

Canine Stem Cell Transplantation

Joseph Impelizzeri, DVM, DACVIM (Oncology) www.oncologyvet.com

Canine patients can benefit from stem cell transplantation in the treatment of Lymphosarcoma. This procedure was pioneered at the Fred Hutchinson Cancer Research Center in Seattle, Washington and dogs were the original species in which the stem cell transplantation (SCT) procedures were perfected more than twenty years ago. Today, that information is available as a treatment option for dogs with lymphoma, leukemia, multiple myeloma, and other immune system diseases. This article will discuss the process and experience with canine lymphoma.

The transplant process has several steps. The first begins with a diagnosis and classification of the type of lymphoma (including staging and immunohistochemistry or flow cytometry). This information is used to individualize a treatment plan. Depending on the availability of a compatible stem cell donor, the decision to perform either an autologous or an allogenic transplant is considered. An autologous transplant is completed by using the patient's own stem cells to reconstitute the bone marrow after chemotherapy and total body irradiation. An allogenic transplant requires stem cells from a matching donor—with current matching techniques the donor will be a sibling of the patient from the same litter or other litters of the same breeding pair. Twenty-five percent of siblings are expected to be matches.

In most cases, locating and identifying a donor will take weeks or months, and during this time, the patient is started on one of the standard chemotherapy induction protocols. If a donor is found, then plans for an allogenic transplant can be made. This includes completing an induction protocol, confirming remission, and consolidating the patient with total body irradiation to eliminate the bone marrow and allow for the donor's stem cells to repopulate with new bone marrow. Concurrently, the donor is given a medication that causes bone marrow stem cells to be released into the blood stream where they can be harvested using an apheresis machine. This machine is somewhat like a dialysis machine in that blood circulates through the machine where the stem cells are harvested and most of the blood and plasma goes back into the donor. It may also be necessary to harvest some bone marrow from the donor if insufficient numbers of stem cells are obtained from the blood.

Once the stem cells are collected, they are given to the patient through an intravenous catheter. The patient then goes into isolation for 14-21 days and is monitored carefully for evidence of engraftment. Anti-rejection medications are given during this time to prevent graft rejection and prevent graft versus host disease—a serious and potentially fatal complication of an allogenic transplant. When there is confirmation of engraftment, the patient can go home with twice weekly, weekly, and then monthly rechecks. The anti-rejection medications are tapered off after several weeks, and periodic blood tests to confirm engraftment are done. It is expected that during this time the new marrow will seek out and eliminate any remaining tumor cells—the graft versus tumor effect. Some dogs may require long term management of graft versus host disease, and others may require a post transplant infusion of more stem cells from the donor at some time in the future (a DLI, or donor lymphocyte infusion). A DLI is used to ensure engraftment as well as to boost the new immune system to attack remaining tumor cells. An allogenic transplant with a matching donor is currently the preferred procedure, however in many instances a matching donor may not be found and an autologous transplant is considered.

With an autologous transplant the patient's own stem cells are used to reconstitute the marrow after total body irradiation. After the initial staging, a standard chemotherapy protocol is started. Once there is confirmed complete remission, weekly complete blood counts are done to monitor the recovery and rebound of the normal bone marrow cells. At the time of peak cell recovery, the patient is given a medication to mobilize stem cells from the marrow into the peripheral blood. After 4-6 days of monitoring—when the stem cells in the blood have reached a peak—an apheresis procedure is performed (as with the allogenic donors) to collect the stem cells. At this point, the cells can be saved in cryopreservation for future use, or the patient can go straight to total body irradiation and infusion of the harvested cells. After infusion of the cells, the patient goes into isolation for 14-21 days. During this time careful monitoring for engraftment is done, and once the white blood cell and platelet counts return to normal levels the patient can go home. No anti-rejection medications are needed for an autologous transplant. Long term follow-up involves monitoring for evidence of relapse of disease.

Allogenic transplants are expected to be more costly than autologous transplants due to several factors. The allogenic transplant requires the identification of a suitable donor, anti-rejection medications are needed, and post-transplant follow-up includes monitoring for complete engraftment and graft versus host disease. Autologous transplants do not require these things, although the time in isolation is expected to be the same. Allogenic transplants have the advantage of greater likelihood of tumor elimination due to the graft versus tumor effect, yet they are also troubled by the potentially serious side effect of graft versus host disease. Both procedures are associated with potentially life threatening complications—such as failure to engraft, overwhelming infections, hemorrhage due to platelet deficiency, and disease progression.

To date there have been only two dogs that have had successful transplants. Both were allogenic; one Golden Retriever and one Beagle. The Golden Retriever's transplant was completed over two years ago, and he continues to do very well. He has been off all transplant related medications for over a year. The Beagle's transplant was completed nearly four months ago and she too is doing very well. The transplant related medications are being gradually reduced, and studies to confirm engraftment are now being performed. Two additional allogenic transplants are being organized for completion in August 2006, as well as three autologous transplants. Exact costs for these procedures are difficult to predict due to the individual nature of each patient. As an estimate, an allogenic transplant may cost around \$25,000, and an autologous transplant \$15-20,000. Since only two transplants have been completed to date, it is too early to predict what the long term survival will be for dogs that undergo a transplant.

These techniques have been developed in Bellingham, WA by Drs. Theresa Westfall and Edmund Sullivan. If you would like more information, please contact them at bvcc720@yahoo.com or by phone at 360-734-0720.