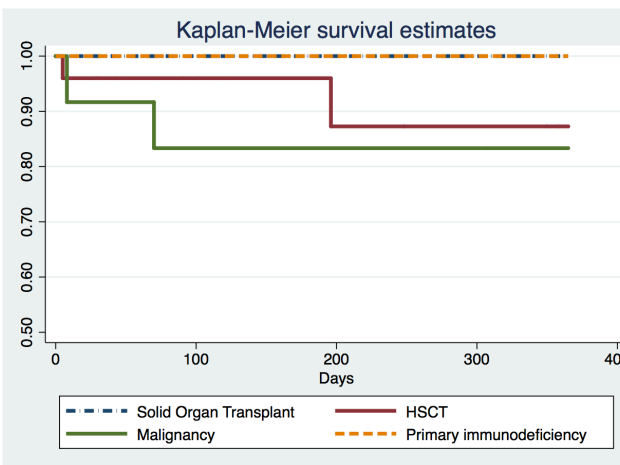
Total N= 67 of Proven and Probable IMI per EORTC definition		
	Proven IMI= 20 (30%)	Probable IMI=47(70%)
Gender		
Male	11	21
Female	9	26
Race		
Caucasian	13	31
African American	1	3
Hispanic/Latino	2	7
Asian/Pacific islander	2	1
Middle-Eastern	1	5
Other	1	
Underlying diagnosis		
SOT	4	8
BMT	9 ¹	21 ²
Malignancy	6	8
PID	1	8
Rheumatologic/inflammatory diseases and Hyperimmune states		2
Other diseases/entities	1	1
Clinical site of infection		
Lung	12	16
Tracheobronchial		19
Sinus		3
Skin and soft tissue	4	1
CNS		2 ³
Abdominal	3 ⁴	1 ⁵
Skeletal	1	
Other		5 ⁶
Modality of diagnosis		
Microbiology alone	12	
Fungal PCR alone	1	
Histopathology alone	-	
Galactomannan alone	19	
Microbiology + pathology	7	
Microbiology + Galactomannan	6	
Fungal PCR and pathology	3	
Fungal PCR and Galactomannan	1	
Histopathology and Galactomannan	7	
Microbiology+Histopathology+ Galactomannan	10	
Microbiology+Pathology+Fungal PCR+Galactomannan	1	

Table 1: Clinical and diagnostic characteristics

¹ One BMT patient had concomitant Lung transplant
² One BMT patient had concomitant Liver transplant
³ Patient with CNS imaging concerning for IA in addition to positive galactomannan. Patient with CNS and lung radiographic imaging concerning for IA in addition to positive galactomannan.
⁴ Aspergillus growing from peritoneal cavity. Aspergillus PCR positive from an omental biopsy. Aspergillus PCR positive from colon biopsy
⁵ Radiographic liver lesions with positive galactomannan
⁶ Aspergillus positive culture from a throat swab, with accompanying radiographic findings and positive galactomannan. 4 positive aspergillus cultures from sputum

	Hazards Ratio Unadjusted (95% CI)	p-value	Hazards Ratio Adjusted (95% CI)	p-value	Average days of survival if patient died in one year (number of deaths)	Deaths n (%) (95% CI)
BMT	1.29 (0.53-3.15)	0.56	1.17 (0.37-3.66)	0.78	56 days (15/67)	15 (50%) (312-0.68)
Malignancy	0.71 (0.23-2.13)	0.54	.98 (0.30-3.18)	0.97	4 days (2/67)	2 (14%) (0.01- 0.42)
Primary Immune Deficiency	0.78 (0.26-2.34)	0.66	0.85 (0.16-4.33)	0.84	272 days (1/67)	1 (11%) (0.0-0.48)
Solid Organ Transplant	--	--	--	--	0	0
Other immunocompromised conditions*	--	--	--	--	0	0
Usage of:					Number (%) (95% CI)	
Corticosteroids	1.12 (0.42-2.95)	0.82	1.07 (0.35-3.28)	0.90	21 (31.3%) (0.23-0.65)	
Calcineurin	0.79 (0.26-2.42)	0.69	0.41 (0.08-1.90)	0.25	23 (34.3%) (0.21-0.65)	
IMDH	1.80 (0.60-5.33)	0.28	1.48 (0.39-5.60)	0.56	17 (25.3%) (0.01-0.98)	
Amphotericin	0.84 (0.28-2.56)	0.77	0.88 (0.19-4.09)	0.87	23 (34.3%) (0.34- 0.76)	
Voriconazole	1.49 (0.34-6.5)	0.59	2.53 (0.32-19.65)	0.37	48 (71.6%) (0.59-0.82)	
Micafungin	0.26 (0.03- 2.03)	0.20	0.25 (0.03-2.03)	0.19	11 (16.4%) (0.30-0.89)	
	Number n (%)	95% CI				
6 week mortality	12 (18%)	(0.09-0.29)				
12 week mortality	17 (25.4%)	(0.16-0.37)				
Total deaths	33 (49%)	(0.37-0.62)				

Table 2: Risk Factors associated with mortality



Disclosures. All authors: No reported disclosures.

270. T2MR: A New Tool for Anti-Fungal Stewardship

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Background. Candidemia is associated with mortality rates between 30 and 50%. T2 magnetic resonance assay (T2MR) is a costly, rapid diagnostic technology that can detect the five most common Candida species in blood with a sensitivity of 91% and specificity of 99.4%. The clinical role of this tool remains unclear but this study shares our clinical experience with T2MR.

Methods. We conducted a retrospective chart review of patients with T2MR testing performed from April 25, 2017 through April 25, 2018. T2MR ordering was restricted to Infectious Diseases pharmacists and physicians without specific ordering criteria. Variables cataloged included the time between order and result in the medical chart, T2MR result, anti-fungal therapy and duration. Descriptive statistics were reported on collected variables.

Results. Sixty-eight unique patients had T2MR ordered at least once during the study time period. The median age was 62.5 years (interquartile range (IQR), 22-92) and 42 patients (62%) were male. The median time between order and result appearing in the medical chart was 6.21 hours (IQR, 3.55-40.93). Out of 72 tests performed, 4 were positive (2 for *C. parapsilosis* and 2 for *C. krusei/glabrata*). Only 1 of 4 T2MR positive patients had concurrent candidemia while 1 patient had suspected fungal endophthalmitis, 1 patient was managed for a fistula, and 1 patient had cutaneous candidiasis.

Of the negative tests, 1 patient had a false negative T2MR result despite blood cultures growing *C. glabrata*. There was only 1 invalid test in our sample. Thirty-six patients were initiated or maintained on anti-fungal therapy at the time of the T2MR test, with micafungin being the most commonly prescribed anti-fungal agent. Negative T2MR patients had a median anti-fungal therapy duration of 2 days (IQR, 0–16). Sixteen patients (44%) had their anti-fungal therapy discontinued within 1 day of the negative T2MR result. There were no patients with a negative T2MR result who subsequently developed candidemia within 30 days after T2MR testing.

Conclusion. Our study showcases the benefit seen with T2MR in curtailing unnecessary anti-fungal exposure. Study limitations include a small cohort and evaluation at a single center. There is an opportunity for this technology to be utilized in anti-fungal stewardship.

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271. Fungal Diagnostic Studies in Histoplasmosis

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Background. Histoplasmosis (histo) is a common cause of invasive fungal infection in endemic regions and accurate diagnosis is difficult without direct tissue culture or pathology. Indirect fungal antigen testing for various fungal pathogens is typically performed to assist with diagnostic workup though cross-reaction can lead to difficulty interpreting results. We aimed to evaluate the prevalence of positive antigen testing for non-*Histoplasma* fungal pathogens in patients with proven invasive histo.

Methods. We performed a retrospective review of adult patients with proven invasive histo from 2010–2018 at our institution. For inclusion purposes, histo was confirmed by either fungal culture and/or cytology. Patient demographics, clinical characteristics and results of fungal antigen testing for *Histoplasma*, *Blastomyces*, *Aspergillus*, *Cryptococcus* and β -D-glucan were evaluated. Two different urine *Histoplasma* antigen assays were used during the study period.

Results. 57 (31%) of 182 patients diagnosed with histo during the study period had culture or cytology evidence of disease and were included in all further analysis. Thirty-two (56%) of these patients were male, 35 (61.4%) were Caucasian and the mean age was 50.1 years. HIV (20; 35%) and being on immunosuppressive medications (21, 37%) were common in this population. The majority of cases were classified as disseminated histo (40, 70%) followed by acute pulmonary (10; 18%) and chronic pulmonary (7, 12%) disease. Results of fungal antigen testing are documented in the table. Chi-squared analysis was performed.

Conclusion. There is a frequent cross reaction of non-*Histoplasma* fungal tests in patients with histo. In our review, there was a high rate of cross reaction with *Blastomyces* antigen, which can be confusing in regions where both pathogens coexist. Elevation of β -D-glucan was high in these patients. Urine *Histoplasma* antigen sensitivity was higher with MiraVista testing for disseminated disease in our review. While noninvasive fungal tests are helpful in diagnosis of these infrequent infections, clinicians must still maintain knowledge of the clinical differences between these fungal pathogens and be aware of the limitations of these tests. A prospective study is needed to better define differences between individual *Histoplasma* tests.

TABLE

TABLE showing results of *Histoplasma* and non-*Histoplasma* urine antigen tests

Histoplasmosis Presentation N=57	Urine <i>Histoplasma</i> Antigen (%)	Urine <i>Blastomyces</i> Antigen (%)	Serum <i>Cryptococcus</i> Antigen (%)	Serum <i>Aspergillus</i> Antigen (%)	Serum Beta D glucan Antigen (%)
Acute pulmonary (n=10)	4/5 (80)	1/2 (50)	0/1 (0)	1/4 (25)	0/2 (0)
Viracor	0/0 (-)				
Miravista* (NS)	4/5 (80)				
Chronic Pulmonary (n=7)	0/4 (0)	0/4 (0)	0/2 (0)	0/2 (0)	0/2 (0)
Viracor	0/2 (0)				
Miravista* (NS)	0/2 (0)				
Disseminated (n=40)	26/37 (70)	25/27 (93)	1/19 (5)	12/20 (60)	21/24 (88)
Viracor	8/16 (50)				
Miravista* (p=0.019)	18/21 (86)				
Total	30/46 (65)	26/33 (79)	1/22 (5)	13/26 (50)	21/28 (75)
Viracor	8/18 (44)				
Miravista (p=0.017)	22/28 (79)				

* Chi square analysis

Disclosures. All authors: No reported disclosures.

272. Invasive Pulmonary Aspergillosis: Comparative Analysis in cancer patients with Underlying Hematologic Malignancy vs. Solid Tumor

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Background. Over the years, the profile of patients with invasive pulmonary aspergillosis (IPA) has extended beyond the commonly associated population with hematologic malignancy (HM) and is now comprising patients with solid tumors and patients with lung diseases. We therefore aimed to compare the clinical characteristics, diagnostic approach and therapeutic outcome of IPA in cancer patients with hematologic malignancies vs. solid tumor (ST).

Methods. We conducted a retrospective study evaluating consecutive cases of proven and probable IPA from March 2004 to December 2016 in a tertiary cancer center. We included patients >18 years with an underlying ST, HM, or Hematopoietic Cell Transplantation (HCT) within 1 year of IPA diagnosis.

Results. A total of 311 patients were analyzed: 225 had HM including HCT and 86 ST. Patients with ST were more likely to have had COPD (33% vs. 8%, $P > 0.01$) or other underlying pulmonary diseases when compared with HM patients (76% vs. 43%, $P < 0.01$). Radiation therapy prior to the infection was also notably higher in the ST group than the HM group (48% vs. 14%, $P < 0.01$). Patients with HM were more likely to have received steroid (38% vs. 15%, $P = 0.0001$) and have concurrent neutropenia 37% vs. 2%, $P < 0.0001$. *A. fumigatus* was most commonly recovered in patients with ST than in patients with HM (66% vs. 38%, $P < 0.01$). Monotherapy and voriconazole-based primary antifungal therapy were more often prescribed in patients with ST than in patients with HM (87% vs. 56%, $P < 0.0001$ and 77% vs. 53%, $P = 0.0002$ respectively). Complete or partial successful response to therapy was recorded in 66% of patients with ST compared with 40% in the HM group ($P = 0.0001$). IPA attributable mortality within 12 weeks was significantly higher in the HM than in the ST group (30% vs. 18%, $P = 0.04$).

Conclusion. Monotherapy with voriconazole were more often prescribed in patients with ST than in patients with HM. Patients with ST had a better response to antifungal therapy and a lower IPA attributable mortality within 12 weeks compared with those with HM.

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273. Low Positive Predictive Value of β -D-Glucan in Hematology Patients Receiving Antimold Prophylaxis

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Background. Detection of β -D-glucan (BDG) in serum is recognized as the mycological evidence in the diagnosis of invasive fungal infection (IFI). However, its diagnostic value in low prevalence of IFI has not been elucidated. We aimed to examine the performance of BDG in hematology patients receiving antimold prophylaxis.

Methods. We retrospectively reviewed all BDG results performed for the purpose of diagnosis or surveillance for IFI in hematology patients receiving posaconazole or micafungin prophylaxis from January 2017 to February 2019 in a tertiary hospital. At least two consecutive positive results of BDG were regarded as positive BDG. All the episodes were classified into true-positive (TP, positive BDG with probable/proven IFI), true-negative (TN, negative BDG without probable/proven IFI), false-positive (FP, positive BDG without probable/proven IFI), false-negative (FN, negative BDG with probable/proven IFI), and nonevaluable (could not be determined for the occurrence of breakthrough IFI). When BDG test was performed in the setting of persistent fever ≥ 72 hours in spite of broad-spectrum antibiotics or with a suspicion of IFI, it was defined as a diagnostic BDG episode, while others were defined as a surveillance BDG episode.

Results. Of a total of 140 episodes, 24 episodes were non-evaluable. Among 116 evaluable episodes, 75 received induction chemotherapy for acute leukemia or myelodysplastic syndrome, 35 underwent stem cell transplantation, and 10 had intensive treatment for graft-vs.-host disease. There were three episodes of probable/proven IFI (2.6%). Ninety-one (78.4%) were performed with diagnostic purpose, while 25 (21.6%) were performed for surveillance. TP, TN, FP, and FN were 2 (1.7%), 91, 22, and 1, respectively. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value were 66.7%, 80.5%, 8.3% and 98.9%, respectively. PPV was 13.3% and 0% in diagnostic and surveillance BDG episodes, respectively.

Conclusion. The PPV of BDG was low in hematology patients receiving antimold prophylaxis, even in the diagnostic-driven episodes. The routine screening of BDG is not helpful, and the BDG test may be used for exclusion of IFI rather than for diagnosis in these patients.

