of pulmonary surface nodules about 3 weeks after tumor implantation. The antimetastatic activity of N-CWS depended upon the dose, time and route of its injection. Intravenous injection of N-CWS after removal of the implanted tumor caused the greatest inhibition of development of pulmonary metastases. Therapy with N-CWS plus CPA prolonged significantly the survival of mice with metastases.

The cytotoxic activities of peritoneal macrophages and macrophages in the lung against 3LL cells were enhanced in mice treated with N-CWS. Intravenous injection of peritoneal macrophages activated with N-CWS inhibited pulmonary metastases.

In conclusion, biological response modifiers such as N-CWS showed antitumor activity by intratumoral application.

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REFERENCES

Supplementary (1) Bone Marrow Transplantation in the Treatment of Acute Leukemia

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Twenty-two patients with acute leukemia including 10 with acute non-lymphocytic leukemia (ANL), 9 with acute lymphocytic leukemia (ALL) and 3 with leukemic non-Hodgkin's lymphoma were treated with high-dose cyclophosphamide (CY) and 1,000 cGy total body irradiation (TBI) followed by bone marrow transplantation from an HLA-identical sibling donor. The patients ranged from 8 to 46 yr in age (the median, 32 yr). Eight patients were transplanted at relapse and 14 during first or later remission. All patients were isolated in a laminar air-flow room with total intestinal decontamination. Intensive cares included blood component therapy, total parenteral nutrition and infection prevention programs. Prophylactic methotrexate was given to prevent graft-vs-host disease (GVHD) as scheduled. No antileukemic therapy was given after bone marrow transplantation. Engraftment was confirmed by conversion of sex chromosome and red cell antigens to the donor type.

At the time of analysis (March, 1984), 7 transplant patients are alive in complete remission 71, 36, 21, 17.5, 6, 5.5 and 1 mo respectively posttransplant; 1 out of these 7 patients received bone marrow at relapse while the remaining 6 in remission. Primary causes of death in 15 patients were as follows: Interstitial pneumonia in 6 patients, leukemic relapse in 3, hepatic veno-occlusive disease in 2, sepsis in 2, acute GVHD in 1 and pneumonia associated with chronic GVHD in 1.

When results were analysed in 19 evaluable patients on the basis of 1 yr survival, factors such as recipient's age, pretransplant condition and GVHD were associated with the survival. One year survival was obtained in 3 of 4 evaluable patients under 20 yr old, 1 of 3 between 21-30
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yr old, 1 of 7 between 31–40 yr old and none of 4 over 41 yr old. Only one of 8 (13%) patients transplanted at relapse has survived more than 1 yr after transplantation while 4 of 11 (36%) transplanted in remission have survived. As for GVHD, 1 yr survival rates were 50% (2/4) and 14% (2/14) in patients with and without acute GVHD respectively; they were 50% (1/2) and 75% (3/4) in patients with and without chronic GVHD respectively.

These observations clearly demonstrate that allogeneic bone marrow transplantation can produce relatively high long-term survival rates in the treatment of acute leukemia. One patient is now surviving in unmaintained remission almost 6 yr after transplantation. In this patient, acute leukemia is probably cured. Another patient with T cell-ALL was transplanted during first remission because poor prognosis was expected. The patient has survived more than 3 yr after transplantation. Patients with ALL are usually transplanted during second or later remission because the disease is curable in a considerable portion of the patients by conventional chemotherapy. Since posttransplant relapse rates have been high in patients with ALL, bone marrow transplantation during first remission will be an effective approach in the treatment of high risk ALL with poor prognosis.

When results were analysed in relation with posttransplant survival, younger age of the recipients, transplantation during remission and the presence of acute GVHD are factors which favorably influence 1 yr survival after transplantation. Therefore, long-term survival will be highly expected in younger patients with acute leukemia when bone marrow transplantation is performed during complete remission. Furthermore, transplantation during remission will have advantages in reducing major or fatal complications compared with that at relapse. Among transplantation-related complications, interstitial pneumonia is one of the most important problems to be solved.

Supplementary (2) Differential Sensitivities of Long-Term Cultured Cell Lines Derived from Human Haematopoietic Malignancies to Various Anti-Cancer Drugs

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We investigated anti-cancer drug sensitivities of long-term cultured cell lines derived from patients with haematopoietic malignancies in vitro. The 15 cell lines used in this experiment consist of 3 non-T, non-B cell leukemia cell lines, 4 T-cell lineage cell lines derived from lymphoblastic leukemia, 6 B-cell lineage cell lines derived from B-cell leukemia and lymphoma and 2 myeloma cell lines, 2 myeloid cell lines derived from myeloid leukemia. As for anti-cancer drugs, following drugs are tested: antibiotics; daunorubicin HCl(DAU), doxorubicin HCl(ADR); anti-metabolites; methotrexate (MTX), cytarabine (CA); vinca alkaloid; vincristine sulfate (VCR); steroid hormone; dexamethasone (DX); alkylating agent; cyclophosphamide (CY). Anti-cancer antibodies have strong cytotoxic effects to each cell line. Among them, B-cell lineage cell lines were less sensitive to the drugs than T-cell lineage cell lines. Some non-T, non-B cell line which is belong to lymphoid stem cell was the most resistant cell to any drugs. Anti-metabolites showed a tendency that they were more effective in cytotoxicity to immature cell lines than to more-differentiated cell lines of both T- and B-lineage cells. Vinca alkaloid showed