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CIRCULATING ENDOGENOUS GRANULOCYTE COLONY-STIMULATING FACTOR LEVELS AFTER BONE MARROW TRANSPLANTATION

To the Editor:

Endogenous circulating granulocyte colony-stimulating factor (G-CSF) levels after bone marrow transplantation (BMT) have been reported previously by us and others.[1,2] In this ongoing study, we have evaluated 19 transplant patients (16 allogeneic and 3 autologous) for a follow-up period of mean 29 months (4 to 72 months) once a week. Analyses are performed with a commercial enzyme immunoassay (EIA) kit (Amgen Diagnostics, Thousand Oaks, CA). Ten healthy control subjects are also included to the study. The study by Cairo et al[3] is interesting in regard to our results which, in part, are similar. The cytoreductive regimen and the patient characteristics in both studies are comparable.[3] Although their follow-up frequency occurs more often than ours, we have also observed a negative correlation between white blood cell (WBC) and G-CSF levels in uncomplicated transplants on week 0 and +4 (respectively, $r = .555$ and .788). The endogenous G-CSF levels are within the limits of 0 to >3,000 pg/mL (Fig 1). A

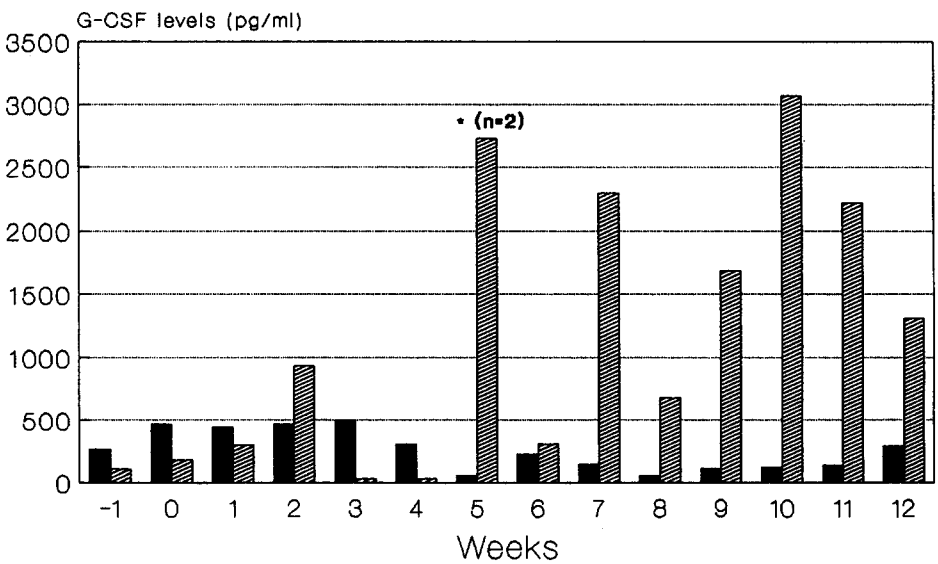


Fig 1. Circulating endogenous G-CSF levels after BMT. (■) Uncomplicated (n = 16); (▨) engraft, failure (n = 3); (•) after the PBSCT.

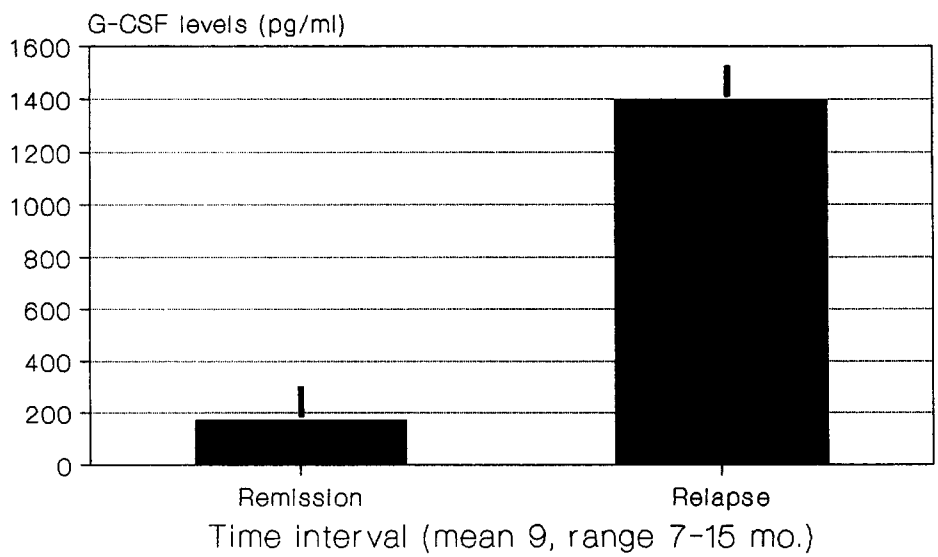


Fig 2. Circulating G-CSF levels during remission and relapse after BMT.

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parameter that is not mentioned in Cairo's study is the G-CSF level during infectious episodes. In our experience, G-CSF levels during infections (temperature over 38°C) are higher (mean: 585 ± 272) compared to days without fever (mean: 328 ± 180) ($P = .0177$). When patients were evaluated according to the take in time, preengraftment G-CSF levels (mean: 654 ± 506) decreased after take in (mean: 273 ± 209) ($P = .0214$). In three patients who developed engraftment failure serum G-CSF increased compared with preconditioning values, but not significantly. However, no WBC increase was observed. Peripheral stem cell was infused to two of these patients, which resulted in a G-CSF increase to > 3,000 pg/mL. The cytokine triggering effect of this procedure has also been reported by Baiocchi et al.[4] Another interesting observation was a G-CSF increase that occurred in four cases (1 CML, 1 ANLL, 2 ALL) with clinical relapse from 175 ± 203 to 1,400 ± 979 pg/mL ($P = .0498$) (Fig 2).

The role of interleukin-1 (IL-1) in the pathogenesis of leukemias is under investigation.[5] G-CSF secretion can be stimulated by IL-1.[6] The predictive value of our limited experience warrants further investigation both in regard to engraftment failure and leukemic relapses.

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RESPONSE

The data provided by Beksac et al regarding an inverse correlation between white blood cell count and endogenous granulocyte colony-stimulating factor (G-CSF) levels in uncomplicated bone marrow transplants between week 0 and week 4 are very compatible with the inverse correlation that we have previously demonstrated. It is unclear whether their inverse correlation between endogenous G-CSF levels also occurred with the absolute neutrophil count or just the circulating white blood cell count. The circulating levels of endogenous G-CSF after bone marrow transplantation are also both very similar in each of our studies (0 to 3,000 pg/mL). However, in our study we could not show any difference in the endogenous G-CSF level between those patients who had infections and/or fever greater than 38°C versus those who were either uninfected or afebrile. Additionally, because we only had one patient who demonstrated graft failure, it is difficult to compare our data to their three patients who developed graft failure. However, their three patients with graft failure did not demonstrate a significant increase in endogenous G-CSF levels compared with preconditioning values, which was similar to our one patient.

Most interesting, however, is their finding of increased G-CSF levels in four patients with leukemia who developed a clinical relapse post marrow transplantation. Because none of our leukemia patients relapsed during the time of study, we have no comparative data or correlate these findings. However, an increase in certain hematopoietic growth factors (especially G-CSF) during clinical relapses for acute and chronic leukemias may either represent a cause-and-effect relationship or possibly an epiphenomena associated with leukemogenesis and increase in granulocyte production during relapse. Further investigation is warranted to expand this observation and determine the mechanisms associated with this finding.

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