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To the editor:

Hematopoietic progenitor cell harvest and functionality in Fanconi anemia patients

Recently, Croop et al[1] reported the feasibility of mobilizing and collecting peripheral blood $CD34^+$ progenitor cells from patients with Fanconi anemia. The authors performed successful apheresis collection in 6 of 8 patients. They showed that prolonged granulocyte colony-stimulating factor (G-CSF) administration (median 10 ± 4 d) and days of apheresis (4 ± 3 d; range, 2-8 d) were required and that such procedure led to significant adverse events. This study supported evidence that patients with Fanconi anemia can be mobilized, but the authors did not answer the question of whether these hematopoietic progenitors were functional and could efficiently participate to autologous reconstitution after infusion. In this scope, data concerning granulocyte-macrophage colony-forming unit (GM-CFU) assays would have been of great interest.

We would like to report our experience with G-CSF–mobilized peripheral blood $CD34^+$ cells ($n = 4$) or bone marrow (BM) harvest ($n = 2$) in patients with Fanconi anemia, using a standard collection method. At the time of harvest, none of the patients had criteria of severe aplastic anemia (defined by hemoglobin level below 80 g/L [8 g/dL], absolute neutrophil count below 0.5×10^9/L, and platelet count below 20×10^9/L) and were transfusion independent (Table 1). All 4 mobilized patients, with a mean age of 17.3 y (range, 4-31 y), received G-CSF at the daily dose of 10 μg/kg for 5 days. Two of them failed to mobilize, while the other 2 underwent apheresis with a number of initial peripheral blood $CD34^+$ counts of 9.4/μL and 9.8/μL. Within 2 days of apheresis, the numbers of total nucleated cells collected in these 2 patients were 84.86×10^9/kg and 90.14×10^9/kg and the numbers of $CD34^+$ cells were 1.53×10^6/kg and 0.9×10^6/kg. GM-CFU assays were performed by seeding 1×10^3 $CD34^+$ cells in a conventional methylcellulose culture assay in order to determine myeloid progenitors cell growth. Interestingly, $CD34^+$ progenitor cells failed to generate GM-CFU colonies with numbers of 0.42×10^4 or 1×10^4 GM-CFU/kg patient weight, thus suggesting a low clonogenic capacity of $CD34^+$ cells even in patients without severe bone marrow failure. We determined that $CD34^+$ cells from Fanconi anemia patients have 5 to 12 times lower levels of GM-CFU/kg, as compared with 72 patients with hematologic malignancies for whom apheresis, performed with the same standard conditions, led to a median of 1.1×10^6 $CD34^+$/kg (median GM-CFU/kg, 5.1×10^4). The same pattern of dramatic decrease in $CD34^+$ cells (0.03×10^6/kg and 0.12×10^6/kg) and GM-CFU (0×10^4/kg) was observed in both patients that underwent BM harvest. These results contrast with a relatively normal blood count that cannot be predictive of CD34 cell recovery or functionality.

Similar to a murine model of FANCC disruption clearly demonstrating a reduced repopulating ability of hematopoietic stem cells,[2] our results tend to support the hypothesis of a qualitative and quantitative defect of hematopoietic progenitor cell compartment.

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Table 1. Patients characteristics and analysis of collection and clonogenicity of bone marrow or peripheral blood progenitor cells

Patient no.	Product	Sex	Age, y	Weight, kg	WBC, $\times 10^9$/L	ANC, $\times 10^9$/L	Hb, g/dL	Plt, $\times 10^9$/L	WBC at apheresis, $\times 10^9$/L	$CD34^+$ count/μL	Days of apheresis	Liters processed	TNC, $\times 10^9$	$CD34^+$, $\times 10^6$/kg	GM-CFUs, $\times 10^4$/kg
1	PBSCs	F	26	50	4	1.79	12.2	144	14.7	9.4	2	27.8	90.14	0.9	0.42
2	PBSCs	M	4	20	2.5	0.88	7.8	9	5.6	1.4	—	—	—	—	—
3	PBSCs	F	12	27	1.9	0.67	7.9	37	4.2	1.2	—	—	—	—	—
4	PBSCs	M	17	47	4.3	1.83	13.2	118	19.2	9.8	2	21.7	84.86	1.53	1
5	BM	M	31	61	4.2	2.27	13.5	72	—	—	—	—	0.88	0.03	0
6	BM	M	14	52	3.8	1.06	12.2	62	—	—	—	—	0.79	0.12	0

WBC indicates white blood cell count; ANC, absolute neutrophil count; Hb, hemoglobin level; Plt, platelet count; TNC, total nucleated cell count; PBSCs, peripheral blood stem cells; F, female; and M, male.