Session: 151. Viruses and Bacteria in Immunocompromised Patients
Friday, October 5, 2018: 12:30 PM

Background. Non-meningococcal and nongonococcal *Neisseria* spp. are usually commensal and rarely cause invasive disease in humans. Eculizumab, a terminal complement inhibitor, increases susceptibility to meningococcal disease, but data on atypical *Neisseria* spp. disease in persons receiving eculizumab are lacking. This case series describes postmarketing reports of disease by commensal *Neisseria* spp. in patients receiving eculizumab.

Methods. The FDA Adverse Event Reporting System (FAERS) database and the medical literature were searched for cases of disease by any nonmeningococcal and nongonococcal *Neisseria* spp. in patients receiving eculizumab. Included cases had a diagnosis of disease by any atypical *Neisseria* spp. with onset on or before January 31, 2018 and ≥1 dose of eculizumab in the 3 months prior to disease.

Results. The search identified seven FAERS cases, including one case also reported in the literature. Patient ages ranged from 4 to 38 years. Five patients had positive blood cultures, of which three had an indwelling catheter for vascular access (n = 2, *N. sicca/subflava*) or hemodialysis (n = 1, *N. cinerea*). Two patients with bacteremia had *N. cinerea* septic shock with possible cholecystitis, and *N. mucosa* sepsis with concurrent *Streptococcus* bacteremia after gastroenteritis. The remaining two cases in the series included one with *N. sicca* bacterial peritonitis associated with a peritoneal dialysis catheter (negative blood cultures, other cultures not specified), and one with a diagnosis of *N. flavescens* sepsis while neutropenic (specimen source not specified). All seven patients were hospitalized and three had sepsis or septic shock. All cases resolved with antibiotics and supportive care.

Conclusion. We identified seven cases of serious disease caused by atypical *Neisseria* spp. among eculizumab recipients. Since these organisms are typical inhabitants of the oropharynx and urogenital tract and are not skin flora, the source of disease was unclear. Our data suggest that eculizumab may confer increased risk for disease by usually commensal *Neisseria* spp. Healthcare professionals are encouraged to treat all *Neisseria* spp. isolated from sterile sites as pathogenic, and not as contaminants, in patients receiving eculizumab.

The views expressed are those of the authors and do not necessarily represent those of, nor imply endorsement from, the U.S. Food and Drug Administration, the Centers for Disease Control and Prevention, or the U.S. government.

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1559. Hematopoietic Cell Transplantation with Post-transplant Cyclophosphamide: Impact of Donor Type on Pre-engraftment Blood-Stream Infections

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Session: 151. Viruses and Bacteria in Immunocompromised Patients
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Background. The aim of the study was to estimate the cumulative incidence of pre-engraftment blood stream infections (PE-BSI), its predictive factors and the infection-related mortality (IRM) after hematopoietic cell transplantation (HCT) from any donor type, with post-transplant cyclophosphamide (PT-Cy).

Methods. Retrospective cohort study on 235 adults who underwent peripheral blood HCT from every donor type with PT-Cy platform, from 2013 to 2017 at San Raffaele Scientific Institute. The Poisson regression was used to estimate the crude incidence rate (IR) of PE-BSI. The Fine-Gray competing risk model was applied to estimate the cumulative incidence function (CIF) of the first PE-BSI and its predictive factors and of IRM.

Results. Patients' characteristics are reported in Table 1. During 5,316 person-days of follow-up (PDFU), 77 PE-BSI episodes occurred in 72 patients: IR = 1.45 per 100-PDFU [95% confidence interval (95% CI) 1.13–1.77]. The median time to PE-BSI was 13 days (IQR: 7–17) and the estimated CIF at 28 days was 32% (95% CI: 26–39%); no differences in CIF according to donor type [30% vs. 34% vs. 32% in match-related, match-unrelated and haploidentical donor, respectively; Gray's test: P = 0.968]. Among the 87 isolated pathogens, 60% were Gram-positive bacteria (GPB), 39% Gram-negative bacteria (GNB) and 1% nontuberculous mycobacteria. CIFs of GNB and GPB PE-BSI by type of donor are shown in Figure 1. By multivariate analysis (Table 2), after adjustment for age, sex, year of HCT, donor type and disease phase at HCT, the CIF of any PE-BSI was higher in subjects with absolute neutrophils count ≤500 for ≥7 days before HCT [adjusted hazard ratio (AHR) = 2.90] and in multi-drug resistant (MDR) GNB rectal carriers before HCT [AHR = 2.68]. These covariates were confirmed as independent factors also for GNB PE-BSI. Overall, IRM at 30 days was 5% (95% CI: 2–8%) with no differences by donor type (Gray's test: P = 0.106).

Conclusion. HCT with PT-Cy platform showed a 32% of cumulative incidence of PE-BSI at 28 days and donor type did not affect its occurrence, which was conversely increased by prolonged and severe neutropenia and MDR GNB rectal carriage before HCT. Haploidentical setting did not retain a higher IRM at 30 days than match-related and match-unrelated donors.

Table 1. Characteristics of patients who underwent hematopoietic cell transplantation with PT-Cy platform (all patients received antibiotic prophylaxis with levofloxacin).

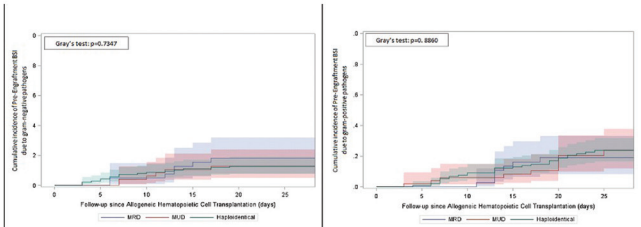
Patients' Characteristics		Overall (n =235)	MRD (n =40)	MUD (n =50)	haplo (n =145)	p-value
BASELINE						
Age at HCT, yr, median (IQR)		49.6 (37.0-62.0)	48.1 (40.9-59.4)	50.6 (37.4-57.0)	51.6 (36.4-63.1)	0.863
Male gender, n (%)		147 (63%)	25 (63%)	33 (66%)	89 (62%)	0.844
Year of HCT, median (IQR)		2016 (2014-2017)	2016 (2015-2017)	2016 (2016-2017)	2015 (2014-2016)	<0.0001
ANC ≤500 for ≥7 days before HCT		66 (28%)	10 (25%)	5 (10%)	51 (35%)	0.003
Diagnosis§, n (%)	Acute myeloproliferative diseases	157 (67%)	27 (68%)	29 (58%)	101 (70%)	0.260
	Acute and chronic lymphoproliferative diseases	65 (27%)	11 (27%)	15 (30%)	39 (27%)	
	Chronic myeloproliferative diseases	12 (5%)	2 (5%)	5 (10%)	5 (3%)	
	Benign/immune-mediated diseases	1 (1%)	0	1 (2%)	0	
Disease phase at HCT, n (%)	>CR1	40 (17%)	1 (2)	9 (18%)	30 (21%)	0.001
	CR1	63 (27%)	16 (40%)	20 (40%)	27 (19%)	
	Active disease	131 (55%)	23 (58%)	20 (40%)	88 (61%)	
	Not applicable	1 (1%)	0	1 (2%)	0	
Conditioning regimen, n (%)						0.286
	Myeloablative conditioning	184 (78%)	35 (88%)	39 (78%)	110 (76%)	
	Reduced intensity conditioning	51 (22%)	5 (12%)	11 (22%)	35 (24%)	
MDR-GNB rectal carrier within 30 days before HCT, n (%)		18 (8%)	3 (8%)	1 (2%)	14 (10%)	0.214
Number of HCT, n (%)	First allogenic HCT	201 (87%)	39 (98%)	50 (100%)	115 (79%)	0.001
	Second allogenic HCT	27 (12%)	1 (2%)	0	26 (18%)	
	Third allogenic HCT	4 (3%)	0	0	4 (3%)	
GVHD prophylaxis*, n (%)	PT-Cy/sirolimus/(t)MMF	231	40 (100%)	50 (100%)	141 (98%)	0.387
	PT-Cy/cyclosporine A/MMF	3	0	0	3 (2%)	
FOLLOW-UP						
Follow-up, days, median (IQR)		276 (137-580)	289 (197-577)	316 (174-531)	259 (114-618)	0.579
ANC engraftment, n (%)		225 (96%)	39 (98%)	50 (100%)	136 (94%)	0.144
Time to engraftment, days, median (IQR)		20 (17-24)	20 (16-24)	22 (19-29)	19 (17-24)	0.046
PE-BSI, n (%)	none	164 (70%)	28 (70%)	34 (68%)	102 (70%)	
	Single BSI episode	72 (31%)	12 (30%)	16 (32%)	44 (30%)	0.972
	Two BSI episodes	5 (2%)	0	1 (2%)	4 (3%)	0.563
At least 1 BSI due to Gram-positive bacteria, n (%)		46 (20%)	7 (18%)	10 (20%)	29 (20%)	0.936
At least 1 BSI due to Gram-negative bacteria, n (%)		30 (13%)	7 (18%)	6 (12%)	17 (12%)	0.615
Time to the first BSI after HCT among subjects who developed≥1 BSI, days, median (IQR)		13 (7-17)	13 (12-15)	13 (7-20)	10 (7-18)	0.549
Antimicrobial resistance score, n (%)						0.051
	Susceptible to 1st line antibiotic therapy (PTZ)	13 (18%)	1 (8%)	7 (44%)	5 (11%)	
	Susceptible to 2nd line antibiotic therapy (MEM,VAN)	49 (68%)	9 (75%)	8 (50%)	32 (73%)	
	Resistant to 2nd line antibiotic therapy (MEM,VAN)	10 (14%)	2 (17%)	1 (6%)	7 (16%)	
Septic shock, n (%)		12 (17%)	2 (17%)	2 (17%)	8 (18%)	0.873

Abbreviations: HCT, hematopoietic cell transplantation; MRD, match-related donor; MUD, match-unrelated donor; haplo, haploidentical donor; ANC, absolute neutrophils count; CR, complete response; MDR-GNB, multi-drug resistant Gram-negative bacteria; GVHD, graft-versus host disease; PT-Cy, post-transplant cyclophosphamide; MMF, mofetil mycophenolate; PE-BSI, pre-engraftment blood-stream infection; PTZ, piperacilin/tazobactam; MEM, meropenem; VAN, vancomycin.

§ Acute myeloproliferative diseases: acute myeloid leukemia, myelodysplastic syndrome; Acute and chronic lymphoproliferative diseases: acute lymphoblastic leukaemia, Hodgkin lymphoma, non-Hodgkin lymphoma, multiple myeloma; Chronic myeloproliferative diseases: chronic myelogenous leukemia, idiopathic myelofibrosis, myeloproliferative neoplasm; Benign/immune-mediated diseases: chronic granulomatous disease.

* 1 patient died because of ESBL-producing Escherichia coli BSI before receiving GVHD prophylaxis

Figure 1 - Cumulative incidence function (CIF) of the first pre-engraftment BSI due to Gram-negative and Gram-positive bacteria according to the type of donor [CIF estimated according to the Fine-Gray method, with engraftment, pre-engraftment death or second HCT as competing events].



	% cumulative incidence (95%CI)		
	MRD	MUD	Haploidentical
7 days	5% (0.9% - 15.0%)	4.2% (0.8% - 12.7%)	7.2% (3.7% - 12.3%)
14 days	12.7% (4.6% - 25.2%)	10.6% (3.8% - 21.3%)	11.1% (6.5% - 17.1%)
21 days	18.3% (7.9% - 32.0%)	12.7% (5.1% - 24.0%)	12.7% (7.7% - 19.1%)
28 days	18.3% (7.9% - 32.0%)	12.7% (5.1% - 24.0%)	12.7% (7.7% - 19.1%)

	% cumulative incidence (95%CI)		
	MRD	MUD	Haploidentical
7 days	0%	6% (1.5% - 15.0%)	5.2% (2.3% - 9.9%)
14 days	13.5% (4.8% - 26.5%)	8.2% (2.6% - 18.2%)	12.2% (7.3% - 18.5%)
21 days	19.1% (8.2% - 33.2%)	20.4% (9.9% - 33.6%)	20.5% (13.9% - 28.0%
28 days	19.1% (8.2% - 33.2%)	23.7% (11.9% - 37.8%)	23.8% (16.5% - 31.8%

Table 2 - Multivariate Fine-Gray models to assess baseline factors associated with the incidence of any or Gram-negative bacteria (GNB) pre-engraftment BSI (PE-BSI)

Characteristic at HCT	Risk categories	Adjusted HR of any PE-BSI (95%CI)	p-value	Adjusted HR of GNB PE-BSI (95%CI)	p-value
Age	per 3-years older >50 vs ≤50 years	1.010 (0.959-1.063)	0.716	0.943 (0.866-1.027)	0.178
Gender	Female vs Male	0.877 (0.524-1.467)	0.616	0.767 (0.340-1.730)	0.523
Year of HCT	per 2 more recent years >2015 vs ≤2015	0.942 (0.628-1.411)	0.770	1.024 (0.515-2.036)	0.947
ANC ≤500 for ≥7 days before HCT	Yes vs No	2.895 (1.542-5.435)	0.0009	4.866 (1.992-11.89)	0.0005
MDR-GNB rectal carrier within 30 days before HCT	Yes vs No	2.683 (1.253-5.749)	0.011	3.885 (1.288-11.72)	0.016
Type of donor			0.496		0.367
	Haploidentical vs MRD	0.929 (0.480-1.801)	0.828	0.656 (0.255-1.688)	0.382
	MUD vs MRD	1.493 (0.758-2.944)	0.387	1.307 (0.417-4.099)	0.646
Disease phase	Active disease vs >CR1/CR1	0.886 (0.483-1.624)	0.694	1.074 (0.432-2.674)	0.877

Abbreviations: HCT, hematopoietic cell transplantation; MRD, match-related donor; MUD, match-unrelated donor; haplo, haploidentical donor; ANC, absolute neutrophils count; CR, complete response; MDR-GNB, multi-drug resistant Gram-negative bacteria; PE-BSI, pre-engraftment blood-stream infection.

The multivariate model considered engraftment and pre-engraftment death as competing events; it was constructed by considering the main exposure of interest (type of donor), *a priori* factors known to have a potential effect on the incidence of PE-BSI (age and sex) and other covariates with a p-value<0.2 at univariate analysis.

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1560. Clinical Presentation of BK Virus-Associated Hemorrhagic Cystitis (HC) After Hematopoietic Cell Transplantation (HCT)

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Background. BK polyoma virus (BKPyV) has been associated with hemorrhagic cystitis after HCT. Prior studies have examined risk factors for BKPyV-associated HC, but the characteristics of disease, including duration, common presentations, and the spectrum of clinical outcomes, have not been well described. Precise estimates of major clinical endpoints are critical to design clinical trials of novel prevention and treatment agents.