

Blood-cell transplants slow kidney cancer

Physicians call renal-cell cancer a silent malignancy because it usually develops in people without producing pain or other symptoms. If the cancer, which seldom responds to drugs, is detected while still confined to a kidney, removing that organ can save a patient. In most cases, however, this stealthy cancer spreads before it's found and on average, is fatal within a year of diagnosis.

Researchers now report some success in fighting this kidney cancer by using blood from a healthy sibling donor and enabling immune cells in it to take control of the cancer patient's immune system. In 8 of 19 patients given this therapy, donor immune cells attacked the cancer, sending it into full or partial remission, the scientists report in the Sept. 14 *NEW ENGLAND JOURNAL OF MEDICINE*.

The study "opens new therapeutic possibilities not only for metastatic renal-cell cancer but also for other solid tumors that are resistant to conventional chemotherapy and radiotherapy," says Shimon Slavin of Hadassah University Hospital in Jerusalem in the same issue.

To prepare a transplant, the researchers first treated a donor with a drug that flushes bone-marrow cells into the bloodstream. The researchers then extracted the bone-marrow stem cells—which can differentiate into various cell types—and many of the donor's white blood cells, the body's immune-system warriors.

The scientists treated the cancer patients with immune-suppressing drugs while giving them up to three infusions of the donor cells. As the researchers decreased the patients' doses of the immune suppressants over several months, the donor's immune cells destroyed the patients' immune cells and bone-marrow stem cells. This cleared the way for donor cells to replace the patients' cells, says study coauthor Richard W. Childs, an oncologist at the National Heart, Lung, and Blood Institute in Bethesda, Md.

In some cases, the result has been stunning, Childs says. When the 19 patients began their treatment, during 1998 or 1999, all had had a cancerous kidney removed but still had cancer. Also, the best available drugs—interferon alpha and interleukin-2—had failed in these patients. Their life expectancy was 6 to 8 months at best, Childs says.

Since treatment, two patients have survived more than 2 years, and six others have lived for more than a year. Cancer is undetectable in four of these eight patients. In the others, tumors have shrunk by at least half.

The study is "the first intriguing evidence" in a long time of a beneficial treatment for renal-cell cancer, says Robert Dreicer, a urologic oncologist at the Cleveland Clinic Foundation. "Given the lack of therapies for this disease, for selected patients [with appropriate sibling donors], this clearly is a glimmer of hope."

About 30,000 people receive diagnoses of kidney cancer each year in the United States. Renal-cell cancer makes up about 85 percent of these cases.

The treatment is far from perfect, Childs says. The other 11 patients in the study have died. Ten succumbed to the cancer or its complications. The other patient died from graft-versus-host disease—a condition that arises when immune cells in a transplant attack the recipient's blood or tissue cells too aggressively.

The study suggests the researchers turned the graft-versus-host reaction to some patients' advantage, making it a graft-versus-tumor response. However, inducing graft-versus-host disease is the medical equivalent of playing with fire. "You need to be cautious," Dreicer says.

Thus, the patients' treatment can be described as "a balancing act," Childs says. The scientists had to risk inducing some graft-versus-host destruction by donor immune cells as they were easing back on immune-suppressing drugs in order to give these cells enough latitude to

seek and destroy tumor cells.

Childs and his colleagues are now culturing donor immune cells in laboratory dishes with tumor cells from a potential recipient. Their goal is to orient the donor immune cells to their malignant targets before injecting them into patients.

—*N. Seppa*