Early Trilineage Recovery by Granulocyte Colony-Stimulating Factor in a Patient with Aplastic Anemia

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Among the cytokines active in hematopoiesis, granulocyte colony-stimulating factor (G-CSF) has functions mainly on cells of neutrophilic granulocyte lineage [1]. A large number of clinical trials have suggested that G-CSF can accelerate the recovery of neutrophils when used after high-dose cytotoxic chemotherapy or bone marrow transplantation [2, 3]. In addition, G-CSF have been shown to have beneficial effects in patients with aplastic anemia (AA) who suffer from severe neutropenia [4]. With the exception of rare instances, however, G-CSF is known to have little or no effect on erythrocyte or platelet counts [2, 4-7]. We report here a unique case with acquired AA who showed trilineage recovery shortly after administration of rhG-CSF.

Case Report

A 57-year-old man was referred to Osaka University Hospital because of pancytopenia in April 1993. He had a 3-month history of pancytopenia and had received a total of 800 ml of red blood cell (RBC) in a previous hospital. Laboratory data were as follows: hemoglobin (Hb), 11.2 g/dl (immediately after RBC transfusion); reticulo-cytes 88 × 10^9/l, white blood cells (WBC), 3.2 × 10^9/l with differentials of 35% neutrophils and 56% lymphocytes; and platelets (PLT) 73 × 10^9/l. Bone marrow aspirate and biopsy revealed uniform hypocellularity (nucleated cell count, 14 × 10^9/l) with megakaryocytes and no morphological abnormalities. Based on these findings, he was diagnosed as having mild AA [8]. Daily anabolic steroids were thus administered orally at a dose of 30 mg/kg body weight in April 1993. This treatment did not improve the hematologic parameters and hemoglobin decreased (fig. 1).

Because RBC transfusions were required every 2 or 4 weeks, the patient was admitted to our hospital on September 21, 1993. Hemoglobin was 8.6 g/dl, reticulocytes 80 × 10^9/l, WBC 2.71 × 10^9/l (47.8% neutrophils, 3.8% eosinophils, 39.9% lymphocytes, 8.1% monocytes), and PLT
56 × 10⁹/1. Bone marrow aspirate revealed severe hypocellularity, and cytogenetic examination showed normal karyotype. After admission, his neutrophil count gradually decreased to less than 1.0 × 10⁹/1. Because of little response to anabolic steroid therapy, daily rhG-CSF was administered at the initial dose of 250 μg (5.0 μg/kg) subcutaneously. A rise of the WBC and neutrophil counts was seen 1 day after the initiation of this treatment. After a 1-week course, G-CSF was discontinued, and WBC and neutrophil counts rapidly decreased. The daily subcutaneous injection of rhG-CSF was returned after a 1-week interruption, but its dose was reduced to 125 μg/day. Shortly (< 2 weeks) after the treatment, RBC and PLT counts started to increase in addition to the expected rise of neutrophil count. Also, the number of reticulocytes increased and reached a maximum (246 × 10⁹/1) at the 8th week of rhG-CSF treatment. The anabolic steroid was then stopped. Since the WBC and neutrophil counts exceeded 30 × 10⁹/1 8 weeks after the initiation of therapy, the schedule of rhG-CSF administration was changed (250 μg two or three times a week). This rhG-CSF treatment maintained the WBC count between 4 × 10⁹/1 and 10 × 10⁹/1. Unexpectedly, both hemoglobin and PLT gradually increased the normal range. In addition to the improvement in peripheral blood, bone marrow aspirate exhibited normocellularity with almost normal differentials 6 weeks after the initiation of treatment. However, despite a slight increase in the number of multilineage progenitor cells (CFU-Mix), the numbers of granulocyte-macrophage progen-
Table 1. Numbers of hematopoietic progenitor cells in bone marrow before and after rhG-CSF treatment

- Numbers of progenitor cells (per 5 × 10⁴ cells) were measured using methylcellulose cloning cultures [9]. All cultures were performed with a combination of interleukin-3 (10 ng/ml), granulocyte-macrophage colony-stimulating factor (10 ng/ml), granulocyte colony-stimulating factor (10 ng/ml), and erythropoietin (2 U/ml). The results are shown as the mean ± SEM of triplicate cultures. CFU-E = late erythroid progenitor cells; CFU-GM = granulocyte-macrophage progenitor cells; BFU-E = erythroid progenitor cells; CFU-Meg = megakaryocytic progenitor cells; CFU-Mix = multilineage progenitor cells.
- Control value was obtained from 2 male volunteers (ages 57 and 68) showing normal hematopoiesis. The results are shown as the mean ± SEM of the 2 controls.

References

Hashimoto et al. Effect of G-CSF on Aplastic Anemia