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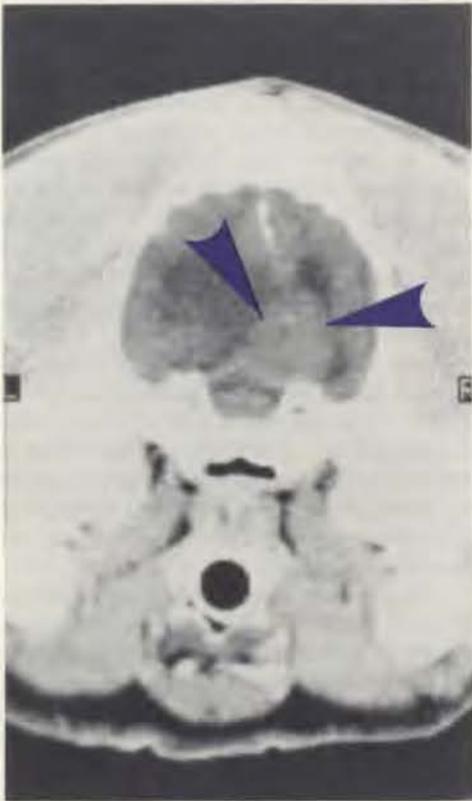
Treatment of Brain Tumors

Until recently, the diagnosis of a brain tumor in a dog or cat meant that nothing could be done to prevent the disease from taking its course. But that is slowly changing. Veterinarians at teaching institutions are borrowing from human medicine and are treating brain tumors in small animals aggressively.

"We are taking the human protocol and are adapting it to our patients," said Dr. Betsy Dayrell-Hart, a neurologist and lecturer in medicine at the University of Pennsylvania School of Veterinary Medicine. "Human medicine is more experienced with the treatment of brain tumors, and at VHUP we frequently consult with neurologists from Children's Hospital when we are considering surgery to remove a brain tumor."

Clinicians at VHUP perform about six brain surgeries on dogs and cats annually. "Usually such surgery is just one element of the treatment," said Dr. Dayrell-Hart. "Most of the animals also require chemotherapy or radiation treatment or both to reduce or eliminate the tumor. The different specialties cooperate closely in these complex cases."

Treatment is not undertaken lightly. "The top priority is the quality of life the animal will have after treatment," she said. "Will it be able to function normally without pain and will its life be extended by a significant period? We must also consider the owners. Brain tumor treatment requires a commitment, financially and in terms of time and emotion, during the animal's recuperation period. Many trips to the veterinarian are needed for follow-up treatment, and the owners may have to put up with temporary loss of training and sometimes impaired other functions in the pet. And then, despite all these efforts, treatment is not always successful. However, each animal we treat teaches us something new, enabling us to go a step further with the next case."



CT-scan, pretreatment. Arrows indicate tumor.



Snapshot of Cindy.

Cindy, a six-year-old bullmastiff, is a recent patient of Dr. Dayrell-Hart. She had lymphoma of the brain and underwent surgery, chemotherapy, and radiation therapy. Dr. Dayrell-Hart first met Cindy early one Wednesday morning in April. Cindy had been admitted to VHUP with signs of severe neurologic disease. "She was blind in her right eye, was confused and kept circling, even though she had trouble walking."

From the history provided by JoAnn Duarte, Cindy's owner, Dr. Dayrell-Hart knew that Cindy had been healthy until two weeks prior when she suddenly showed signs of depression and failing vision. Tests had ruled out infectious diseases and poisoning as reasons for the symptoms.

Cindy received a thorough physical and then a CT scan to determine the cause of her troubles. "The physical exam is still most important in neurologic cases as it allows us to determine brain function and helps to pin-point the affected area," she said. "Additionally, the scan then helps to precisely locate the troubled area, and it provides visual images of the changes in the brain." Cindy's scan showed an inflammatory area over the left side of her brain. "We treated and stabilized her and sent her home with antibiotics and other medications."

Shortly thereafter, Cindy had seizures which increased in intensity. "We took her back to Penn," said Ms. Duarte. A second CT scan revealed a mass which had formed in the left side of the brain, and it showed that the entire brain had shifted in the skull case due to pressure.

"We knew that we had to perform surgery to relieve the pressure or we would lose the dog," said Dr. Dayrell-Hart. "We also wanted a biopsy to determine the nature of the mass." After the risks of the procedure were discussed, Ms. Duarte opted for the procedure.

"Brain surgeries are difficult operations and take a lot of planning because the brain is so delicate and does not tolerate changes well," said Dr. Dayrell-Hart. One of the biggest dangers is bleeding, and surgeons have to be very careful to avoid blood vessels to minimize bleeding. "The physical exam and the CT scan help us locate the affected area, and we can then determine how to approach the surgery." In Cindy's case it wasn't clear whether surgery could even help her due to the shifting of the brain. "In people, this condition is usually fatal."

A neurosurgeon from Children's Hospital (CHOP) took great interest in the case and was present during the operation to offer advice. "We have a close relationship with the specialists at CHOP, and they provide us with the delicate instruments needed for this type of surgery. Our instruments are larger; we hope to eventu-

ally acquire our own set." Brain surgery requires special anesthetics and monitoring devices to ensure that the brain does not swell during surgery. "It takes quite a bit of preparation on our part to coordinate such surgery," said Dr. Dayrell-Hart. "The anesthesia team is crucial to the success of the surgery. Dr. Kim N. Oisen headed this team. Cindy was in good physical condition and relatively young compared with our previous patients. So she was a 'good' risk."

On the day of the surgery, the dog's head and neck were shaved. A long incision was made so skin and muscles could be peeled back. "We try very hard to not damage the muscles and nerves so the animal can have a normal appearance after surgery." The brain of a large dog is about the size of an adult's fist. In Cindy's case, almost half of this mass was affected by the growth. "We drilled a nickel-size hole to relieve the pressure and to perform a biopsy. The tumor location was such that we couldn't remove much of the tumor." During surgery, a pathologist stood by to examine the tissue samples to determine the type of tumor. "It was a puzzle and only later were the tissues identified as a lymphoid tumor, an extremely rare condition when it is only in the brain." The surgery did not go smoothly. The tumor had a great number of arteries supplying it with blood and there was much bleeding. "We had to use suction to remove the blood and electrocautery to close some of the blood vessels. Some were clamped with metal clamps which are still in Cindy's head."

When the dog woke up from anesthesia, she got up and walked over to her food bowl to eat. "The pressure had been relieved and the hole in her skull provided continued relief," said Dr. Hart. "The muscle mass over the opening was sufficiently thick to protect the brain from external injury."

"We visited her a few days after the surgery and couldn't believe that she was up and around," said Ms. Duarte. "Of course, she was not out of the woods as it was explained to us that she had a lymphoid tumor in her brain and that radiation therapy and chemotherapy were needed to shrink the remaining tumor. We opted for the treatment as we are extremely attached to the dog and wanted her to get well again."

"Primary lymphomas in the brain are very rare in dogs and when they occur in people, they are often fatal," said Dr. Dayrell-Hart. "Usually these growths are secondary to a tumor elsewhere. We checked Cindy and could not find any evidence of lymphoma anywhere else and concluded that the growth in her brain probably was primary."

The dog was referred to Dr. Ann Jeglum, an oncologist at the School who devised a treatment plan to

shrink or eliminate the tumor. Cindy received a five-day infusion of chemotherapy drugs. A course of radiation treatment lasting longer than a month was also prescribed. This was administered by Dr. Sydney Evans.

As her treatment had to be performed at VHUP, Cindy became a regular resident. "We visited her once a week as we live three hours away," said Ms. Duarte. "The dog was cheerful and seemed pleased to see us. She obviously knew all the nurses and her way around the ward. She seemed quite comfortable during her stay and was not fretting or whining when we left."

Cindy stayed at VHUP for eight weeks. "When she left, many staff members came to say 'Good Bye,'" said Ms. Duarte. "It was quite emotional and I never expected the concern all these people showed for our dog." Cindy is home now and her hair is growing back. She was sent home with two courses of chemotherapy which are being administered by her veterinarian. Her blood is being monitored weekly to catch any adverse effects quickly. "Our veterinarian has worked closely with the specialists at Penn, and getting the follow-up treatments at his office has made it easier for us."

Recently, Cindy returned to VHUP for another CT scan. It showed no evidence of the tumor. "We are elated," said Ms. Duarte. "The dog is her old self, her memory has returned, and she can do her obedience exercises. She acts like a three-year-old. We are even thinking about taking her into the show ring again, in the veteran's class!"

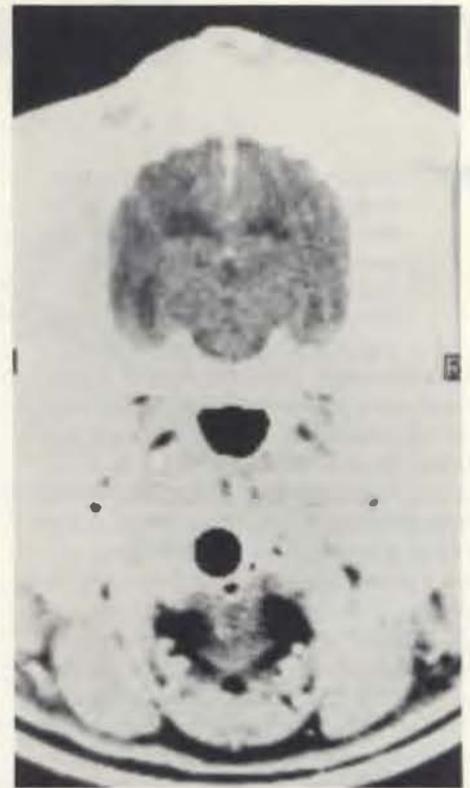
Cindy is not the norm. "She is a lot younger than our other brain surgery patients," said Dr. Dayrell-Hart. "Most of the cats and dogs we operate on are much older and not as good risks. But we have had a good

rate of success." Most frequently, surgery is just part of the treatment, as in the case of Cindy, animals often also receive chemotherapy and radiation treatment. "We have some patients which were treated for brain tumors three years ago; there are others who lived only another year longer. But with each patient we learn more, and this helps the next case," said Dr. Dayrell-Hart. "We ask the owners to bring the animal back if it is failing. If it has to be euthanized, we do it here and then conduct an autopsy. This helps us evaluate the treatment and ascertain the changes in the brain. Owners do go along with this as they realize that this knowledge will help another animal."

When Ms. Duarte was asked whether she would have another dog treated should the problem ever arise again, she said that she didn't know. "Cindy is special to us and we wanted to do anything to save her. But it was an emotionally draining experience and I don't know whether I could face that again, the worry, the shock seeing her with her head shaved, and the concern as to whether she might be suffering. It is hard."

Dr. Dayrell-Hart and her colleagues are cautiously optimistic about Cindy's prognosis. "We think that it was a primary lymphoma. Blood and bone marrow tests show no evidence of other tumors." Neurosurgery in small animals is a new field, and each case contributes to the knowledge. "We are fortunate in that we have the different specialists here and the physicians from CHOP. Without all these people, a case like Cindy's could not have been treated here."

Dr. Dayrell-Hart graduated from Penn in 1983. She completed her residency in neurology here last year and was appointed a lecturer in medicine.



CT-scan, posttreatment.

Inherited Immunodeficiency in Irish Setters

Ten years ago, a syndrome characterized by recurrent bacterial infections and very high white blood cell counts was reported in young Irish setters. Their white blood cells were apparently unable to kill bacteria. But the molecular defect has only recently been elucidated by researchers at the School of Veterinary Medicine of the University of Pennsylvania.

Over the last two years, Dr. Urs Giger, assistant professor of medicine and medical genetics, and Dr. Mark A. Bronstein (V'73), a practitioner in Ardmore, PA, have been treating an inbred Irish setter cross which has chronic recurrent bacterial infections. Since a few weeks of age, the dog has had a variety of infections, including skin, gum and bone infections, pneumonia, and recently pyometra. They appeared poorly responsive to antibiotics, the only treatment presently available. "Interestingly, the white blood cell or leukocyte count of this dog was always incredibly high, being at times over 200,000," said Dr. Giger. "Such leukocyte counts are generally only seen in dogs with leukemia. These leukocytes were obviously unable to fight any infection, although they appeared morphologically normal and were present in large numbers."

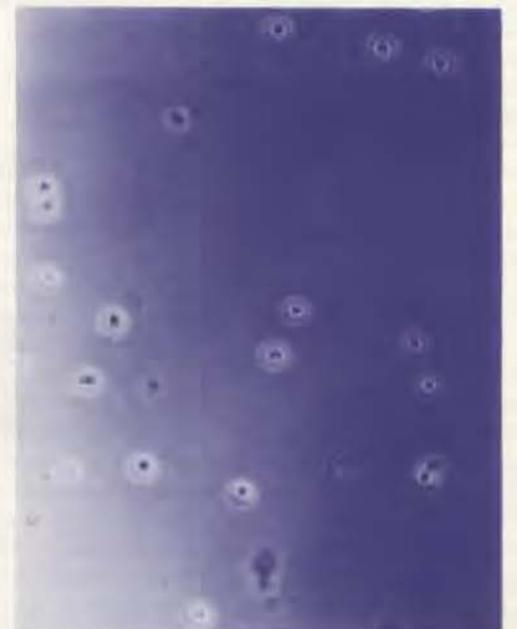
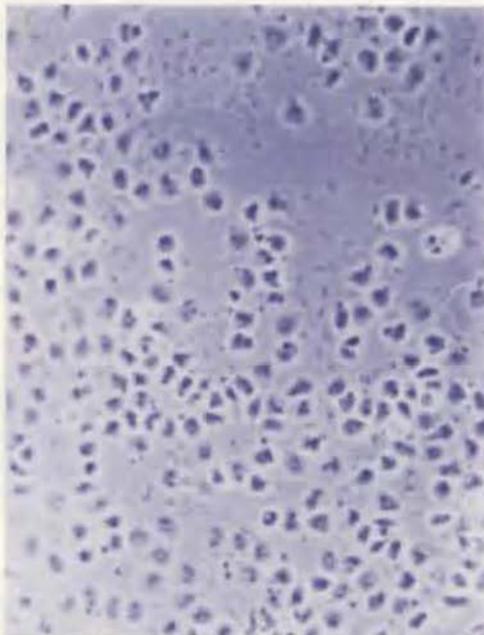
Dr. Giger and his collaborators, therefore, studied the function of these leukocytes and found that they had diminished capability of adhering to any surface because adhesion-promoting proteins on their cell surface were missing. "The process of adhesion is vital in the function of leukocytes and includes cell adher-

ence to blood vessel walls, cell migration to the site of infection, and binding of bacteria," explained Dr. Giger. "Our patient's leukocytes remained in the blood stream because they were unable to travel to the infected tissue and kill bacteria."

Based on data of limited functional and monoclonal antibody studies from related dogs, this disorder appears autosomal recessive inherited and occurs rarely in the Irish setter breed. A leukocyte adhesion defect

similar to the disorder in this dog has also been reported in children with recurrent infections.

Dr. Giger presented the results of these studies at the National Meeting of the American Society of Hematology in San Francisco. The leukocyte adhesion deficiency in Irish setters is only one of the inherited immunodeficiency syndromes recognized and investigated in dogs by members of the Section of Medical Genetics here at the School.



White blood cell adhesion to plastic surface; cells from control dog adhere readily and spread on surface (left), whereas few cells from the affected dog are adhering (right).