Anti-LFA-1 Antibody Treatment of a Patient with Steroid-Resistant Severe Graft-Versus-Host Disease

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OHASHI, Y., TSUCHIYA, S., FUJIE, H., MINEGISHI, M. and KONNO, T. Anti-LFA-1 Antibody Treatment of a Patient with Steroid-Resistant Severe Graft-Versus-Host Disease. Tohoku J. Exp. Med., 1992, 167 (4), 297-299 — For treatment of steroid-resistant severe graft-versus-host disease, a murine monoclonal antibody (25.3) against the α chain (CD11a) of the lymphocyte function-associated antigen 1 (LFA-1) was infused into a patient with posthepatitic aplastic anemia who had undergone allogeneic bone marrow transplantation. The monoclonal antibody infusion was well tolerated and resulted in appreciable improvement in symptoms of gastrointestinal illness such as diarrhea and abdominal pain, suggesting that this antibody may be useful for controlling severe acute graft-versus-host disease. —— graft-versus-host disease; monoclonal antibody; CD11a

Recently, the in vivo efficacy of a murine monoclonal antibody (mAb) against the α chain (CD11a) of the lymphocyte function-associated antigen 1 (LFA-1) has been investigated in patients with steroid-resistant grade III-IV acute graft-versus-host disease (GVHD) with beneficial results and minimal toxicity (Stoppa et al. 1991). We also applied the mAb to a case of steroid-resistant severe GVHD with noted improvement in symptoms.

The patient, an 8-year-old boy with severe aplastic anemia following acute non-A and non B hepatitis, underwent allogeneic bone marrow transplantation (BMT) from an HLA identical sibling donor. For GVHD prevention cyclosporin A and short-term methotrexate were given. Nevertheless, after engraftment severe acute GVHD (grade III) did develop, associated with abdominal pain, profuse watery diarrhea (> 1,500 g/day), generalized erythrodermia, and mild hepatic dysfunction. Administration of prednisolone (60 mg/day) and high dose methylprednisolone (1,500 mg/day) were ineffective.

In view of the minimal toxicity of anti-LFA-1 α chain murine mAbs used for prevention of graft failure in HLA non-identical BMT (Fischer et al. 1986, 1991; Maraninchi et al. 1988), we decided to try infusion of an anti-LFA-1 α chain mAb 25.3, which had been supplied by Immunotech, Marseille, France. The preparation was sterile and free of pyrogen, and the dosage was 0.2 mg/kg body weight/day, applied by intravenous infusion over a 6-hr period for 7 successive days.

As shown in the Fig. 1, diarrhea appeared to be improved from day 3 and the severity of abdominal pain began to be alleviated at day 5. After completion of the course of mAb administration, abdominal pain continued to decrease in severity and disappeared within 10 days, followed by remarkable further improvement in diarrhea. However, erythrodermia was little changed. The infusions of mAb were well tolerated without any apparent

Received July 29, 1992; revision accepted for publication August 27, 1992.
toxicity. The first 24-hr kinetics of serum mAb showed a peak level (2μg/ml) at the 8th hr and an estimated half-life of approximately 40 hr. Serum anti-CD11a mAb levels increased cumulatively during the treatment but began to drop rapidly after the last infusion. Antimouse IgG antibodies were not detected when examined at the 2nd and 4th week of the therapy. Although further clinical trials are needed to confirm the efficacy of this approach, the present observation offer support for the use of anti-LFA-1 antibodies in controlling severe acute GVHD.

Acknowledgments

We are grateful to Dr. Michel Delaage, Immunotech, Marseille CEDEX 9, France for providing the mAb 25.3. The work was supported in part by grants from the Ministry of Education, Science and Culture, and from the Ministry of Health and Welfare.

References
