https://doi.org/10.17221/140/2021-VETMED

Surgical management of a metastatic vertebral tumour originating from a mammary adenocarcinoma in a dog

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Citation: Nam A, Hong SH, Jee HC, Lee WJ, Myung H, Kim DH (2022): Surgical management of a metastatic vertebral tumour originating from a mammary adenocarcinoma in a dog. Vet Med-Czech 67, 644–650.

Abstract: An 11-year-old spayed female Toy Poodle presented with acute tetraparesis. A small subcutaneous mass was found in the right trunk region, and the magnetic resonance revealed a compressive spinal cord lesion due to an irregular bone proliferation at the third cervical vertebra. After surgical resection of the vertebral lesion, the neurological symptoms improved, and the patient could walk on her own. The excised vertebral and subcutaneous masses were diagnosed as a mammary adenocarcinoma on the histopathological examination, with Ki-67 and HER-2 immunohistochemistry staining. This case report highlights the importance of defining the primary tumours of metastatic vertebral tumours and the necessity of palliative surgery to improve the patient's quality of life.

Keywords: bone tumour; canine; mammary cancer; metastasis; palliative surgery

Mammary gland tumours (MGTs) are the most common neoplasms in intact female dogs (Dorn et al. 1968; Salas et al. 2015). Recent studies have also reported higher incidence rates of malignant tumours than that of benign tumours, similar to epidemiologic trends in women (Salas et al. 2015; Vascellari et al. 2016). Although all malignant MGTs imply a metastatic risk to various organs, including the lymph nodes, liver, and lungs, bone metastases are rare (Chun and de Lorimier 2003).

Bone tumours account for ~2% of all canine tumours (Gruntzig et al. 2015), with metastatic bone tumours being less predominant than primary bone tumours (Chun and de Lorimier 2003; Thompson and Dittmer 2017). Notably, primary tumours can be difficult to identify in cases where the initial clinical manifestation results from metastatic lesions (Cooley and Waters 1998). There are many types of symptoms related to the bone tumour location, such as neurological signs (e.g., ataxia, paresis, and paralysis) if the spinal cord is affected (Valentim et al. 2016).

Although few studies on canines with MGTs developing skeletal metastases have been reported (Misdorp et al. 1972; Trost et al. 2014; Zuchi et al. 2020), the decision to undergo surgery in cases with distant metastasis remains unclear, as surgery may negatively impact the life expectancy (Milch 2005). To further investigate this topic, this report describes a case of palliative surgery to relieve tetraparesis in a canine with a metastatic cervical vertebral tumour.

https://doi.org/10.17221/140/2021-VETMED

Case description

An 11-year-old spayed female Toy Poodle dog weighing 3.2 kg was referred for sudden lethargy and astasia. The patient had neck pain and neurologic symptoms, including tetraparesis, upper motor neuron signs, and systemic tremors without any previous traumatic history.

On physical examination, cranial proprioception and motion reflex were absent, and the deep pain reflex was decreased in all four limbs. Furthermore, a subcutaneous mass of ~1 cm in diameter was found in the right trunk region.

No remarkable laboratory findings were observed, with the exception of an elevated alkaline phosphatase activity (555 µkat/l; reference range: 15–127 µkat/l). The radiography revealed a radiolucent amorphous lesion with new bone formation in the third cervical (C3) vertebra (Figure 1A). The abdominal ultrasonography showed a hyperechoic liver, hyperechoic renal cortex, and renal calculi in the left kidney, and no other masses were found in the abdominal organs. On the computed tomography (CT), a 6.3 × 12.0 mm calcified subcutaneous mass connected to the surrounding mammary gland was identified on the right abdominal wall (Figure 1B). Irregular bone lysis and proliferation arising from the lamina of the C3 vertebra were also observed, and a contrast-enhancing lesion protruding into the left dorsal side of the spinal canal was found on the post-contrast transverse CT (Figure 1C,D). In addition, a round-shaped, heterogeneously hyperintense mass at the third and fourth cervical (C4) level was seen on the T2-weighted magnetic resonance imaging, which caused the dorsal compression of the spinal cord and focal expansion of the subarachnoid space immediately cranial to the lesion (Figure 1E,F). Aside from the subcutaneous and vertebral lesions, there

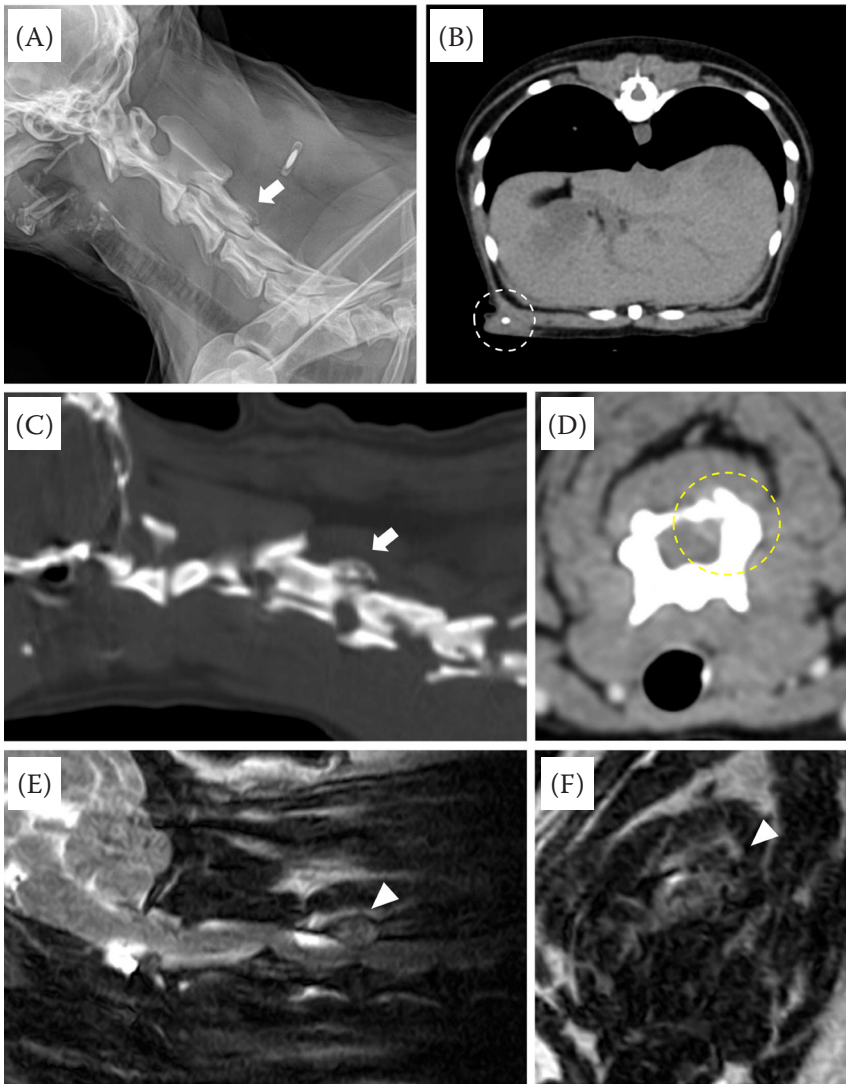

Figure 1. Diagnostic images of the vertebral mass
(A) Lateral radiography and (C) sagittal computed tomography (CT). Bone lysis and new bone formation (arrows) in the lamina of the third cervical (C3) vertebra. (B) Transverse CT image of the thorax. A subcutaneous nodule with calcification is shown in the right abdominal wall (white circle of dots). (D) Contrast-enhanced C3 lamina (yellow dotted circle) on the post-contrast transverse CT image. (E) Sagittal T2-weighted and (F) transverse T2-weighted magnetic resonance images at the C3–4 vertebral level. Irregular bony proliferation from the caudal lamina of the C3 vertebra (arrowheads)

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were no other specific findings. Based on these findings, a tentative diagnosis of a primary or secondary vertebral tumour was made.

Surgical resection of the vertebral mass was planned to relieve the patient's clinical symptoms, as per the owners' wishes. Premedication with butorphanol (0.2 mg/kg) and midazolam (0.3 mg/kg) were administered intravenously, and general anaesthesia was induced with intravenous propofol (6 mg/kg) and maintained with 2% isoflurane inhalation. The patient was positioned in ventral recumbency, and a routine surgical preparation was performed. When the C3 and C4 vertebrae were exposed, a reddish, granulomatous tissue proliferation was identified in the dorsal part of the C3 vertebra (Figure 2A). The normal bony tissues along the margin of the abnormal tissues were carefully removed using an ultrasonic surgical aspirator (Cavitron Ultrasonic Surgical Aspirator; Cavitron Ultrasonics, Cavitron Corporation, Long Island City, NY, USA) to minimise spinal cord damage and tumour cell seeding (Figure 2B). There was no adhesion between the mass and the spinal cord, and no serious haemorrhage was associated with the surgical procedure. The vertebral bone flap and mass were subsequently separated from the vertebrae (Figure 2C). After inspecting the spinal cord to ensure no lesions remained, an orthopaedic wire was placed between the C2 and C4 vertebrae to provide mechanical spine stabilisation. The nuchal ligament was briefly retracted, holes were made for the wiring at the spinal processes of the C2 and C4 vertebrae using a 1.0 mm diameter-drill bit, and an orthopaedic wire with a diameter of 0.3 mm was implanted to fix the two vertebrae (Figure 2D). After confirming no further vertebral instability, the surgical site was flushed several times with sterile saline and routinely closed. Finally, removal of the subcutaneous mass was conducted. Post-operative radiography (Figure 2E) and CT images (Figure 2F) were acquired immediately after surgery.

The patient was then administered a 2.5 ml/kg/h continuous infusion of normal saline containing tramadol (0.4 mg/ml), lidocaine (0.3 mg/ml), and ketamine (0.15 mg/ml) for analgesia. The following medications were prescribed for the post-operative care: intravenous cefazolin (22 mg/kg); subcutaneous carprofen (2.2 mg/kg); and oral drugs, including omeprazole (0.5 mg/kg), gabapentin (10 mg/kg), and liver supplements.

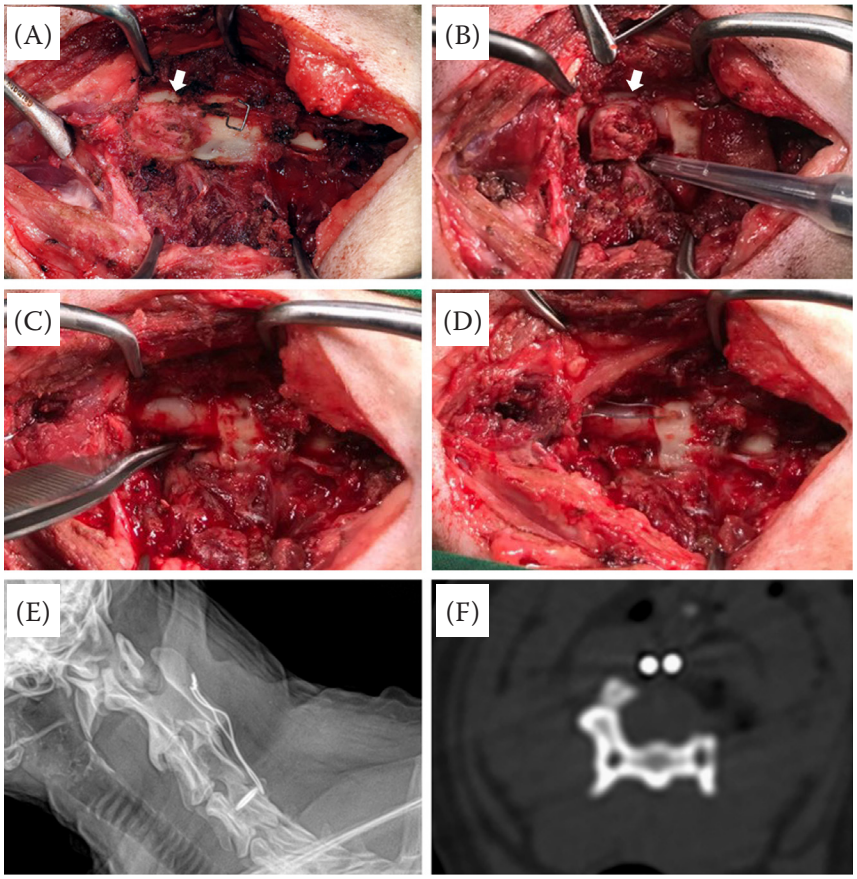

Figure 2. Intraoperative photographs and post-operative diagnostic images

(A) A reddish, irregular shaped mass (arrows). A staple was temporally placed at the spinal process of the fourth cervical vertebra. (B) After the adjacent bony tissue around the mass was removed using an ultrasonic surgical aspirator, (C) a whitish spinal cord was observed. (D) An orthopaedic wire loop was placed to improve the stability of the vertebrae. (E) Post-operative lateral radiography shows the radiolucent third cervical vertebra and orthopaedic wire loop. (F) Post-operative transverse CT shows an opening in the left lamina

https://doi.org/10.17221/140/2021-VETMED

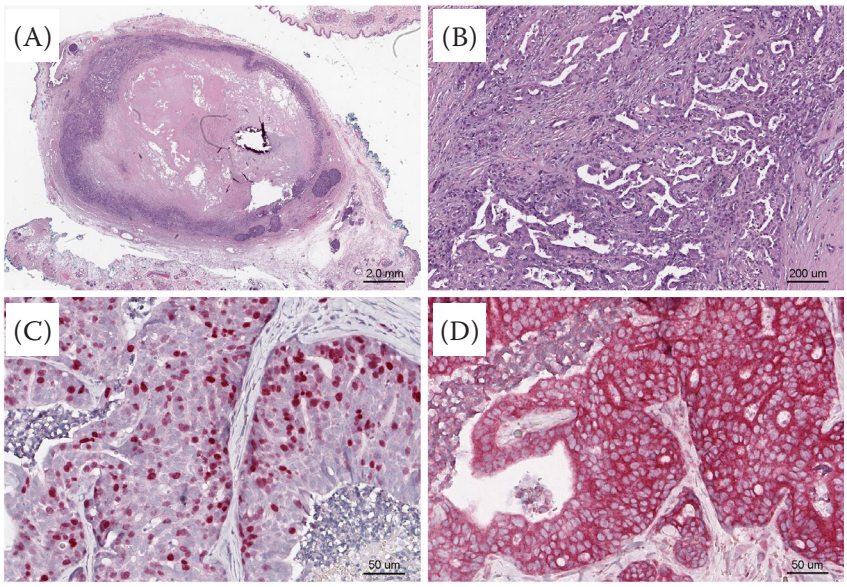

Figure 3. Histological and immunohistochemical images of the mammary gland mass
(A) Low magnification image shows proliferation of epithelial cells, with a large central area of necrosis on haematoxylin and eosin staining. (B) Tumour cells are characterised as variably sized round ovoid hyperchromatic nuclei, with a moderate pale eosinophilic cytoplasm and indistinct cell borders at high magnification. (C–D) The nuclei and cytoplasm of the tumour cells are strongly stained with Ki-67 and HER-2 markers, respectively. Scale bar: A = 2.0 µm, B = 200 µm, C–D = 50 µm

By the 4th day post-operatively, the patient was able to stand up independently, and her neck pain seemed to completely disappear. Moreover, the patient was able to walk around independently and exhibited normal motion reflex two weeks post-operatively. Despite the medical teams' strong recommendation of post-operative adjuvant chemotherapy and radiation therapy, the owners' decided otherwise.

The subcutaneous mass was diagnosed as a mixed mammary adenocarcinoma on the histopathological examination, which consisted of a neoplastic proliferation of epithelial cells, with variably sized round ovoid hyperchromatic nuclei, finely stippled

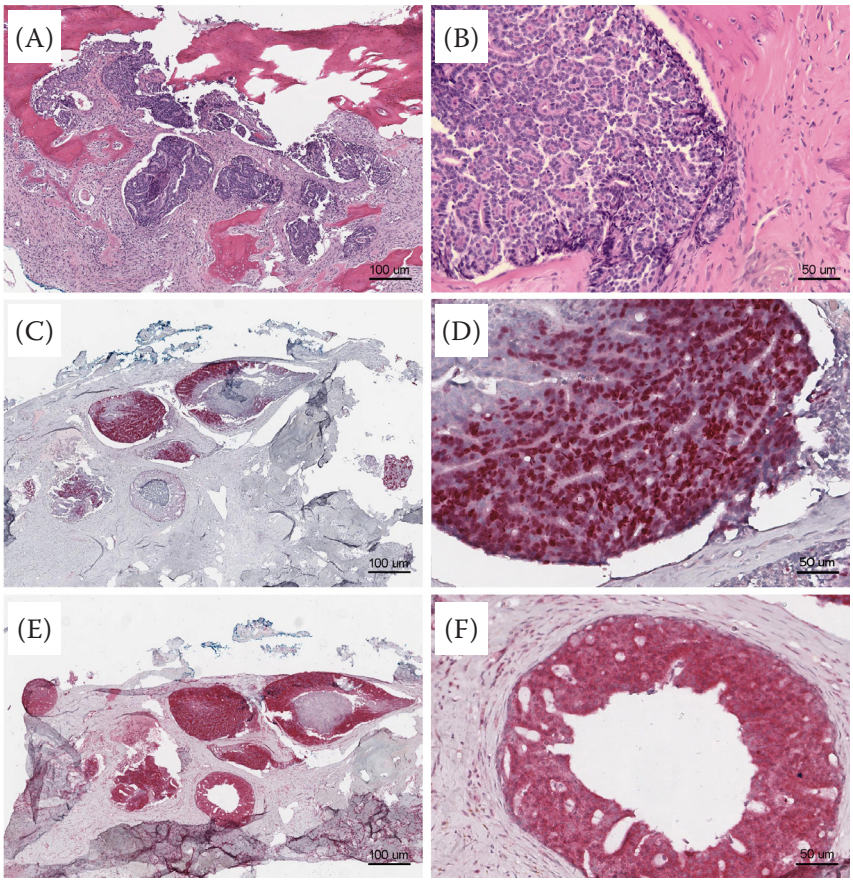

Figure 4. Histological and immunohistochemical images of the vertebral mass
(A) Mass showing a multinodular benign neoplastic process consistent with an adenocarcinoma with a severe periosteal bone proliferation on haematoxylin and eosin staining. (B) High magnification shows that the neoplastic proliferation of epithelial cells formed an irregular acinar structure. The nuclei and cytoplasm of the tumour cells show strongly positive staining with Ki-67 (C–D) and HER-2 (E–F). Scale bar: A, C, E = 100 µm; B, D, F = 50 µm

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chromatin, and prominent nucleoli (Figure 3A,B). The cytoplasm was scant to moderate and pale eosinophilic with indistinct cell borders, and the mitoses ranged up to three per high-power field (Figure 3B). Furthermore, there was a large central area of necrosis. On the immunohistochemistry, the mass was stained intensely positive for both Ki-67 and HER-2 markers (Figure 3C,D).

The vertebral mass section was characterised by a neoplastic proliferation of epithelial cells, which formed multiple variably sized discrete nodules of irregular acinar and ductular structures, or occasional dense sheets supported by modest to abundant collagenous connective tissue stroma. It was alternated with bone trabeculae effacing normal architecture (Figure 4A,B). The histopathologic findings of the cell nuclei, nucleoli, and cytoplasm were similar to those of the subcutaneous mass. The neoplastic cells were also strongly positive for both Ki-67 and HER-2 (Figure 4C–F). Therefore, the vertebral tumour was confirmed to be a bone metastasis of a mammary adenocarcinoma with severe periosteal bone proliferation.

The patient was well maintained without any neurological signs for three months. Unfortunately, the vertebral mass relapsed, and the patient eventually died at home one month later.

DISCUSSION

Secondary bone tumours are less common in dogs (Chun and de Lorimier 2003), with few studies reporting on the frequencies of several types of cancer, including primary bone tumours, MGTs, and haemangiosarcomas (Goedegebuure 1979). A report by Egenvall et al. (2007) revealed an incidence rate of 9% for malignant bone tumours localised to the vertebrae in Swedish dogs. Moreover, various diseases, including neoplasia, cause spinal cord disorders in dogs, resulting in symptoms, such as ataxia, paraparesis, paraplegia, tetraparesis, and tetraplegia (Bagley 2010; Valentim et al. 2016). The range and severity of these symptoms also depend on several factors: the spinal region affected, localisation with respect to the spinal cord, cell type, malignancy, and compression rate (Seguin et al. 2000; North and Banks 2009). In this case, a cervical spinal cord disorder was suspected based on the patient's tetraparesis and C3 vertebrae bone lesions on the radiography, which is the primary imaging modality for diagnosing bone tumours (Vanel et al. 2013). Although magnetic resonance imaging allows the detailed evaluation of the spinal cord and surrounding skeletal structure, a histopathological confirmation using bone biopsy should be conducted for a definitive diagnosis (Besalti et al. 2016).

MGTs are the most frequently diagnosed cancer in female dogs, with an incidence rate of 13% in dogs and > 40% of all tumours in intact female dogs (Sorenmo 2003; Pastor et al. 2018). Between 40–50% of canine MGTs are malignant, which has recently increased to reach 88% (Salas et al. 2015; Pastor et al. 2018). Malignant tumours can spread throughout the body. Although the lungs are the most common site for the distant metastasis of canine mammary cancer, metastasis to the skeletal system, including the vertebral bone, occasionally occurs (Cooley and Waters 1998; Valentim et al. 2016). Specifically, metastatic neoplasms account for 65% of spinal tumours in dogs, predominantly originating from the mammary gland (Valentim et al. 2016).

Determining the primary tumour is very important for the appropriate treatment and prognostic evaluation. However, it might be missed if the primary lesion does not cause clinical symptoms and does not spread to other organs (Cooley and Waters 1998). A thorough whole-body examination with a physical examination, diagnostic imaging, and histopathology should be performed. In this case, the patient's cervical vertebral mass was confirmed to be a metastatic tumour originating from a mammary adenocarcinoma based on the histopathological findings and high Ki-67 and HER-2 immunostaining from the bone tumour and solitary subcutaneous mass. According to the patient's medical history from the owners, a small, solitary mammary gland tumour, which did not undergo any histopathology, was removed when the dog was spayed abroad at the age of six years. A strong association between the tumour size and malignancy has been reported, wherein one out of 97 tumours smaller than 1 cm and four out of 54 tumours sized 1–2 cm were malignant (Sorenmo et al. 2009). Nevertheless, a possible malignancy should not be overlooked even if the mammary tumour is small.

The prognosis for spinal tumours depends on the location, degree of invasion of the nervous tissue, and severity of the neurological symptoms during the diagnosis (Asano et al. 2005). Previous research

https://doi.org/10.17221/140/2021-VETMED

revealed a median survival time of 20 days (range 1–202 days), although 50% of spinal tumour-bearing dogs received several forms of surgery, radiation, and chemotherapy (Pancotto et al. 2013). In another study, three out of four dogs with spinal tumours involving the cervical vertebrae were euthanised. One did not receive any treatment, whereas the others underwent surgery, but showed little or no clinical improvement (Besalti et al. 2016). In this case, our patient recovered well with the dramatic relief of neck pain post-operatively, despite the onset and exacerbation of symptoms within hours. Palliative surgery should be considered to improve the quality of life or relieve symptoms in cases of metastatic cancer, as observed in the present case. In conclusion, this report describes a dog with a metastatic cervical tumour originating from a mammary adenocarcinoma that showed improvement in the neurological symptoms following the surgical management. Despite the poor prognosis given its malignant nature, surgery to improve the quality of life is worth considering.

Conflict of interest

The authors declare no conflict of interest.

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Received: November 12, 2021
Accepted: July 27, 2022
Published online: September 12, 2022