Student Paper Communication étudiante

Osteosarcoma in a 6-year-old Newfoundland dog: Limb-sparing surgery and cisplatin chemotherapy

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Abstract — A 6-year-old Newfoundland dog was presented with left forelimb lameness, which was diagnosed as osteosarcoma and treated with an endoprosthetic limb-spare surgery and cisplatin chemotherapy.

Résumé — Ostéosarcome chez un chien Terre-Neuve âgé de 6 ans : chirurgie permettant de préserver le membre et chimiothérapie au cisplatine. Un chien Terre-Neuve âgé de 6 ans a été présenté pour boiterie du membre antérieur gauche. Un ostéosarcome a été diagnostiqué et traité par l'implantation d'une prothèse endomédullaire visant à épargner le membre et une chimiothérapie au cisplatine.

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A 6-year-old, male, Newfoundland dog was presented to the Western College of Veterinary Medicine Small Animal Clinic with a 4-day history of progressive left forelimb lameness. Physical examination revealed pain and swelling on palpation of the distal part of the left radius.

Radiographs of the left antebrachium showed a lytic, expansile area of cortical and cancellous bone with reactive periosteal new bone in the distal part of the left radial diaphysis, characteristic of osteosarcoma. The ulna did not appear to be involved.

The dog was sedated with 0.05 mg/kg bodyweight (BW) of hydromorphone hydrochloride (Hydromorphone HP 10; Sandoz Canada, Boucherville, Quebec), IM, and 0.03 mg/kg BW of acepromazine (Atravet; Ayerst Veterinary Laboratories, Guelph, Ontario), IM. A bone biopsy was harvested with a 13-gauge × 9-cm Jamshidi bone marrow biopsy needle (Allegiance Healthcare, McGraw Park, Illinois, USA) from the dorsolateral aspect of the left radius after infusion of lidocaine as a local anesthetic and submitted for light microscopic examination and aerobic and anaerobic culture. A supportive splint was placed on the left forelimb to reduce the risk of pathologic fracture. The dog was discharged with a 100 μg fentanyl patch (Duragesic; Janssen-Ortho, Markham, Ontario) and instructions to the owner to administer deracoxib (Deramaxx; Novartis Animal Health US, North Carolina, USA), 100 mg, PO, q24h, for pain management.

Light microscopic examination of the bone biopsy confirmed osteosarcoma. Management options included amputation or limb-spare surgery, with or without chemotherapy; medical management; and radiation therapy. The owners elected for an endoprosthetic limb-spare surgery and chemotherapy.

The dog was premedicated with hydromorphone and acepromazine, as described above. Anesthesia was induced with propofol (Abbott Laboratories, St. Laurent, Quebec) and maintained with isoflurane (Isoflo; Abbott Laboratories) and nitrous oxide gas. A morphine (Duramorph; Sandoz, Boucherville, Quebec) epidural was administered at a dose of 0.1 mg/kg BW, as well as a brachial plexus nerve block, using bupivicaine (Marcaine; Abbott Laboratories, St. Laurent, Quebec), 0.5 mL/kg BW, to assist in perioperative and postoperative pain management.

A craniolateral incision was made over the left radius and extended dorsally over the carpometacarpal region. Care was taken to ensure that the pseudocapsule of the tumor was not incised. The abductor pollicis longus and extensor carpi radialis muscles were isolated and transected, and the tumor was dissected from its soft tissues. The cephalic vein was preserved. A tract was observed extending from the previous bone biopsy. This area was dissected out and removed. The affected portion of the radius was removed by using a sagittal saw 10 cm proximal to the distal extremity of the radius. Radiographs were taken of the excised mass to determine neoplastic margins; the proximal portion did not appear to be clean, so a further 2.7-cm of radius was excised.

An extra large Kuntz limb-sparing plate (Veterinary Orthopedic Implants, South Burlington, Vermont, USA), measuring 3.5 by 2.7 mm, was contoured to the 3rd metacarpal bone and the remaining part of the radius. A stainless steel endoprosthetic spacer (Veterinary Orthopedic Implants) was secured to the limb-sparing plate with 2 screws. The plate was affixed to the radius, radial carpal bone and 3rd metacarpal bone by using 3.5-mm, 3.5-mm, and 2.7-mm screws. A pancarpal arthrodesis was performed. A total of 18 screws were placed.

A Jackson-Pratt closed suction drain was placed next to the prosthesis and the extensor carpi radialis and the abductor

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Figure 1. (A) Radiograph of left antebrachium 3–5 wk postdiagnosis. The osteosarcoma involves the distal diaphyseal radius. (B) Radiograph of the left antebrachium post surgical implantation of an endoprosthetic spacer and Kuntz limb-spare plate.

pollicis longus muscles were sutured over the limb-sparing plate. The incision was closed in 3 layers (fascia, subcutaneous tissue, and skin) by using 2-0 polydiaxanone suture (PDS), 3-0 PDS, and 3-0 polypropylene, respectively. A modified Robert-Jones bandage was placed postoperatively. The excised tissues were submitted for light microscopic examination.

One day postoperatively, the dog was weight-bearing. Pain management was achieved with a morphine (Duramorph, Sandoz) epidural, 0.1 mg/kg BW, q12h, for 2 treatments. The hydromorphone was discontinued, as the dog became very sedate, even on low doses. Thirty-six hours postoperatively, a swab was taken of the fluid from the wound and submitted for culture and sensitivity testing. A 100-μg fentanyl patch and deracoxib, 100 mg, PO, q24h for 14 d (refills allowed if needed) were prescribed and the dog was discharged. The dog was to be administered cephalexin (Nu-cephalex; Nu-pharm, Richmond Hill, Ontario), 1500 mg, PO, q8h for 10 d. Limited exercise was recommended, with gradual increases to a 20-min walk per day within 6 wk time. A mild mechanical lameness was present.

Unfortunately, light microscopic examination confirmed incomplete tumor excision. Both the primary tumor excision and the additional 2.7 cm of radius removed had dirty margins, with tumor cells infiltrating the entire medullary cavity. A *Staphylococcus* sp. was identified on subculture of the wound fluid.

Two weeks postoperatively, a cisplatin (Platinol; Bristol Myers-Squibb Company, Princeton, New Jersey, USA) chemotherapy protocol was initiated. Results from a complete blood (cell) count (CBC), serum biochemical profile, and urinalysis were obtained prior to initiating chemotherapy. Prior to receiving chemotherapy, the dog was placed on 0.9% NaCl IV fluids for 4 h at a rate of 999 mL/h and butorphanol (Torbugesic; Wyeth Animal Health, Madison, New Jersey, USA), 0.4 mg/kg BW, IV, was given 30 min prior to chemotherapy. Cisplatin, 60 mg/m^2 (diluted in 370 mL of saline) was administered, IV, over 20 min. The dog was maintained on IV fluids (0.9% NaCl) at a rate of 999 mL/h for 2 additional hours.

The dog was lethargic for 2 d postchemotherapy, but recovered well. Chemotherapy was scheduled every 3 wk for 6 to 8 treatments, pending signs of renal toxicity and myelosuppression. Limb and thoracic radiographs were scheduled every 3 mo.

The dog did very well for 1 mo postoperatively and then developed an acute left forelimb lameness, and a swelling on the medial aspect of the limb was noted. Fine needle aspirate and cytologic examination confirmed a hematoma and anaplastic mesenchymal neoplastic cells. Radiographic examination confirmed a mottled and lytic radius. The endoprosthetic spacer and implant appeared stable in position. Thoracic radiographs revealed 4 obvious pulmonary metastases. Results from a CBC, serum biochemical panel, and urine specific gravity revealed slightly elevated urea 13.8 mmol/L (reference range, 3.5 to 11.4 mmol/L) and creatinine 153 μmol/L (reference range, 41 to 121), concentrated urine (USG 1.055), mild neutropenia (segs 2.460 $\times$ 10^9/L; reference range, 3.0 to 10.0 $\times$ 10^9/L), and thrombocytopenia (platelets 101 $\times$ 10^9/L; reference range 200 to 900 $\times$ 10^9/L). Amputation and radiation therapy were discussed. The owners elected to pursue palliative radiation therapy to alleviate pain.

A CBC and serum biochemical panel revealed that the renal enzymes and thrombocyte count had improved; urea 11.0 mmol/L, creatinine 139 μmol/L, platelets 204 $\times$ 10^9/L, while the neutrophil numbers had decreased, 1.677 $\times$ 10^9/L. Radiation therapy was postponed due to the neutropenia. Subsequently, results from a CBC showed that the neutrophil count had increased, 2.346 $\times$ 10^9/L, so radiation therapy was initiated at a total dose of 1600 cGy over 2 d.

The chemotherapy was discontinued due to further elevations of renal enzymes (creatinine 126 μmol/L and then 146 μmol/L; urea 12 mmol/L) and also insufficient response to single agent chemotherapy for treatment of osteosarcoma with pulmonary metastases (1). Pain management included the administration of deracoxib, 50 mg, PO, q24h, and tramadol (WCVM Veterinary Teaching Hospital Pharmacy, Saskatoon, Saskatchewan), 120 mg, PO, q8h.

Four weeks later, the dog's lameness had progressed. Radiographs revealed tumor progression both in the left forelimb and in the lungs. The stability of the implants was questioned. The owners elected for amputation. Three weeks later the dog became inappetent and lethargic due to the progressive pulmonary metastasis. The dog was euthanized.

Osteosarcoma is the most common primary bone neoplasm of dogs (2,3). Unfortunately, this neoplasm has a very high

metastatic rate, with 98% of dogs having micrometastasis in the lungs at the time of diagnosis (3). These metastases are generally not evident on radiographs in the early stages. Without treatment, many of the patients are euthanized within 16–20 wk from initial diagnosis due to unmanageable pain (4).

Amputation has been the primary treatment option, although limb-spare surgery, chemotherapy, and radiation therapy are now available (4). The combination of surgery, either amputation or limb-spare, and chemotherapy has provided the longest survival time, with a median of 235 to 366 d (2).

Amputation has traditionally been the most common treatment for appendicular osteosarcoma (2,3,5). This procedure usually ensures complete removal of the primary tumor and provides pain relief, relatively short anesthesia times, decreased risk of postoperative complications, and decreased expense in comparison with limb-spare procedures (2). This option is viable for nearly all patients, except those with compromising orthopedic or neurologic problems, or both, and obesity. The mean survival time with amputation alone is 4 mo (6).

Limb-sparing (limb salvage) removes all of the primary tumor, while providing a pain-free, functional limb. No more than 50% of the limb can be affected by the tumor (2,6). This technique is favorable for owners who refuse to amputate the limb, and for dogs with compromising neurologic or orthopedic problems (2,3,5). Various options exist for limb-sparing, including frozen cortical bone allograft implantation, pasteurized tumoral autografting, bone transport osteogenesis, and endoprosthesis (2). Eighty percent of limb-spare dogs have good to excellent limb function (3,5). Mild mechanical lameness due to the arthrodesed carpal joint will be present. Potential complications of limb-spare include local tumor recurrence, implant failure, and infection (3). Mild infection is actually desirable postoperatively, as these dogs tend to have a survival time of 480 d with infection, compared with 228 d without infection (7). This has been attributed to local immune system upregulation (7).

The best survival times result from a combination of surgery and chemotherapy (2). Three anti-cancer drug options are available; they include doxorubicin (potentially cardiotoxic), cisplatin (potentially nephrotoxic), and carboplatin (no toxicity but renally eliminated) (2,5). Alternating cisplatin and doxorubicin or carboplatin and doxorubicin can minimize potential toxicities. All of the chemotherapeutic agents are administered once every 3 wk for 6–8 treatments or until signs of toxicity occur (2,5). Most oncologists agree that an appropriate time between surgery and initiating chemotherapy is 2 wk (2). Mean survival times based on amputation or limb-spare surgery and chemotherapeutic agent(s) are as follows: cisplatin 262–322 d, doxorubicin 366 d, carboplatin 275–321 d, alternating cisplatin and doxorubicin 300–345 d, and alternating carboplatin and doxorubicin 275–320 d (2).

Radiation therapy can be used in combination with surgery or chemotherapy, or both, or simply on a palliative basis. Most often, palliative treatment with 8–10 Gy is administered on days 0, 7, and 21. Patients improve within 3 wk, with the response lasting up to 4 mo (6). Alternatively, 2 treatments of 800 cGy each on day 0 and day 1, as used in this patient, have been reviewed (6). Radiation and chemotherapy yields a mean survival time of 7 mo (5).

With the continued research both in oncology and surgery, the survival time for appendicular osteosarcoma has been significantly prolonged, 33% to 65% of dogs live 1 y, postdiagnosis, and 16% to 28% live 2 y, postdiagnosis (4).

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References

1. Ogilvie G, Straw R, Jameson V, et al. Evaluation of single-agent chemotherapy for treatment of clinically evident osteosarcoma metastases in dogs: 45 cases (1987–1991). J Am Vet Med Assoc 1993;202:304–306.
2. Jehn C, Farese J, Lewis D, Ehrart N, Kuntz C. Current treatment options for dogs with appendicular osteosarcoma. Vet Med 2005;100:295–305.
3. Gassel A, Bilbrey S. Limb-sparing surgery for appendicular osteosarcoma in dogs. Vet Med 2003;98:119–124.
4. Morello E, Buracco P, Martano M, et al. Bone allografts and adjuvant cisplatin for the treatment of canine appendicular osteosarcoma in 18 dogs. J Small Anim Pract 2001;42:61–66.
5. Liptak J, Dernell W, Ehrhart N, et al. Canine appendicular osteosarcoma: Curative-intent treatment. Compend Contin Educ Pract Vet 2004; 26:186–197.
6. Moore A. Osteosarcoma in dogs: Managing a destructive disorder. Vet Med 2001;96:539–546.
7. Duncan B, Lascelles X, Dernell W, et al. Improved survival associated with postoperative wound infection in dogs treated with limb-salvage surgery for osteosarcoma. Ann Surg Oncol 2005;12:1073–1083.