Serial Granulocyte Transfusions as a Treatment for Sepsis Due to Multidrug-Resistant Pseudomonas aeruginosa in a Neutropenic Patient

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The emergence of multidrug-resistant Pseudomonas aeruginosa (MRPA) has become a major clinical problem. We successfully treated MRPA sepsis in a neutropenic patient undergoing peripheral blood stem cell transplantation with serial granulocyte transfusions. Granulocyte transfusion should be considered as a treatment for severe infection in patients with neutropenia.

CASE REPORT

An 11-year-old girl with acute myeloid leukemia achieved complete remission after a course of induction antileukemic chemotherapy and relapsed during courses of the consolidation therapies. She was treated with allogeneic bone marrow transplantation from her brother, whose human leukocyte antigens (HLA) were fully matched. She relapsed again on day 150 after bone marrow transplantation and failed to achieve complete remission. Subsequently, she suffered from sepsis and cellulitis of the labia majora caused by multidrug-resistant Pseudomonas aeruginosa (MRPA). Antibiotic susceptibility tests revealed that the bacteria were resistant to piperacillin (MIC, 128 mg/liter), ceftazidime (MIC, ≥128 mg/liter), cefazolin (MIC, ≥32 mg/liter), aztreonam (MIC, 16 mg/liter), ciprofloxacin (MIC, ≥64 mg/liter), gentamicin (MIC, ≥64 mg/liter), imipenem (MIC, 16 mg/liter), and meropenem (MIC, 16 mg/liter). The bacteria were, however, sensitive to amikacin (AMK; MIC, 16 mg/dl). Although blood cultures became negative for MRPA after the administration of AMK, the labia majora fell into necrosis and culture still yielded numerous MRPA bacteria.

Since the patient deteriorated from leukemia, we decided to treat her with peripheral blood stem cell transplantation (PBSCT) from her mother (one HLA locus mismatched) with a double conditioning regimen. The first part consisted of cytarabine, etoposide, and nimustine, and the second part consisted of fludarabine, melphalan, and total-body irradiation. Immunosuppressive therapy consisting of methotrexate and tacrolimus was administered for prophylaxis of graft-versus-host disease.

Fever developed, the C-reactive protein level became elevated, and a blood culture yielded MRPA during the first part of the conditioning therapy despite the administration of AMK and meropenem (3) (Fig. 1). We chose the patient’s father and aunt as donors for granulocyte transfusion (GT) to avoid a immunological response to the PBSCT donor since there was a possibility of infusing lymphocytes simultaneously from the granulocyte donors. Each GT donor was stimulated with a single dose of subcutaneous granulocyte colony-stimulating factor (G-CSF; 600 µg/body) and oral dexamethasone (8 mg/body) simultaneously 20 h before leukapheresis (1, 7). Granulocytes were collected by standard centrifugation leukapheresis (CS3000; Baxter) by using hetastarch with processing of 8 liters of blood in approximately 2.5 h via peripheral venous access. The collected granulocytes were irradiated with 30 Gy. GTs were performed on days −10, −7, −5, −3, 0, 2, 4, 6, 7, and 10 since neutrophils could not survive for more than 48 h and moreover began to lose their function in less than 6 h (6). The donor on days −10, −5, 0, 4, and 7 was her father. The donor on days −7, −3, 2, and 6 was her aunt. The donor on day 10 was her mother (PBSCT donor). The amount of granulocytes we transfused (harvested) resulted in a mean of 31.4 × 10⁹ (range, 8.10 × 10⁹ to 65.3 × 10⁹) cells. The in vivo neutrophil increment was determined 14 to 16 h after GT and resulted in a mean of 1,215/µl (range, 0 to 2,900/µl). The fever subsided, the C-reactive protein level decreased, and the blood culture became negative for MRPA when the neutrophil count was kept above 500/µl and the absolute neutrophil count with- out GT reached 500/µl on day 16. Although culture of the labia majora yielded MRPA during the entire course of PBSCT, it eventually became negative for MRPA on day 17. Bone marrow aspiration on day 60 showed complete remission and replacement by the mother’s cells.

P. aeruginosa is the bacterial pathogen most frequently responsible for infection in immunocompromised patients. The prevalence of MRPA isolates has been increasing and has become a major clinical problem (2, 8).

The use of GT is complicated by the technical difficulty of daily procurements of granulocytes for patients. The complex-
ity of donor recruitment, screening, and care is also prohibitive as part of routine treatment for the infected patients with neutropenia. In addition, before the widespread clinical use of G-CSF, GT had a limited role in the treatment of infections because of the inadequate dose of granulocytes. However, the use of a combination of G-CSF and dexamethasone to mobilize granulocytes resulted in a sufficient yield of granulocytes (1, 7). The efficacy of GT and the availability of G-CSF allow us to consider the feasibility of using GT for severe infection in patients with prolonged neutropenia (4, 5, 9).

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REFERENCES

FIG. 1. Clinical course of PBSCT. MTX, methotrexate; FK506, tacrolimus; MEM, meropenem; WBC, white blood cells; CRP, C-reactive protein.