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New promise in treatment of leukemia

Transplanting the patient's own bone marrow eliminates the graft-versus-host problem and permits chemoradiotherapy.

Results of a new bone marrow transplantation technique, reported in the July 17, 1986 issue of *The New England Journal of Medicine,* hold out promise for victims of acute leukemia who relapse after chemotherapy. The article describes the results of treating 25 leukemia patients, who had a relapse of their leukemia after one or more remissions on chemotherapy, by infusions of their own bone marrow collected during remission and chemically treated.

Leukemia was one of the first major cancers to yield to modern chemotherapeutic treatment. Since the pioneering studies by Sidney Farber on the treatment of childhood leukemias, a number of types of this otherwise uniformly lethal, malignant proliferation of white blood cells, have become curable diseases.

Many cases of acute non-lymphocytic leukemia go into prolonged remission (absence of symptoms and normal blood picture) following intensive chemotherapy. Some of these patients may well remain in remission for the rest of their lives and thus be cured of their leukemia.

In other cases, these patients experience one or more recurrences of leukemic proliferation of their white blood cells. These patients have a poor prognosis for ultimate leukemia-free survival.

Chemotherapeutic treatment involves administering cytotoxic (cell-killing) agents to kill the leukemic cells in the bone marrow. These agents also kill normal cells. Therefore, there is always the possiblity of leaving the patient without any white blood cells at all.

Such patients are severely immunosuppressed and rapidly fall victim to infections similar to those which afflict victims of AIDS.

One method of dealing with this problem has been to go ahead with extensive chemotherapy and radiation therapy to completely destroy the leukemic cells, and the patient's immune system, and then transplant new bone marrow into the patient.

The new bone marrow can come from one of two sources: a genetically related donor, or the patient himself.

Marrow from a genetically related donor (allogeneic marrow) must be carefully matched against the prospective recipient to avoid graft-versus-host disease. In this situation, the marrow graft perceives the tissues of the host as foreign antigens and attacks them, ultimately killing the host.

Only 25 to 40% of patients who might benefit from allogeneic marrow transplants, will be sufficiently compatible with a potential donor to justify the attempt. Immunosuppressive therapy, in addition to the anti-leukemic treatment, is required.

Transplantation of the patient's own bone marrow (autologous marrow), collected during remission and frozen, eliminates the graft-versus-host problem and enables the adminstration of intensive chemoradiotherapy to the leukemic marrow, followed by reinfusion of the stored marrow. The main problem in autologous marrow transplantation, especially after the second remission, is that the marrow may contain viable leukemia stem cells which then go on to reestablish the disease.

The *New England Journal* article describes the application of a technique of treating the removed bone marrow with a chemical, 4-hydroperoxycyclophosphamide. This chemical had been demonstrated to remove leukemic cells from bone marrow suspensions at concentrations which did not impair the ability of the remaining normal cells to repopulate the marrow.

A number of techniques to remove leukemic cells from bone marrow suspensions, utililizing monoclonal antibodies, have been developed. While this technique works well for lymphocytic leukemias, monoclonal antibodies to non-lymphocyte white cells have been difficult to identify and develop.

Thus the ability to chemically purge leukemic cells from the marrow of patients with non-lymphocytic leukemia represents a significant breakthrough for treatment of such patients who lack compatible marrow donors.

The results of this study, conducted at the John Hopkins University School of Medicine, are very promising. Median leukemia-free survival was over 400 days, and ranged up to 1,653 days. While the number of leukemic relapses in this group was higher than in patients treated by allogeneic marrow transplants, the overall results were much better than with chemotherapy alone.

These preliminary results indicate that this technique must be considered to offer the first real possibility of extended survival to patients with non-lymphocytic leukemia who have relapsed and do not have a compatible donor of normal marrow.