All from Ria's Rib

Pasarin Aujchariyapirom

Mississippi State University College of Veterinary Medicine

Class of 2021

Clinicopathologic Conference

August 28th, 2020

Advisor

Hayley Gallaher, DVM, DACVS-SA

INTRODUCTION

Primary rib tumors are usually uncommon in dogs or cats.[1,4,12] Among primary rib tumors, osteosarcoma (OSA) is the most common bone tumor in dogs, followed by chondrosarcoma and hemangiosarcoma respectively.[1,2,12] Rib OSA commonly originate at or near the costochondral junction.[4,12] In two studies that examined incidence of location, ribs five to nine were the most commonly affected and the right side was involved twice as often as the left side.[3,5] Due to the high metastatic rate, osteosarcoma typically has a poor prognosis at the time of diagnosis.[1,8,12] Clinical signs can vary, from the patient being asymptomatic to presenting with dyspnea, depending on the location of the tumors.[3,12] Thoracic radiographs and computed tomography or magnetic resonance imaging are extremely helpful for aiding with diagnosis and surgical planning.[13] Although no form of treatment is curative,[12] a combination of surgical thoracic wall resection and reconstruction along with chemotherapy are reported to be effective at prolonging median survival time in dogs.[1,2,12,13] The gold standard for diagnosis of osteosarcoma test is histopathology.[7,12]

HISTORY AND PRESENTATION

Ria is a 12-year-old female spayed Australian Shepherd mix dog who presented to MSU-CVM Small Animal Emergency Service on October 9th, 2019 for a progressing lameness in her right front limb. She is up to date on vaccination and preventatives. At presentation to MSU-CVM she currently has osteoarthritis and atopic dermatitis. She had had TTA (Tibial Tuberosity Advancement) performed on her left stifle when she was young and a TPLO (Tibial-plateau-leveling osteotomy) on right stifle in early 2019. She also received rehabilitation exercise including cold laser therapy and underwater treadmill therapy for treatment of her osteoarthritis. She is currently on grapiprant occasionally for osteoarthritis. In early September 2019, the owner

noticed lameness of right forelimb and has been progressively worsening. On September 24th, 2019, Ria's lameness was evaluated by her primary veterinary care veterinarian where she routinely goes for rehab exercise. Her orthopedic examination revealed a grade 2/5 right forelimb lameness and pain on palpation of the shoulder/elbow joint. Radiographs of the forelimb were obtained, and consideration was given to a possible possibly soft tissue injury. Her primary veterinarian offered conservative management and physical therapy for the possible of soft tissue injury with cold laser therapy. Ria was also prescribed gabapentin 30 mg twice daily and the owner were told to continue using grapiprant 60 mg once daily orally for 2-3 weeks. They were also told that if her lameness was not better, they recommend performing further diagnostic tests at MSU-CVM.

On presentation to MSU-CVM Small Animal Emergency Service on October 9th, 2019 Ria's lameness had continued, and her activity level had decreased in the last 3 weeks, but she had maintained a good appetite. She was eating, drinking, urinating, and defecating normally. She lived primarily indoors.

On exam, Ria was quiet, alert, and responsive. She had a heart rate of 80 beats per minute, a respiratory rate of 44 breaths per minute, and a rectal temperature of 101.3 degrees Fahrenheit. Her mucous membranes were pink with a capillary refill time of 2 seconds. She weighed 26.4 kg and had a body condition score of 4/9 with mild generalized loss of muscle mass. Her triage exam was within normal limits. On orthopedic exam, she had grade 3/5 lameness in the right front limb visible while she was walking. She had decreased flexion in her right carpus. She was mildly reactive on extension of her right elbow and extension and flexion of her right shoulder, and had mild laxity on shoulder abduction. There was moderate to severe muscle atrophy of her right forelimb. Her left forelimb was unremarkable. On her right stifle, a

bone plate could be felt on the medial surface, and there was firm swelling on the lateral surface. There was no tibial thrust on her right hind limb. Segmental reflexes were intact in all four limbs except forelimb withdraw was slightly decreased in the right forelimb. Proprioception was also intact in all four limbs but delayed in her right forelimb.

DIAGNOSTIC APPROACH

On the day of presentation, blood was taken for a complete blood count and a serum chemistry, with results displaying a slight hyperchromasia, mildly decreased blood urea nitrogen (7 mg/dl), and mildly increased alkaline phosphatase; ALP (194 U/L).

Thoracic radiographs revealed a round, soft tissue opaque mass with amorphous mineral opaque material centrally which was located at the region of the right first rib and measured approximately 7.3 x 6.1 x 5.0 cm. The mass caused the right cranial lung lobe to be caudally displaced and the trachea within the thoracic inlet was focally deviated to the left. There was complete destruction of the first right rib.

Thoracic computed tomography with contrast was then performed which revealed a large, smoothly marginated, soft tissue attenuating, heterogeneously contrast-enhancing mass within the region of the right first rib, which was confluent with the right lateral thoracic body wall. The mass extended from the ventral thoracic inlet to the level of the intervertebral foramina and was causing expansion and nearly complete destruction of the right first rib. This mass measured approximately 8.8 x 5.4 x 7.2 cm. This mass was causing severe leftward deviation of the trachea and cranial vena cava and caudal displacement of the right cranial lung lobe. There were multiple enlarged sternal and cranial mediastinal lymph nodes, with the largest of these measuring up to 1.2 cm in thickness. Thoracic radiographs and computed tomography interpretation were given

to possible organs of origin for the described mass include the thoracic body wall and rib. Differentials for this mass included neoplasia (as with a primary bone tumor or sarcoma) with lesser consideration given to granuloma formation. Metastatic neoplasia or reactive lymphadenopathy were considered for the enlarged lymph nodes. Atelectasis was considered for the changes to the lung lobes.

Following CT, while still under sedation, an ultrasound- guided Tru-cut biopsies was obtained of the mass. Histopathology of the biopsy revealed that the largest section was composed of inflamed irregular collagenous connective tissue and atrophied striated muscle fibers. The remaining sections consisted of fragments of a neoplastic mass composed of polygonal mesenchymal cells arranged in random patterns and multifocally forming chondroid matrix and much smaller quantities of densely eosinophilic matrix suggestive of osteoid. Multinucleate cells were noted occasionally, 4-5 mitoses can often be seen in a single high-power field, and some of the mitoses were of an atypical type. The histopathology was consistent with a diagnosis of chondrosarcoma.

Ria underwent thoracic wall resection removing 1st – 4th ribs with the mass on October 14th, 2019. The resected thoracic wall with the mass attached, prescapular and sternal lymph nodes were sent to perform histopathology which is the gold standard of diagnostic tests. There was a poorly demarcated, fairly well encapsulated multilobular mass composed of polygonal to elongate cells with scant to moderate pale staining slightly eosinophilic sometimes vacuolated cytoplasm, and large round to ovoid nuclei with dispersed to vesicular chromatin and multiple small nucleoli. Moderate anisocytosis and anisokaryosis was noted. Mitotic figures were 20 per 10 high powered field with occasional bizarre mitotic figures. The rib mass was an osteosarcoma (OSA), which can vary widely in their histologic appearance, but in all cases a definitive

diagnosis was based on the production of osteoid by malignant mesenchymal cells. The tumor matrix may contain variable amounts of cartilage and collagen as well. There were scattered areas of both cartilage and collagen matrix production. The presence of osteoid, as in this case, denoted a diagnosis of OSA. Although numerous studies have investigated tumor grading of canine OSA, no histological grading system has been accepted in veterinary medicine. No neoplastic cells were seen in prescapular and sternal lymph nodes.

PATHOPHYSIOLOGY

Osteosarcoma (OSA) is a malignant bone tumor that characterized by the formation of neoplastic bone tissue with expression of rapid and invasive growth.[9] Histologically, OSA is a malignant mesenchymal tumor of primitive bone cells that is characterized by the production of osteoid.[9] Its etiology remains unknown.[9,12] However, there is evidence that OSA can associate with higher weight bearing bones, previous sites related to metallic orthopedic implants, ionizing radiation, genetic mutations and viral infections.[9,12] OSA most commonly affects middle aged animals,[3,4,12] medium-sized and large-breed dogs are over-represented.[4] Sex and breeds affected by OSA can vary.[2,4] It primarily occurs in the appendicular skeleton.[2,7] Within the axial skeleton, primary osteosarcoma is rare but may occur in the ribs, sternum, vertebrae and skull.[4,7] Clinical signs can vary, depending on the location of the tumors.[3,12] In rib bone OSA, the typical clinical signs are commonly included dyspnea and a localized swelling on the thoracic wall which is usually a consequence of the tumor's extension into the surrounding soft tissues.[3] In Ria's case, the lameness and muscle atrophy of her forelimb were mostly likely as a result of the impingement on the brachial plexus by the mass.

TREATMENT AND MANAGEMENT

There is no curative treatment for OSA.[12] Surgical resection of thoracic wall tumors is the treatment of choice with adjunctive therapy to prolong the median survival time.[1,2] Recommendations for surgical resection for thoracic wall masses are at least 3 cm margins of normal tissue, and include one rib cranial and one rib caudal to the lesion.[5,6] Full-thickness or *en bloc* resection of ribs that will require surgical reconstruction to reestablish thoracic wall continuity are recommended for the management of primary rib sarcomas because of their aggressive local behavior, and this frequently involves multiple ribs and occasionally adjacent organs and structures.[5,6] There are several options for reconstruction of the thoracic wall defect after rib resection or true en bloc resection, which depends on the location and size of the tumors.[5,12,13] These options include the use of prosthetic mesh nonabsorbable implants such as polypropylene mesh (Marlex mesh, Prolene mesh), polytetrafluoroethylene (PTFE) mesh and sheets.[5,12,13] Marlex is the most commonly reported implant used in veterinary thoracic wall reconstruction techniques.[5,13] Autogenous techniques, local tissue flaps including latissimus dorsi, superficial and deep pectoral muscles, and diaphragm have also been reported either alone or in combination with prosthetic mesh which is called a composite technique.[5,6,12,13] Autogenous techniques alone are sufficient for craniolateral chest wall defects less than 5 cm diameter or less than 3 resected ribs, and for posterior chest wall defects less than 10 cm diameter.[5] Prosthetic or composite techniques are preferred for the reconstruction of large thoracic wall defects as the additional rigidity reduces paradoxical chest wall motion which can result in ventilatory compromise and provides superior protection of intrathoracic organs and vessels.[5] However, there are reports that complications such as mesh-related infection and fistula formation secondary to adhesions were higher for prosthetic and composite techniques compared with autogenous reconstruction.[5,12] If major early complications from surgery occur, including

pneumothorax or pleural effusion, then it is recommend that a thoracic drain be placed.[12,13] Also patients should be carefully monitored for respiratory and cardiovascular sequelae by electrocardiogram, pulse oximetry, arterial blood gas, or end-tidal CO2 measurements.[12,13]

Chemotherapy adjunctive therapy is commonly performed post-operatively.[1,2] Carboplatin and/or doxorubicin are reported to be used effectively but neither of them can inhibit metastasis.[1,2] Carboplatin has fewer and less severe side effects than doxorubicin. However, some studies reported extravasation reactions in dogs,[11] which happened to Ria and lead to a necrotic wound.

Radiation therapy is also considered to be a palliative method of treatment.[1,10] The intent is to provide pain relief and prolong median survival time.[1,10] However, particularly for a cranial thoracic wall mass, the reduced accessibility and adjacent sensitive areas, as well as the requirement for general anesthesia reduce the practicality of this.[10]

PROGNOSIS

Many studies suggested the location of OSA in axial bones increases the hazard of metastasis and mortality.[4,7,8] Tumors arising from the rib and scapula had the highest prevalence of metastasis and the patient had shorter survival times.[7,8] The majority of dogs with primary rib OSA survive less than 3-4 months after the diagnosis.[3,8] One study demonstrate a significant association between the shorter survival time and the percent elevation of alkaline phosphatase (ALP) above normal.[7] Surgical resection of the tumor as a treatment option has better outcome than conservative management alone.[1,2,6] There were reports that suggested the animals that received postoperative adjuvant chemotherapy had longer median disease-free intervals (225 days) and median survival times (240 days) than dogs with OSA treated by surgery alone

(median disease-free interval, 60 days; median survival, 90 days).[1,2] Due to the high rate of pulmonary metastasis, the prognosis for dogs with OSA is poor.[12,13]

CASE OUTCOME

On October 14th, 2019, thoracic wall resection with an autogenous reconstruction technique using superficial and deep pectoral muscle were performed. The owner elected to spare her right forelimbs and monitor the degree of neurologic function of her forelimb post-operatively. Following surgery Ria received oxygen therapy, drainage of the chest tube, surgical wound care and blood gas monitoring to evaluate her respiratory status. Ria's right forelimb had progressed to grade 5/5 lameness. Three days post-operative, bilateral clear nasal discharge was noted, thoracic radiograph was performed, and interpretation was given to infectious etiologies pneumonia, pulmonary thromboembolism, hemorrhage, or atelectasis. Antibiotics were prescribed for a 3 weeks course which were ampicillin+sublactam and enrofloxacin. Multimodal analgesia including fentanyl, then later acetaminophen+codeine, gabapentin, grapiprant and trazodone was used. Within a few days, Ria was able to maintain her blood oxygen and oxygenation without oxygen therapy, and follow-up thoracic radiographs were performed to confirm improvement of pulmonary abnormalities. She was discharged on October 23rd, 2019.

After Ria went home, the owners were able to visualize her inability to use her right forelimb. They elected to perform Ria's right forelimb amputation with placement of a polypropylene mesh on her thoracic wall defect to add rigidity on October 30th, 2019 at MSU-CVM. During her second surgery, a chest tube was placed through right caudal lung lobe accidentally. The perforation was then repaired, but did not ultimately affect her outcome. Ria's post-operative care was similar to her first surgery. One week post-operative Ria was doing well

and she received first chemotherapy with Carboplatin via her left dorsal pedal vein and was discharged on November 7th, 2019.

November 11th, 2019, she presented to MSU-CVM Oncology Department to have the left metatarsus and hock swelling examined. The swelling was suspected to be a reaction to her carboplatin chemotherapy treatment or mild vasculitis from her time in ICU post-operatively. Radiographs were performed to rule out hypertrophic osteopathy and results were unremarkable. Recommendations were to warm pack and massage her left hind limb for 3 days.

December 3rd, 2019, Ria presented to MSU-CVM Oncology Department for second chemotherapy. At this visit the necrotic wound on her left metatarsus was noted. She was transferred to Small Animal Surgery Department for intensive wound management. Her owner noticed a black spot on her left hock area getting wider and starting to scab. Her owner thought it to be a healing wound. Later on, Ria started licking the scabbed wound. The scab came off, and the owner then noticed gray malodorous discharge in a deep necrotic wound. Additionally, at this appointment, a new firm and round mass was palpated on the right cranial thoracic wall, which was approximately 10x10x10 cm in size. Aspiration and cytology interpretation was suggested to be the recurrence of osteosarcoma. Thoracic radiographs and computed tomography were repeated, and the pulmonary metastatic neoplasia was noted. The owners elected to manage her wound at MSU-CVM until it could be closed surgically. She was discharged on December 11th, 2019. On Dec. 23rd, 2019, she became severely anorexic and lethargic. Ria was humanely euthanized by her primary care veterinarian.

REFERENCES

1. Baines SJ, Lewis S, White RAS: Primary thoracic wall tumours of mesenchymal origin in dogs: a retrospective study of 46 cases. Vet Rec 150:335–339, 2002
2. Pirkey-Ehrhart N, Withrow SJ, Straw RC, et al: Primary rib tumors in 54 dogs. J Am Anim Hosp Assoc 31:65–69, 1995
3. Feeney DA, Johnston GR, Grindem CB, et al: Malignant neoplasia of canine ribs: clinical, radiographic, and pathologic findings. J Am Vet Med Assoc 180:927–933, 1982
4. Heyman, SJ, Diefenderfer, DL, Goldschmidt, MH. Canine axial skeletal osteosarcoma: a retrospective study of 116 cases (1986 to 1989). Vet Surg;21:304–310, 1992
5. Liptak, JM, Dernell S, Rizzo SA, et al: Reconstruction of chest wall defects after rib tumor resection: a comparison of autogenous, prosthetic and composite technique in 44 dogs. Vet. Surg 37:479-487, 2008
6. Matthiesen DT, Clark GN, Orsher RJ, et al: En bloc rib resection of primary rib tumors in 40 dogs. Vet Surg 21:201-20, 1992
7. Kruse, M. A., Holmes, E. S., Balko, J. A., Fernandez, S., Brown, D. C., & Goldschmidt, M. H. Evaluation of Clinical and Histopathologic Prognostic Factors for Survival in Canine Osteosarcoma of the Extracranial Flat and Irregular Bones. Veterinary Pathology, 50(4), 704–708, 2013
8. Hammer AS, Weeren FR, Weisbrode SE, Padgett SL. Prognostic factors in dogs with osteosarcoma of the flat or irregular bones. J Am Anim Hosp Assoc 31:321-326, 1995
9. Júnior Gardinalli Benedito, Martelli Anderson. Clinical and pathophysiological aspects of osteosarcoma in dogs. Science and animal health V.3 N.1 Jan/Jun: 13-30, 2015

10. Eric M. Green, William M. Adams and Lisa J. Forrest. Four Fraction Palliative Radiotherapy for Osteosarcoma in 24 Dogs. J Am Anim Hosp Assoc 38:5, 445-451, 2002
11. Miller, Lejeune, Regan, Szivek, Kow: Suspected Carboplatin Extravasation Reactions in Seven Dogs. J Am Anim Hosp Assoc; 54:360–367, 2018
12. Fossum, T. W., & Duprey, L. P. Thoracic wall neoplasia. In: Small animal surgery. 3rd ed. St. Louis: Saunders Elsevier, 2007; 894-896
13. Tobias, Karen M. & Johnson, Spencer A. Thoracic wall neoplasia. In: Veterinary small animal surgery. St. Louis: Saunders Elsevier, 2012; 1783-1786