Relating autoimmune cytopenias after hematopoietic cell transplantation (HCT) to transplant-variables and immune reconstitution: a predictor analysis

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Background

- Autoimmune cytopenias (AIC) after allogeneic HCT are serious complications requiring urgent immunosuppressive therapy
- The etiology of AIC remains unclear
- Incidence of AIC post-HCT in children varies from 2.1% to 6%
- Diagnosis of AIC post-HCT is challenging as it is difficult to distinguish the newly occurring AIC from more common infectious diseases or treatment-related toxicity and cGVHD

Aims

- In this retrospective, pediatric study we aim to compare incidence of AIC between stem cell sources
- Identify and analyze risk factors of AIC
- Relate markers from immune reconstitution and inflammation events to AIC

Conclusions

We identified multiple risk factors for development of AIC:

1. **Cordblood as cell source**
2. **No previous chemotherapeutic treatment**
3. **aGVHD prior to development of AIC**

IgM, IgG and IgA levels are increased prior to AIC diagnosis and may be an interesting immune biomarker

Survival chances were not affected for patients developing AIC

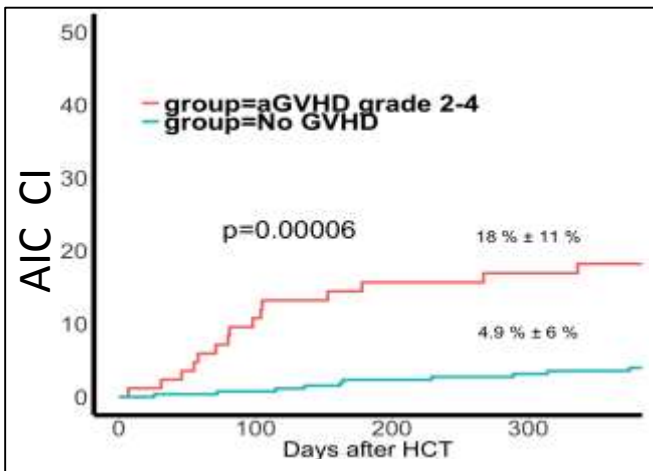

Figure 1. AIC Cumulative incidence curve shows that patients with a GVHD 2-4 have a higher chance (p< 0.001) to develop AIC.

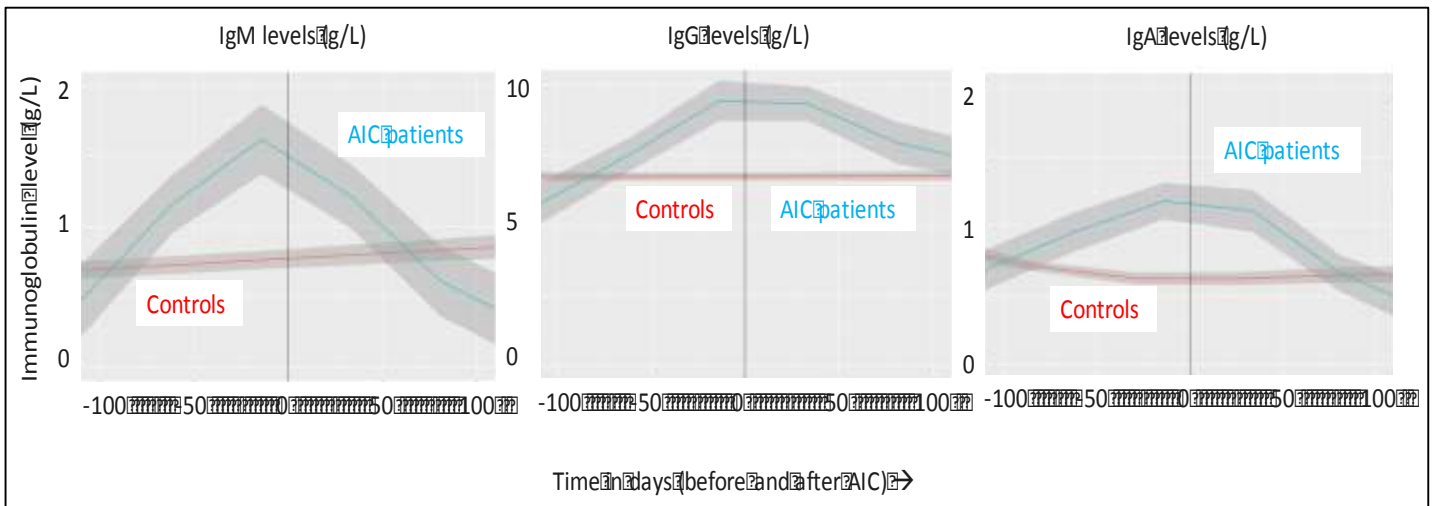

Figure 2: Immunoglobulin profiles show increased levels of IgM, IgG and IgA prior to AIC development

Patient characteristics

	Patients with AIC	Patients without AIC
Gender, n (%)		
Male	20 (74%)	
Female	7 (26%)	
Median age at diagnosis, yr (range)	4.6 (0.2-17)	
Type of underlying disease, n (%)		
Malignant	9 (33%)	
Non-malignant	18 (66%)	
Graft source, n(%)		
Cordblood	23 (85%)	
Bonemarrow	3 (11%)	
Peripheral blood	1 (4%)	
Chemotherapy prior to HCT		
Yes		
No		
Acute GVHD		
Yes		
No		
Lineages, n (%)		
AIHA	24 (89%)	Na
AIT	25 (93%)	Na
AIN	19 (70%)	Na

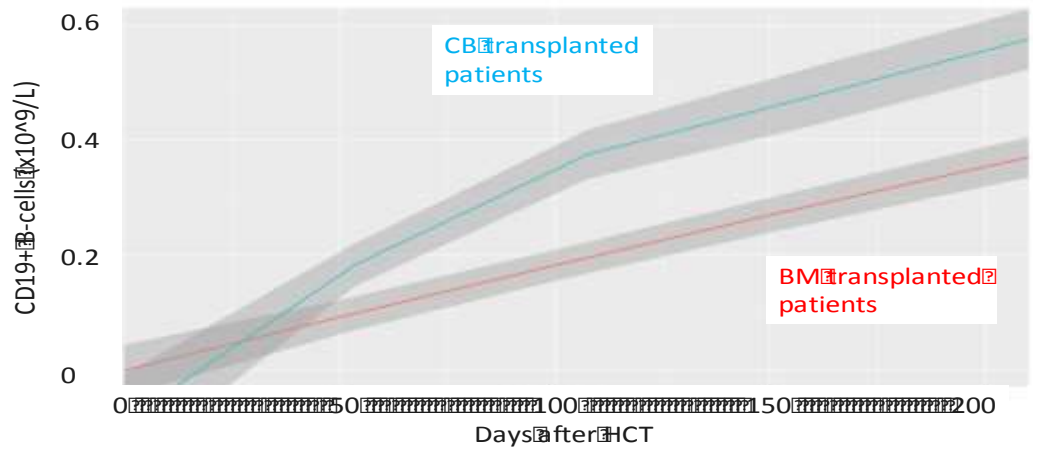

Figure 3: B-cell reconstitution after HCT stratified in CB (n=193) and BM (n=157) transplanted patients

Methods

- All patients who underwent their 1st allogeneic T-replete HCT at the UMC Utrecht between 2004-2016 were included
- AIC were defined as a rapid decrease of hemoglobin, thrombocyte and/or neutrophil count in combination with positive coombs test and/or detection of auto-immune antibodies
- AIC were treated with prednisone, MMF, IVIG and rituximab.
- Cox regression analysis was performed to identify predictors
- Immune reconstitution was monitored longitudinally from day 14 post HCT till day 100 including various subsets of T cells, B cells, NK cells, IgG, IgA and IgM levels.
- Immune reconstitution was related to development of AIC by setting the time point of AIC development at zero. For non AIC patients (controls), the zero point was set at the median of AIC development
- Effect of immune reconstitution on AIC development was estimated using cause specific hazard models. Gray's test was used to correct for competing risks.

Results

- 7.7% of patients developed AIC in 1 (n=3), 2 (n=7) or 3 (n=17) lineages at a median of 136 days post HCT
- Predictors for AIC were cordblood as donor source (HR=3.5, 95%-CI 1.3-9.8, p=0.01), no previous chemotherapeutic treatment (HR=3.03, 95%-CI, p=0.02) and aGvHD grade II-IV (HR=4.4, 95%-CI 2.0-9.3, p<0.001)
- Development of AIC was preceded by an increased level of IgM (p=0.0007), IgA (p<0.0001) and IgG (p=0.088), and lower absolute lymphocyte counts
- B cell reconstitution was faster after cordblood transplantation compared to bonemarrow transplantation
- Overall survival was comparable between AIC patients (86%) and controls (72%, p=0.077)