Expression of HLA-DR (Major Histocompatibility Complex Class II) on Neutrophils From Patients Treated With Granulocyte-Macrophage Colony-Stimulating Factor for Mobilization of Stem Cells

To the Editor:

Gosselin et al\(^1\) have shown in vitro that granulocyte-macrophage colony-stimulating factor (GM-CSF) can induce the expression of HLA-DR (major histocompatibility complex [MHC] class II) on mature neutrophils isolated from the blood of normal individuals. To determine if GM-CSF can have a similar effect in vivo, we used flow cytometry to measure HLA-DR expression on blood neutrophils obtained from two patients treated with GM-CSF for stem cell mobilization in preparation for autologous transplantation. For comparison, we also measured HLA-DR expression on blood neutrophils obtained from normal individuals and from a patient treated with granulocyte colony-stimulating factor (G-CSF) for stem cell mobilization.

As expected, we did not detect HLA-DR on neutrophils from several normal individuals or on neutrophils from the patient treated only with G-CSF. However, we detected HLA-DR on neutrophils from both patients treated with GM-CSF. The first patient was treated with GM-CSF in two separate courses 30 days apart. In both courses, this patient received GM-CSF (Immunex, Seattle, WA; 300 µg/day, subcutaneously [SC]) on days 1 through 10 and G-CSF (Amgen, Thousand Oaks, CA; 600 µg/d, SC) beginning on day 3 and continuing through day 10. The percentages of HLA-DR\(^+\) neutrophils increased from less than 1% immediately preceding GM-CSF administration to 63% and 47% by day 3 after the initiation of GM-CSF therapy for the first and second treatment course, respectively. Beginning on day 4 of GM-CSF administration in each course, after the addition of G-CSF, the percentages of HLA-DR\(^+\) neutrophils began to decrease. On days 6 through 10, neutrophils were negative for HLA-DR. Figure 1 shows the results for the first patient for the first 5 days of the first course of GM-CSF/G-CSF. The second patient was treated with a similar course of GM-CSF/G-CSF. Neutrophils from this patient were less than 1%, 29%, and 3% HLA-DR\(^+\) on treatment days 0, 3, and 6, respectively. These percentages were consistent with levels of HLA-DR \(\alpha\)-chain detected in neutrophil lysates by Western blot.

Neutrophils from the patients treated with GM-CSF had mature characteristics. These characteristics included appropriate light-scatter in the forward and 90° direction, expression of CD16b, low (dim) expression of CD14, and lack of expression of CD34. These characteristics clearly distinguished these cells from monocytes and, together with the observed absence of blasts or other immature myeloid forms in the blood smears, suggested that the HLA-DR\(^+\) neutrophils were relatively mature cells. This is an important distinction because early myeloid forms, including committed progenitor cells through early myeloblasts, express HLA-DR.

GM-CSF administration modulated several other parameters relative to pretreatment values in these patients. Most of these changes were similar to those observed after the administration of G-CSF to normal individuals.\(^2\) These included the white blood cell count and differential, the mean fluorescence intensity of CD14\(^-\) and CD16b\(^-\) neutrophils, and the ratio of band to segmented neutrophil forms.
However, neutrophil HLA-DR expression did not correlate with any of these changes. Nevertheless, the appearance of HLA-DR on these cells may be linked to the potent direct or indirect effects of GM-CSF on myeloid progenitor cells, neutrophil proliferation and maturation kinetics, the systemic distribution of neutrophils, neutrophil priming/activation status, or other parameters.1,4 Because cellular HLA-DR expression generally correlates with the ability of a cell to present antigens to helper T cells, these observations imply that neutrophils may be capable of a more active role in the immune response than previously suspected.5

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REFERENCES

Detection of minimal residual disease in acute leukemia [letter; comment]

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