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721.ALLOGENEIC TRANSPLANTATION: CONDITIONING REGIMENS, ENGRAFTMENT AND ACUTE TOXICITIES

Impact of Concurrent and Previous Multidrug Resistant Bacteria Colonization in Adult Allogenic Hematopoietic Stem Cell Transplant Patients with Acute Leukemia: A Single Center Retrospective Study

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Background
Multidrug resistant bacteria (MDRB) pose a major challenge in allogenic hematopoietic stem cell transplant (allo-HSCT) since patient colonization with Gram - or Gram + MDRB has been identified as a risk factor for infections, acute graft versus host disease (aGVHD) and reduced overall survival (OS). Nevertheless, data on the prognostic value of MDRB colonization are still scarce, and whether it should represent a limit to allo-HSCT eligibility is controversial. Few data are also available on the impact of previously detected colonization that are absent at transplant time.

Methods
This is a retrospective single center study on 60 patients with acute myeloid or lymphoblastic leukemia who underwent allo-HSCT from January 2014 to March 2023 according to JACIE standards.All patients were treated at our department starting from induction. In each hospital stay MDRB colonization was assessed by rectal swabs performed at admission, and thereafter weekly. In case of fever 3 sets of blood culture from peripheral vein and central venous catheters, urine culture and chest X-ray were performed, and empiric antibiotic therapy initiated. In MDRB colonized patients, targeted antibiotic therapy was administered if clinically indicated. All patients received fluroquinolones as antimicrobial prophylaxis. Data were retrieved from hospital records.

Aim of the study
To assess the epidemiology of MDRB colonization and the related impact on allo-HSCT outcome in terms of MDRB-related infections, aGVHD within day 100, OS and non-relapse mortality (NRM).

Results
MDRB colonization was detected in 26/60 (43.4%) patients, in 13 (21.7%) at hospital admission and in additional 13 (21.7%) after allo-HSCT. Overall, 33 MDRB strains were isolated (Table 1).
Among patients colonized at hospital admission, Gram - MDRB accounted for 10/16 (62.5%) strains, mostly *Escherichia Coli* producing extended-spectrum beta-lactamases (ESBL) and *Klebsiella Pneumoniae* ESBL, while Gram + MDRB were 6 (37.5%), mostly represented by vancomycin-resistant *Enterococcus faecium* (VRE). In 14/16 (87.5%) cases the colonization has been previously detected, in 78.5% since the first two hospital stays.
Among patients with positive rectal swabs after allo-HSCT, Gram - MDRB accounted for 16/17 (94.1%) strains, mostly *Escherichia Coli* ESBL and *Klebsiella Pneumoniae* ESBL (1 producing carbapenemases). In these patients the rectal swab turned out positive after a median time of 10 (2-24) days after allo-HSCT, mostly during neutropenia. Albeit absent at hospital admission, 13/17 (76.5%) MDRB strains had been previously isolated in the same patients, being firstly identified during the first two hospital stays in 76.9% cases.
No significant differences in patient baseline characteristics, leukemia classification, type of donor and conditioning or hospitalization length were observed between MDRB carriers (26, 43.4%) and non-carriers (34, 56.8%) (Table 2).
During the whole hospital stay, 18/26 (69%) carriers and 32/34 (94%) non-carriers reported at least one febrile event (p=0.01). Only carriers experienced MDRB (Gram -) infections based on blood (4, 22%) and urine (7, 38%) culture, while the rate of positive chest X-ray (4, 22,2% vs 5, 15.6%, p=0.5) did not differ. Targeted antibiotics were administered to 14/18 (77.8%) febrile

carriers, in 10 (71%) at fever onset and in 4 (29%) at fever persistence. Four (22.2%) did not receive treatment because not clinically indicated. Intensive care unit was never required in both cohorts.
The incidence of aGVHD was similar between carriers and non-carriers (10, 38.5% vs 17, 50%, p=ns), but the proportion of grade 2-4 tended to be higher in the first group (70% vs 35.5%, p=0.08).
Overall, 73% patients are alive with a median follow-up of 18 (0.8-49) months. Median OS was not reached in both groups (p=0.09). There was no difference in NRM between carriers and non-carriers (5, 19% vs 2, 6%, p=0.11).

Conclusion

In our series 43.3% of allo-HSCT patients were colonized by MDRB that, in line with recent literature, were mostly Gram -. The absence of life-threatening infections and the non-significantly inferior OS and NRM in colonized patients suggest that a careful investigation of concurrent and previous colonization and a prompt use of targeted antibiotics may temper the negative impact of MDRB-related infections in adult acute leukemia patients undergoing allo-HSCT. Larger prospective studies are awaited.

Disclosures No relevant conflicts of interest to declare.

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Table 1

MDRB STRAIN	HOSPITAL ADMISSION n (% all strains)	POST HSC INFUSION n (% all strains)	Total n (%)
Escherichia coli ESBL	5	4	9 (27.3)
Klebsiella pneumoniae ESBL	4	4 (1>KPC)	8 (24.2)
Klebsiella oxytoca ESBL		1	1 (3)
Klebsiella aerogenes ESBL		1	1 (3)
Enterobacter cloacae ESBL	1	2	3 (9.2)
Stenotrophomonas maltoph. MDR		2	2 (6.1)
Citrobacter freundii ESBL		1	1 (3)
Burkholderia cenocepacia ESBL		1	1 (3)
Enterococcus faecium VRE	5	1	6 (18.2)
Enterococcus faecalis VRE	1		1 (3)
	16 (48.4)*	17 (51.6)*	33 (100)

* fraction/total strains

Table 2

	MDRB carriers 26	non carriers 34	p
Age	59.2 (22.8-75.1)	56.8 (20.8-71.2)	0.55
Male sex	15 (57.7%)	17 (50%)	0.55
Acute myeloid leukemia	19 (73.1%)	28 (82.4%)	0.38
Acute lymphoblastic leukemia	7 (26.9%)	6 (17.6%)	0.39
Myeloablative conditioning	18 (69.2%)	25 (73.5%)	0.7
Donor			
HLA-matched sibling	9 (34.6%)	7 (20.6%)	0.22
Haploidentical sibling	3 (11.5%)	1 (2.9%)	0.18
Unrelated HLA-matched	14 (53.9%)	26 (76.5%)	0.06
Hospital stay length (days)	29 (20-131)	28 (19-87)	0.14

Figure 1