Use of three-dimensional conformal radiation therapy for treatment of a heart base chemodectoma in a dog

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Case Description—A 9-year-old spayed female mixed-breed dog was evaluated because of a progressively worsening, nonproductive cough and gagging of 1 year’s duration.

Clinical Findings—Physical examination results were unremarkable. A cranial mediastinal mass was identified at the heart base with 3-view thoracic radiography. A CT scan of the thorax revealed an invasive mass surrounding major vessels at the heart base that was not considered surgically resectable. Thoracoscopic biopsy specimens of the cranial mediastinal mass were obtained, and histologic evaluation revealed that the tumor was a chemodectoma.

Treatment and Outcome—On the basis of results of the CT scan, a 3-D conformal radiation therapy plan was generated with computer treatment-planning software. The patient was treated with external beam radiation therapy; a 6-MV linear accelerator was used to deliver a prescribed dose of 67.5 Gy in twenty-three 2.5-Gy fractions. The cough improved following radiation therapy. Prior to treatment, the tumor volume was calculated to be 126.69 cm³. Twenty-five months following radiation therapy, a follow-up CT scan was performed and there was a >50% reduction in tumor volume at that time. Disease progression causing pericardial, pleural, and peritoneal effusion and syncopal episodes occurred 32 months following radiation therapy, which were treated with pericardectomy and additional radiation therapy. The dog was still alive and doing well 42 months following initial radiation treatment.

Clinical Relevance—Conformal radiation therapy provided an additional treatment option for a nonresectable heart base chemodectoma in the dog of this report; conformal radiation therapy was reasonably tolerable and safe. (J Am Vet Med Assoc 2012;241:472–476)
Given the invasive appearance of the mass at laparoscopy, it was considered unresectable. Computed tomography was performed in preparation for radiation therapy. Positioning was accomplished with a custom-formed mold to permit more repeatable positioning during radiation therapy. Computed tomography revealed a large soft tissue mass at the heart base with irregular peripheral and central contrast enhancement (Figure 2). The mass surrounded the aortic arch and portions of the descending aorta, brachycephalic trunk, and left subclavian artery. The mass was also adjacent to the pulmonary arteries and veins but did not surround them.

Computed tomographic images were transferred to a computerized radiation treatment–planning system. This system provides 3-D reconstruction and conformal radiation treatment planning. Total tumor volume was calculated to be $126.69 \text{ cm}^3$ before treatment. A dose of 57.5 Gy was prescribed in twenty-three 2.5-Gy fractions administered daily (Monday through Friday) and completed in 30 days. The dose was delivered through 4 orthogonal beams with a 6-MV linear accelerator. A multileaf collimator was used with each beam to provide better targeting of radiation for each treatment.

For radiation therapy, the patient was premedicated with butorphanol (0.2 mg/kg [0.09 mg/lb], IV), and anesthesia was induced with propofol (4 mg/kg [1.8 mg/lb], IV), given to effect. Isoflurane was used for maintenance of general anesthesia. The patient was placed in dorsal recumbency in the mold already described, and the beam of the linear accelerator was aligned to the center of the treatment volume. Lasers mounted on the wall of the radiation therapy vault were used to assist with positioning of the patient. Portal radiographs were obtained weekly to readjust patient positioning and assure quality control.

Radiation therapy was associated with minimal acute adverse effects. There was 1 incident of vomiting immediately following radiation therapy on 1 day during the second week of treatment. The patient received fluids IV and recovered sufficiently to undergo anesthesia for radiation therapy the next day. This episode is unlikely to have resulted from irradiation. No other adverse events occurred throughout the patient’s treatment.

Twenty-one months following radiation therapy, the patient was reevaluated for an episode of vomiting after dietary indiscretion at an emergency hospital. An irregular hypoechoic spleen was noted on abdominal ultrasonography consistent with splenic torsion. A rounded isoechoic mass on the left lateral lobe of the liver was also noted. An echocardiographic evaluation was performed and revealed normal cardiac function. Although a mass was still present, the area of left atrial compression noted in the previous echocardiogram was absent. An exploratory laparotomy was performed. The spleen and the irregular area on the left lateral liver lobe were removed. Histologic examination determined that samples taken from the spleen and liver were consistent with benign processes. The spleen was found to be thrombosed, and the irregular area of the left lateral liver lobe was determined to be nodular hyperplasia.

A follow-up CT scan of the thorax was performed 25 months after the completion of radiation therapy to

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Figure 1—Ventrodorsal radiographic views of the thorax of a 9-year-old spayed female mixed-breed dog evaluated because of a progressively worsening, nonproductive cough and gagging of 1 year’s duration. A—Radiograph obtained at admission. Notice a cranial mediastinal mass measuring 7 × 4 cm at the level of the left hemithorax between the third and sixth rib spaces (arrows). B—Radiograph obtained 884 days after completion of radiation therapy. Notice that the mass extends from the fourth to sixth rib space (white arrows).
evaluate chronic coughing of several weeks' duration. The mass was digitally reconstructed with radiation treatment–planning software, and the tumor volume was found to be 55.98 cm$^3$ (Figure 2). Bronchoscopy was performed, and no significant abnormalities were grossly revealed. Results of microbacterial culture and antimicrobial susceptibility testing of bronchoalveolar lavage fluid revealed an infection with *Mycoplasma* spp, which was treated with doxycycline. This treatment appeared to partially ameliorate the coughing.

Seven months later (32 months after completion of radiation therapy), the dog was examined again for dyspnea and gagging. Pericardial, thoracic, and abdominal effusion were identified. On echocardiographic evaluation, myocardial function appeared normal; however, there appeared to be right ventricular outflow obstruction, as evidenced by greatly increased velocity and pressure gradient in the pulmonary outflow tract. Pericardiocentesis and thoracocentesis were performed to provide clinical relief. A pericardectomy was performed 2 months later. Episodic weakness and syncope continued following pericardectomy. Echocardiography continued to demonstrate evidence of obstruction of the right ventricular outflow by the mass. A CT scan revealed some enlargement of the mass and further encroachment on the great vessels. An additional course of definitive irradiation was prescribed (60 Gy in 2-Gy fractions), and the syncopal episodes resolved. The dog was still alive and doing well 42 months following the initial course of radiation and 4 months following the second course of treatment.

**Discussion**

Chemodectomas of the heart base are uncommon tumors in dogs, with only 24 histologically confirmed cases at 1 diagnostic laboratory from 1967 to 1979. In another more recent study of biopsy specimens submitted to a diagnostic laboratory, 2 of 11 cardiac biopsy specimens obtained during necropsies performed over a period of 2 years were confirmed to be chemodectomas of the heart base. Another study that used data from the Veterinary Medicine Database, which consisted of 912 histologically confirmed tumors of the heart from 1982 to 1995, revealed that heart base tumors accounted for 8% of cardiac neoplasms.

To our knowledge, the present report is the first in the veterinary literature of a heart base chemodectoma that has been treated with radiation therapy. There is 1 previous report of 2 dogs that were treated with radiation therapy after surgical resection of carotid body tumors that had similar outcomes to the dog of the present report. Carotid body tumors are distinguished from heart base chemodectomas by the location in which they occur. In the human literature, chemodectomas of either the heart base or carotid body are classified as paragangliomas, with lesions of the carotid body being the most common anatomic location. These tumors are radiosensitive and can be treated with radiation therapy alone or in combination with surgery.

Of major concern when planning for radiation therapy are the acute and late effects of radiation on normal tissues. Acute effects, which occur during the course of irradiation and shortly thereafter, appeared to be minimal in this patient. A single episode of vomiting occurred during the early part of the treatment course. It is unlikely that this episode was associated with irradiation for a few reasons. First, the only portion of gastrointestinal tract irradiated was a segment of esophagus, which is not typically associated with vomiting. Second, the episode occurred during the early part of irradiation, and thus a relatively low total dose of irradiation had been delivered. Finally, the episode resolved...
and did not recur during treatment. There are numerous possible explanations for acute vomiting, including anesthetic drugs and acute gastritis associated with dietary indiscretion. However, no further treatment or diagnostic evaluation appeared to be indicated in this patient.

The heart and lungs are susceptible to radiation-induced damage that may cause significant morbidity, including acute pneumonitis and pericarditis as well as pulmonary and myocardial fibrosis, which may occur years after treatment. However, the impact of these toxicities may be minimized through the use of conformal radiation to limit the volume of a tissue treated and through careful consideration of dose variables. Radiation prescription may be rationally guided on the basis of an extensive body of knowledge regarding dose limits for radiation injury. For instance, only 5% of dogs will have an adverse pulmonary reaction when a total dose of 48 Gy is administered in 2-Gy fractions to 67% of the total lung volume. Concomitant cardiac tolerance, irradiation of the entire heart with 44 Gy in 4-Gy fractions will lead to heart failure over a period of 2 years in 5% of dogs. Only 26% of the volume of our patient’s heart received a dose totaling 40 Gy in the initial treatment course, and no abnormalities with regard to cardiac function were detected after nearly 3 years. The pericardial effusion that developed in this dog so long after irradiation is most likely a result of tumor progression rather than a late effect of radiation. Pericardial effusion can occur following radiation therapy but typically develops within several months of irradiation. Given that this effusion developed years later, we believe its origin is most likely associated with tumor progression leading to impaired balance between fluid production and drainage in the pericardium. The right ventricular outflow obstruction that occurred simultaneously with the effusion did appear to be due to further encroachment by the tumor on the pulmonary artery. Constrictive pericardial disease can develop as a late consequence of pericarditis, but this was not consistent with the clinical findings.

Reirradiation of the heart will substantially increase the probability that this dog will develop myocardial dysfunction as a late effect of the treatment. As with the initial course of irradiation, we attempted to limit the volume of heart irradiated. We also lowered the irradiation fraction size to reduce the damaging effects to the late-responding, myocardial tissue. However, in this case, we delivered a relatively high total dose of radiation in an attempt to obtain longer-term tumor control. In other circumstances, a more palliative protocol could also have been used. The literature is still quite sparse with regard to reirradiation. To the authors’ knowledge, there are no data in either dogs or humans with regard to reirradiation of the heart. It is known that many tissues are capable of repairing tissue damage following an initial course of radiation. In general, the longer the interval between initial and subsequent courses of irradiation, the lower the likelihood of radiation injury. A study in rats suggested that the heart might not be as tolerant to reirradiation as are other tissues. However, a number of factors limit the applicability of that experimental study, including the large irradiation fraction size, inclusion of the entire heart in the radiation field, and short interval between courses of irradiation. Additional follow-up time will be needed to evaluate the effects of the second course of irradiation on tumor control and irradiated normal tissues.

Modern radiotherapy equipment permits the delivery of a highly conformal radiation dose. However, several factors limit the degree of radiation dose conformation that is achievable, including tumor invasiveness, precision of patient positioning, and organ motion during treatment. Despite an increasing body of knowledge about the behavior of animal tumors, we are still limited by current imaging techniques. The definition of tumor boundaries is inherently subjective and not standardized in veterinary radiation oncology. Unfortunately, the radiation oncologist must make assumptions about tumor margins on the basis of scant literature and personal experience. In addition, patient setup for radiation therapy is error prone. Positioning aids, such as the custom mold used in this case, can improve the reproducibility of patient position; however, megavoltage portal imaging used to verify positioning lacks the detail and resolution of diagnostic quality of kilovoltage x-ray units. The advent of clinical linear accelerators with kilovoltage imaging (image-guided radiation therapy) now permits extremely precise positioning and highly conformal dose delivery. However, this technology was not available for this patient, nor is it currently available at most veterinary radiation therapy facilities.

Organ motion during treatment, which is particularly problematic in the thorax because of respiration and heartbeat, may also limit highly conformal treatment delivery. State-of-the-art linear accelerators are now equipped with respiratory gating technology that allows for treatment during a given phase of respiration. This technology was not available for the treatment of this patient and, as with image guidance, is not widely available at veterinary centers. It was our assessment of this patient, on the basis of thoracic radiographs, that there was little (perhaps a few millimeters) difference in the mediastinal position during breathing, and our target volume was enlarged to account for this as well for positioning error. However, we could have used artificial ventilation techniques to adjust for respiratory motion. Respiratory motion is particularly problematic for lesions in the pulmonary parenchyma.

There are 2 retrospective studies in the veterinary literature that evaluated factors affecting survival in dogs with aortic body tumors. It was found that animals that underwent pericardectomy had longer survival times, compared with animals that did not. The patient of the present report has survived for nearly 3 years without pericardectomy. However, pericardectomy was indicated 32 months after radiation, when this patient developed effusion. No firm conclusions can be drawn from the present report as to the benefits of radiation therapy over other treatment modalities other than to state it is minimally invasive and appears to be associated with minimal clinically evident toxicity. Further study is needed to assess the long-term survival implications of surgery.
and radiation therapy alone or in combination. However, radiation therapy should be considered, particularly in cases of unresectable heart base tumors.

a. XiO 3D and IMRT, CMS Software, Maryland Heights, Mo.
b. Varian Clinac 2100c, Varian Medical Systems, Palo Alto, Calif.

References

From this month's AJVR

Development of a quantitative multivariable radiographic method to evaluate anatomic changes associated with laminitis in the forefeet of donkeys

Simon N. Collins et al

Objective—To establish and validate an objective method of radiographic diagnosis of anatomic changes in laminitic forefeet of donkeys on the basis of data from a comprehensive series of radiographic measurements.

Animals—85 donkeys with and 85 without forelimb laminitis for baseline data determination; a cohort of 44 donkeys with and 18 without forelimb laminitis was used for validation analyses.

Procedures—For each donkey, lateromedial radiographic views of 1 weight-bearing forelimb were obtained; images from 11 laminitic and 2 nonlaminitic donkeys were excluded (motion artifact) from baseline data determination. Data from an a priori selection of 19 measurements of anatomic features of laminitic and nonlaminitic donkey feet were analyzed by use of a novel application of multivariate statistical techniques. The resultant diagnostic models were validated in a blinded manner with data from the separate cohort of laminitic and nonlaminitic donkeys.

Results—Data were modeled, and robust statistical rules were established for the diagnosis of anatomic changes within laminitic donkey forefeet. Component 1 scores ≤ –0.5 were indicative of extreme anatomic change, and scores from 2.0 to 0.0 denoted modest change. Nonlaminitic donkeys with a score from 0.5 to 1.0 should be considered as at risk for laminitis.

Conclusions and Clinical Relevance—Results indicated that the radiographic procedures evaluated can be used for the identification, assessment, and monitoring of anatomic changes associated with laminitis. Screening assessments by use of this method may enable early detection of mild anatomic change and identification of at-risk donkeys. (Am J Vet Res 2012;73:1207–1218)