Bone Marrow Transplantation

Definition of myeloid engraftment after allogeneic hematopoietic stem cell transplantation

Neutrophil counts continued to rise after reaching 0.5 ×10⁹/L in 78 allograft recipients receiving granulocyte colony-stimulating factor (G-CSF) post-transplant. This was confirmed in 44 subsequent patients not receiving G-CSF. This suggests that the first day of neutrophils ≥0.5×10⁹/L can be considered a valid definition of myeloid recovery after allogeneic transplantation.

haematologica 2004; 88:763-764
(http://www.haematologica.org/journal/2004/6/763)

Myeloid engraftment in hematopoietic stem cell tranplantation (HSCT) is defined as the first of three consecutive days with an absolute neutrophil count (ANC) of 0.5×10⁹/L or greater (ANC500).[1-5] This definition has become the standard for transplant registries such as the International Blood and Marrow Transplant Registry (IBMTR) and peer-review organizations such as the Foundation for the Accreditation of Cell Therapy (FACT). The tempo of myeloid recovery following autotransplantation is steady, making documentation of ANC500 for 3 consecutive days unnecessary.[6]

Serial blood counts on 78 adults with hematologic malignancies (Table 1) allografted after standard regimens were studied. Myeloid growth factors were administered to 69 of 78 patients in the post-transplant period until ANC500 was seen for 3 days; 67 received G-CSF and 2 GM-CSF. ANC included segmented neutrophils as well as bands. A subsequent cohort of 47 patients treated uniformly without G-CSF underwent the same analysis to determine whether the data were reproducible.

Including the first day with ANC500, 3 consecutive ANC levels were available in 65 patients; 2 levels in 10 patients, and 1 level in 3 patients. In the last 3 patients ANC values were available 2-5 days after the first day with ANC500. Table 2 shows the ANC values in these groups and changes in ANC on consecutive days. Of the 75 patients with ANC values available on days 1 and 2, ANC increased from day 1 to 2 in 70 patients and declined in 5. In 4 of 5, it remained above 0.5×10⁹/L. It fell to less than 0.5×10⁹/L in one but increased to >0.5×10⁹/L on day 3. Of the 65 patients with available ANC data for day 3, ANC increased from day 2 to 3 in 57 and declined in 8. None of the 8 had an ANC below 0.5×10⁹/L, and 6 had counts that were higher than those on day 1. The type of graft-versus-host disease prophylaxis, myeloid growth factor administration, stem cell source, and the CD34⁺ cell dose did not affect changes in ANC after myeloid recovery.

In the validation group, potentially acceptable evidence of engraftment, i.e. ANC on the 2 consecutive days following

Table 1. Patients' characteristics (study group).

n	*78*
Age (years)	19-62 (median 43)
Male	49 (62%)
Diagnosis	
Acute leukemia	23 (29%)
Chronic leukemia	18 (23%)
Plasma cell dyscrasias	17 (22%)
Lymphoma	15 (19%)
Other	5 (6%)
Source of stem cells	
Bone marrow	20 (26%)
Blood	16 (21%)
Both	42 (54%)
CD34⁺ cell dose (×10⁶/kg ideal body weight)	0.7-10.8 (median 5.1)
Graft-versus-host disease prophylaxis	
Cyclosporine-Prednisone	46 (59%)
Cyclosporine-Methotrexate	30 (38%)
Cyclosporine alone	2 (3%)
Growth factor post-transplant	69 (88%)

Table 2. Absolute neutrophil counts on days 1, 2, and 3, and per cent change from days 1 to 2, 2 to 3, and 1 to 3 in the Study Group (A). Day 1 is the first day with ANC ≥0.5×10⁹/L.

Documented consecutive days with ANC >0.5	*Day after HSCT (median, range)*	*ANC (10⁹/L; median, range)*			*% change in ANC (median, range)*		
		Day 1	*Day 2*	*Day 1*	*Day 1 to 2*	*Day 2 to 3*	*Day 3 to 3*
Study group 3 (n=65)	12 (8-26)	0,83 (0.50-3.95)	1.50 (0.30-13.78)	2,92 (0.55-25.65)	+117 -46 to +628	+70 -28 to +294	+265 -41 to +971
2 (n=10)	14,5 (10-20)	0,84 (0.57-2.44)	2,01 (0.70-4.57)		+118 +15 to +341		
1 (n=3)	10 (9-11)	2,21 (0.92-2.90)					
Validation group 3 (n=44)	13 (10-23)	0,77 (0.53-2.10)	1,44 (0.36-10.94)	2,52 (0.44-30.74)	+67 -36 to +574	+50 -17 to +1925	+178 -21 to +1793

ANC500, was available for 44 patients (94%). ANC increased from day 1 to 2 in 39 of 44 patients, and declined in 5. It remained $\geq 0.5\times10^9$/L in 2 patients, and declined below 0.5×10^9/L in 3 patients - 2 of whom had an ANC $\geq 0.5\times10^9$/L the next day; 1 with G-CSF and 1 without. ANC increased from day 2 to 3 in 42 of 44 patients, and declined in 2 - but remained $\geq 0.5\times10^9$/L in both. ANC increased from day 1 to 3 in 43 of 44 patients; declining below 0.5 in 1 patient. This patient's ANC was below 0.5×10^9/L on the second day too, but it was $\geq 0.5\times10^9$/L on the fourth day and remained steady thereafter. Thus, in 43 of 46 patients not receiving G-CSF post-transplant, the first day with ANC $\geq$0.5 was also the first of 3 consecutive days with ANC $\geq 0.5\times10^9$/L. Our study shows that myeloid engraftment after allogeneic HSCT is robust and sustained. Only rarely does the ANC fall below 0.5×10^9/L within a couple of days after reaching that threshold level. Thus, the first day with ANC500 is the same as the first of three consecutive days of ANC500 in almost all cases. We therefore propose that myeloid engraftment after allogeneic transplantation be defined as the first day with ANC of $\geq 0.5\times10^9$/L without necessarily having two subsequent days of confirmation whether G-CSF is used or not. It is uncertain whether this can apply to cord blood allografts in which hematologic reconstitution is slower and less predictable.[3]

A change in the standard definition of myeloid engraftment has several implications. If transplant registries and organizations such as FACT changed the traditional definition to the one that we propose, data would less often be considered incomplete or deficient. This would not compromise the quality of the data or patients' care. It is not always clinically necessary to check complete blood counts on the subsequent two days after the ANC reaches 0.5×10^9/L. Checking blood counts only for documentation purposes can result in longer hospital stays, extra clinic visits, and additional use of home care resources. The realization that the first day of ANC500 represents myeloid engraftment could also allow for earlier discontinuation of prophylactic antibiotics, but such steps require further investigation.

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Funding: This work was supported in part by the Auxiliary Board of the Northwestern Memorial Hospital.

Keywords: hematopoietic stem cell transplantation, engraftment, neutropenia.

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