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Influence of prior invasive aspergillosis on outcome of allogeneic hematopoietic stem cell transplantation

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Background

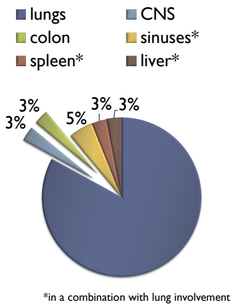
Introducing a new antifungals and diagnostic procedures has improved prognosis of the invasive aspergillosis (IA) in hematological patients. The number of patients with IA who are candidates for allogeneic hematopoietic stem cell transplantation (allo-HSCT) has increased and problems related to the transplant procedure are urgent now. The influence of IA on survival and on transplant related complications has not been investigated in a prospective study under current conditions. The role of the invasive aspergillosis registered prior to the allo-HSCT is still a subject of controversy. ***Specific Aim:*** The aim of this prospective study was to estimate impact of prior proven and probable IA on outcome of allo-HSCT compared to patients without history of IA.

Methodology

In prospective observational single center study 362 allo-HSCT recipients (336 first and 26 second allo-HSCT) were included from Jan 2012 to Dec 2014 (3 years). The median age was 34 y.o., males – 54%. Most of pts had high-risk acute leukemia (70%). Allo-HSCT from MUD were performed in 57%, MRD – 24%, haplo – 11%, MMUD – 8%, predominantly with RIC (80%). Patients received chemotherapy in different regions of Russian Federation where most of the data including history of prior IA were collected. All patients with lesions in CT scan before allo-HSCT have undergone bronchoscopy with BAL microscopy, culture and GM test. For diagnosis of proven and probable IA and evaluation of response to therapy were used EORTC/MSG 2008 criteria. "Active" invasive IA was IA diagnosed just before allo-HSCT. We analyze status of pts before HSCT, donor types, source of HSCT, CMV status, conditioning regimens and type of immunosuppression, relapse or progression of IA, relapse of underlying disease, duration of antifungal therapy and prophylaxis, acute and chronic GvHD. Median of follow up period was 2 y. Overall survival rate (OS) after allo-HSCT was estimated with Kaplan-Meier method and cohorts were compared by log-rank test.

Pts, allo HSCT	Age, median - range, y	Males	Underlying diseases		Donor types				Conditioning	
			Acute leukemia	Other	MRD	MUD	MMUD	Haplo identical	Myelo-ablative	Reduced intensity
336	34									
362	1-67	181	235	101	87	206	29	40	72	290

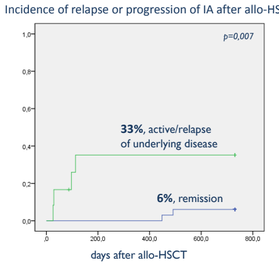
Sites of infection



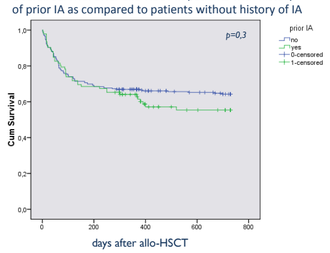
*in a combination with lung involvement

Status of IA at the moment of allo-HSCT				
I.	complete response	26%	n=19	→ secondary prophylaxis
II.	partial response / stabilization	43%	n=31	→ continuation treatment
III.	"active" invasive aspergillosis	31%	n=22	→ first line treatment

Incidence of relapse or progression of IA after allo-HSCT



Overall survival after allo-HSCT in patients with history of prior IA as compared to patients without history of IA



Results

Incidence of IA before allo-HSCT was 20% (n=72/362). According to EORTC/MSG 2008 criteria 92% of pts had probable IA and 8% proven IA. The main sites of infection were lungs – 95%, central nervous system – 3%, and colon – 3%, other localizations were observed mostly in a combination with lung involvement: sinuses – 5%, spleen – 3%, and liver – 3%. The median time from IA to allo-HSCT was 3 months (3 days – 2 years 6 months). Antifungal therapy before allo-HSCT was administrated in 69% pts (voriconazole – 95%, other – 5%) with the median duration of therapy – 2 months. Complete response to antifungal therapy was registered in 19 (26%) pts, partial response or stabilization in 31 (43%), and "active IA" in 22 (31%) pts. After allo-HSCT all pts received antifungal therapy with Voriconazole (first line – 31%, continuation of treatment – 43%, and secondary prophylaxis – 26%). Median length of treatment was 166 days (37 – 394) with the median duration to effect 99 days (31 – 217). No toxicity of the antifungal treatment was registered. Cumulative incidence of relapse or progression of IA at 2 year after alloHSCT was 14% (n=10). "Active" underlying disease before Day+100 post transplant was the only risk factor for the relapse or progression of IA after allo-HSCT (6% vs 33%, p=0,007). 100-days OS after allo-HSCT was 77%, 2-year OS after allo-HSCT was 62%. There was no significant difference in OS in patients with or without IA before allo-HSCT (57% vs 65%, p=0,3). There was no significant difference in OS in patients with or without IA before allo-HSCT (57% vs 65%, p=0,3). Duration of antifungal therapy before HSCT (<90 days *vs* ≥90 days) and status of IA at the moment of HSCT ("active" IA *vs* PR *vs* CR) had no effect on 2-year OS after allo-HSCT in patients with prior IA.

Conclusion

Incidence of proven and probable invasive aspergillosis before allo-HSCT was 20%. Cumulative incidence of relapse or progression of the invasive aspergillosis after allo-HSCT was 14% and progression of underlying disease before D+100 post transplant was the only risk factor.

With effective diagnosis, treatment and secondary prophylaxis prior invasive aspergillosis did not impair the outcome of the allogeneic hematopoietic stem cell transplantation.

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