Diagnosis and treatment of spinal neoplasia in dogs and cats

Bernard Seguin DVM, MS, DipACVS
Colorado State University, USA
Rodney S. Bagley DVM, DipACVIM (Neurology and Internal Medicine)
Gena M. Silver DVM, MS
Washington State University, USA

KEY POINTS

- Tumours of the spine can be in one of three anatomical locations: extradural, intradural-extramedullary, or intramedullary.
- There are several different histological type of neoplasm that can arise at each location.
- Clinical signs can be very variable and a thorough diagnostic approach is required.
- Several diagnostic tests may be required to make a diagnosis and some form of diagnostic imaging is mandatory.
- Surgery remains the cornerstone of therapy for most spinal tumours although radiotherapy may play a role in some cases.
- The prognosis for long-term survival remains poor in patients affected by a malignant neoplasm.

Introduction

Neoplasia is one of the differential diagnoses considered when evaluating a dog or cat with neurological signs referable to the spine. Neoplasms of the spine can be categorised, based on their tissue of origin, as tumours arising from:

- the neuronal tissue itself
- the protective structures of the spine such as the meninges or vertebrae
- a distant metastasis of another primary tumour

Neoplasms affecting the spine can be in one of three anatomical locations: extradural, intradural-extramedullary, or intramedullary (1). Approximately 50% of spinal tumours are extradural, whereas 35% and 15% are intradural-extramedullary and intramedullary, respectively (2).

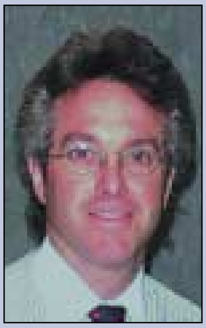
Histological types of neoplasia

Extradural neoplasms

Extradural tumours originate outside the dura mater. These tumours most commonly arise from bone and include osteosarcoma, fibrosarcoma, haemangiosarcoma, multiple myeloma, and chondrosarcoma (1). Osteosarcoma, fibrosarcoma, and haemangiosarcoma of the vertebrae may also be metastases and therefore evaluation for a primary neoplasm should

Bernard Seguin
DVM, MS, DipACVS

Dr. Seguin graduated from the University of Montreal in 1992 and completed an internship in small animal medicine and surgery at the University of Illinois in 1993. He worked in a private practice for two years before going on to gain a Masters degree at Washington State University in 1998. He is currently completing a fellowship in surgical oncology at Colorado State University.



Rodney S. Bagley
DVM, DipACVIM

Dr. Bagley is a Diplomate of the American College of Veterinary Internal Medicine in both Neurology and Internal Medicine. He graduated from the Virginia-Maryland Regional College of Veterinary Medicine in 1986. He is currently an Associate Professor of Neurology and Neurosurgery at Washington State University, College of Veterinary Medicine.

Gena M. Silver
DVM, MS

Dr. Silver graduated from the Atlantic Veterinary College in 1995. She completed a small animal internship and Neurology residency at Washington State University, College of Veterinary Medicine. She is currently an Instructor of Neurology and Neurosurgery at Washington State University, College of Veterinary Medicine.

Illustration courtesy H. W. Scott.

Figure 1 *A dog with a spinal tumour exhibiting neck pain and a rigid stance.*

be performed (2). Other tumours may metastasise to tissue adjacent to the vertebrae and cause secondary spinal cord compression. An example of this would be metastasis from prostatic adenocarcinoma to the sublumbar lymph nodes with eventual invasion into the lumbar vertebrae. Malignancies can also metastasise to the vertebrae via the haematogenous route. Numerous other neoplasms can metastasise to vertebrae, including mammary carcinoma, perianal gland adenocarcinoma, transitional cell carcinoma, Sertoli cell carcinoma, thyroid carcinoma, and pheochromocytoma. The lumbar area is the most common site for spinal metastasis but the cervical and thoracic segments have also been affected.

Lymphosarcoma is the most common soft tissue extradural tumour in dogs (1) and spinal lymphosarcoma is also most commonly seen as an extradural tumour in cats (3). Other tumours found in this location in dogs and cats include meningioma and nerve sheath tumour (4, 5). Other tumours reported in dogs in the extradural location include myxoma, myxosarcoma, plasma cell tumour, and lipoma (5).

Intradural-extramedullary neoplasms

These tumours arise outside the spinal cord but are within the subdural space. In dogs, nerve sheath tumour (Schwanoma, neurofibroma) is one of the two most common tumours in this location (1, 2, 6). There is discrepancy as to the other most common tumour as both meningiomas (1, 2) and haemangiomas (6) are reported. An unusual case of disseminated meningeal tumour in a dog has been reported where the tumour involved almost the entire meningeal surface of the nervous system. A myxoma/myxosarcoma has also been reported in this location (5).

Spinal cord blastoma has been described in young dogs (up to three years of age) of large breeds especially German Shepherd Dogs and retrievers (2). The tumour is consistently located between T10 and L2 (2). The histological origin of the tumour is still being debated. This lesion has been designated ependymoma, medulloepitheloma, neuroepithelioma, and nephroblastoma (2).

In cats over 50% of non-lymphoid tumours are intradural-extramedullary (4). The most common type is a meningioma but nerve sheath tumours are also reported (4). One report describes lymphosarcoma affecting the roots of the brachial plexus and extending into the subarachnoid space in three cats (5).

Intramedullary neoplasms

Intramedullary tumours are situated within the spinal cord substance and are predominantly of glial cell origin. Astrocytoma and ependymoma are the most common (1) but other types reported include oligodendroglioma, undifferentiated sarcoma, choroid plexus papilloma (2), and, interestingly, a meningeal sarcoma. These tumours may be more common in the C6 to T2 region (7). Intramedullary tumours are extremely rare in cats (2). The most common tumours to metastasise to the substance of the spinal cord are haemangiosarcoma and lymphosarcoma although mammary gland carcinoma, malignant melanoma, and thyroid carcinoma have also been reported in dogs (2, 5, 8).

Diagnosis

Clinical signs

Dogs of any age may develop spinal neoplasia. The clinical signs can be insidious, chronic, and progressive but can also be acute. In one study, the majority of animals with intramedullary tumours had an acute onset of neurological signs (9). The neurological signs vary according to the location of the tumour and their severity depends on both the degree of compression, destruction, oedema and haemorrhage of the neuronal tissue and the degree of compensation of the spinal cord (10). Hyperaesthesia is common with many spinal tumours and evidence of pain may also be noted in some case (**Figure 1**).

Neurological signs attributed to the presence of spinal neoplasia can be unilateral, bilaterally symmetrical or asymmetrical, depending on the extent of compression or neural tissue destruction in the transverse plane. Dogs affected by nerve sheath tumours usually display unilateral signs (11, 12), which may be mistaken for lameness, and has been termed 'root signature'.

Spinal hyperaesthesia is common in instances where the tumour is found in the extradural or intradural-extramedullary location and may be the only abnormal finding (2). Animals with intramedullary tumours may not have spinal hyperaesthesia (2, 8) as there are no nociceptors within the spinal parenchyma. If the mass expands to the point of stretching the meninges, or nerve roots, focal spinal hyperaesthesia may result.

Clinical evaluation

A thorough and complete physical examination, as well as a neurological examination, should be performed. A fundic examination may be very helpful as it is a direct examination of part of the nervous system and may reveal evidence of a more diffuse disease, such as lymphoma, rather than one that just affects the spinal cord (13). Peripheral lymph nodes should be palpated and aspirated as necessary. Rectal examination should be performed as the presence of an enlarged asymmetric prostate, or the presence of a mass in the sublumbar or subsacral region, may be detected.

A complete blood cell count (CBC), chemistry panel, and urinalysis are important parts of the initial minimum database. In animals with lymphoma an abnormal distribution or character of cells may be detected with the CBC (13). In one study of cats with spinal lymphoma, 14 out of 19 cats had an abnormality on the CBC including anaemia (58%), leukopaenia (37%), thrombocytopaenia (11%), and circulating lymphoblasts (16%) (14). Examination of bone marrow aspirates may also help to make a diagnosis of lymphoma. Thus the bone marrow was abnormal in 13 of 16 cats with lymphoma (14).

Animals affected by multiple myeloma may have abnormal amounts and distribution of proteins on the chemistry panel, demonstrated by an elevation in the globulin fraction (13). This increase in the concentration of globulin proteins is a result of an overproduction of immunoglobulins by the malignant plasma cells. Elevation of serum alkaline phosphatase activity from dogs with appendicular osteosarcoma indicates a worse prognosis. This prognostic value of alkaline phosphatase in cases of vertebral osteosarcoma, or other bone-invading neoplasm, still needs to be investigated.

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Figure 2 *Lateral radiographic view of the lumbar spine of a 10-year-old male castrated Samoyed. There is an expansile lytic lesion in the lamina of the second lumbar vertebra. Histopathology revealed this mass to be an osteosarcoma.*

Any animal suspected of having a neoplasm should have chest radiographs evaluated for pulmonary metastases or enlarged intrathoracic lymph nodes. This will help to determine the prognosis (2, 13) because if pulmonary metastasis or lymphadenomegaly is detected, suggesting the invasion of neoplasia, then any local therapy of the cancer cannot be curative and the expected survival time is decreased.

Once the minimum database has been completed, electrodiagnostics, survey radiographs of the spine, cerebrospinal fluid (CSF) collection, and myelography or advanced imaging can be performed during a single anaesthetic period.

Cerebrospinal fluid analysis

The sensitivity of this procedure is dependent on the site of puncture. In one study, CSF samples collected from the cerebellomedullary cistern in dogs with a thoracolumbar spinal lesion were abnormal in 27.5%, whereas when the samples were collected from the lumbar cistern 87.5% were abnormal. However, given the practical difficulty associated with thoracolumbar sampling, it is probably wise to take samples from both areas (14). Note that the protein content of CSF collected from the lumbar cistern is normally higher than that of CSF collected from the cerebellomedullary cistern.

Examination of CSF may be normal from animals with spinal neoplasia. The most common abnormality found is an increase in the protein concentration without an increase in the number of cells, referred to as albuminocytologic dissociation (13). Neoplastic cells are rarely found unless the tumour is intradural or involves the meninges (14). The most common tumour associated with neoplastic cells present in the CSF is lymphosarcoma (3, 13, 14). In one study, neoplastic lymphocytes were seen on CSF analysis in six of 17 cats (3). Because dogs with spinal lymphosarcoma have leptomeningeal involvement more frequently than cats, CSF analysis is more commonly diagnostic of this condition (3). The prevalence of positive CSF cytology in animals with intramedullary lymphosarcoma is unknown. In the only reported cases where the cytology was able to provide the diagnosis, leptomeningeal inflitration by the tumour was present (8).

Electrodiagnosis

Electromyography (EMG) is a test to evaluate the status of the motor unit. This test may be useful in localising a spinal lesion as abnormal spontaneous activity may be seen in the muscles whose nerves are damaged by the tumour. However, this test cannot determine the exact aetiology of a dysfunctional unit (13). The greatest diagnostic value of EMG lies in localizing diseases of the nerve roots, nerve sheaths, or cauda equina (13). In two studies, EMG showed evidence of denervation in 100% of the cases where a nerve sheath tumour was present (11, 12). The distribution of the denervated muscles corresponded to the nerves affected histologically (11).

Imaging of the spine and spinal cord

Imaging of the spine and spinal cord is essential in order to plan therapy and to aid in provision of a prognosis in almost all spinal neoplasms, with the exception of lymphoma. Imaging of the spine can be performed with radiography, myelography, computed tomography (CT), magnetic resonance imaging (MRI), and scintigraphy.

Radiographs of the vertebrae are ideally performed with the animal under anaesthesia. Vertebral changes associated with neoplasia may be seen with survey radiographs (**Figure 2**). These changes include cortical destruction, collapse of adjacent disc spaces, destruction of end plates, cyst-like expansile destructive lesions, and pathological fractures of the body or lamina. One study failed to identify pathognomonic changes on radiographs that could differentiate between specific tumour types but found that involvement of more than one vertebra suggested a metastatic neoplasm to the spine. Fluoroscopy can be very useful to guide a fine needle aspiration of a vertebra, or tissue within the vertebral canal, potentially allowing a diagnosis without having to go to surgery (10, 14).

Myelography is an important diagnostic procedure that allows delineation of the subdural space, allowing the clinician to the ability to assess spinal cord compression and make inferences regarding the location and extent of a tumour. Tumours are classified as extradural, intradural-extramedullary, or intramedullary based on the myelographic features. Myelography results in columns of contrast medium, in the epidural space. On the dorsoventral view there is a contrast column, one at each margin of the cord, whereas on the lateral view there are two, one dorsal and one ventral to the cord. Extradural neoplasms cause one or both lines of contrast medium to deviate axially on either the lateral or dorsoventral view (**Figure 3**).

Intradural-extramedullary neoplasms cause one column of contrast medium to expand and outline the lesion. This is referred to as the 'golf tee sign'. This can be seen as a sudden arrest of the contrast medium column

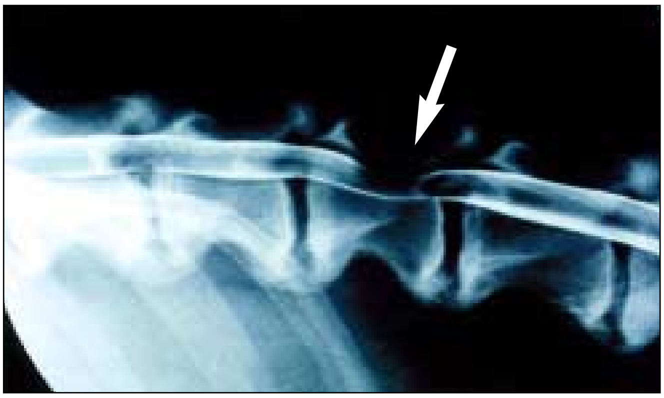

Figure 3 *Lateral radiographic view of a myelogram performed on the same dog as* Figure 1. *The dorsal and ventral contrast columns deviate ventrally depicting an extramedullary mass compressing the spinal cord dorsally.*

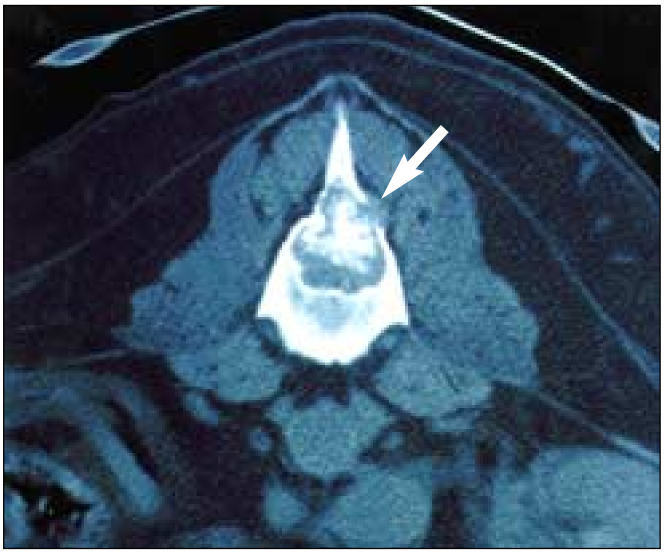

Figure 4 *Transverse computed tomographic view of the second lumbar vertebra in the same dog as* Figures 2 *and* 3. *There is a proliferative lesion invading the spinal canal with some lysis of the right lamina.*

with its end being slightly concave, or as a filling defect in the contrast medium column. The opposite contrast medium column will often deviate abaxially owing to cord swelling. Intramedullary neoplasms cause both contrast medium columns to diverge, indicating spinal cord enlargement. In one study, myelography was very accurate in demonstrating spinal cord or nerve root involvement, or lack thereof, in peripheral nerve sheath tumours in dogs (12). Myelography may have limited value when the tumour is compressing the cauda equina since the dural sac does not extend to this level in most dogs. Other contrast studies such as venous sinography or epidurography poorly delineate this area (13). In these instances, advanced imaging modalities such as CT or MRI are necessary.

Computed tomography (**Figure 4**) has several advantages over conventional radiography:

- CT can discriminate physical density differences as small as 0.5% whereas a 10% difference is needed for visual detection with conventional radiographs (15).
- CT creates the image of a 'slice' of the anatomical area (hence the name tomography) whereas the image created by conventional radiography is the sum of all the structures superimposed in a certain view (e.g. lateral or ventrodorsal).
- CT images can be displayed in different grey scale formats, which can enhance visualisation of specific structures.
- CT images can be reconstructed in multiple anatomical planes (15).

Contrast agent must be injected into the subarachnoid space in order for CT studies to assess spinal cord compression. In one study comparing radiography, myelography, and CT for the evaluation of canine vertebral and spinal cord tumours, CT was more sensitive than radiography in visualising bony changes but myelography was better than CT at differentiating between intradural-extramedullary and intramedullary lesions. This is in contrast to human studies and it was suggested that the reason why myelography was more sensitive than CT was the retrospective nature of the study (15). CT has been used successfully to diagnose brachial plexus tumours in dogs.

MRI is the modality of choice for evaluation of the spinal lesion in humans (16). Like CT, MRI allows tomographic imaging in multiple planes and it therefore provides a more anatomical representation of the spine than does conventional radiography. Anatomical locations involved were accurately determined with MRI in all dogs in a recent study (16). T2-weighted images were helpful to determine the anatomical location, and transverse, TI-weighted images, pre- and post-Gadolinium-based contrast medium administration were helpful for additional localisation and definition of tumour extension. In the same study, bone infiltration was correctly assessed in most dogs but the localisation of the tumour in the intradural-extramedullary compartment was not always possible.

Bone scintigraphy can be performed by injecting technetium-99m-labelled methylene diphosphonate. Scintigraphy is best suited for animals with a known bone tumour where other bony involvement is sought, since the occurrence of multiple skeletal sites of primary and secondary neoplasia has been well documented. Scintigraphy allows for a survey of the entire skeleton. It is estimated that 50 to 75% of the vertebral bone has to be destroyed to be demonstrated radiographically whereas minimal changes in vascularity or bone turnover will be demonstrated with scintigraphy. This modality therefore appears to be more sensitive than radiography at detecting the presence of disease in the vertebrae. Scintigraphy cannot be used to detect spinal neoplasia that does not involve bone. Therefore intradural-extramedullary and intramedullary cancers will not be diagnosed with this modality.

Treatment and prognosis

Spinal tumours

Surgical treatments remain a cornerstone of therapy for most spinal tumours. The goals of surgery are to collect a biopsy for histopathological evaluation, to resect the tumour if possible, and to decompress the spinal cord. Surgical approaches are determined based on the location and extent of the lesion. A dorsal laminectomy or hemilaminectomy is the approach of choice because either can provide wide exposure. A hemilaminectomy in the cervical spine can be challenging because of the proximity of the vertebral artery, which is located ventral to the surgical area. A ventral slot, which is performed in the cervical spine, is rarely beneficial because of the limited access to the spinal canal and nerve roots (10).

Manipulation of the spinal cord should be avoided. Performing a rhizotomy (section of a nerve root) can be helpful in removing a tumour but should be avoided in the brachial and lumbosacral plexuses because of the lower motor neuron deficit that will occur (10). If a nerve requires resection, the ability to achieve a total resection is weighed against the morbidity associated with nerve resection.

Extradural tumours that are invading the dura mater may require a

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durectomy. In order to approach intradural-extramedullary tumours, a durotomy must be performed. Intramedullary tumours are best approached by a dorsal laminectomy or hemilaminectomy with a durotomy and a myelotomy. These tumours can be non-infiltrative which makes surgical excision possible. In one instance, two dogs recovered rapidly back to their preoperative neuralgic status or better after the surgery after a myelotomy was performed to remove an intramedullary neoplasm. In another, an intramedullary spinal paraganglioma in a dog was successfully removed surgically from within the spinal cord. The fibres of the spinal cord were bluntly separated to reach the mass, which was well encapsulated making surgical resection possible.

Results of surgical treatment

In one study, dogs with benign spinal tumours had a median survival time of 1,410 days versus 180 days for dogs with malignant tumours, although the difference was not statistically significant (5). Most dogs had been treated with surgery alone although 3 dogs out of 22 received adjunctive chemotherapy and radiation therapy (5). Two dogs with spinal meningioma survived for 1,410 and 1,440 days, respectively, with surgical excision alone (5). Cats with non-lymphoid vertebral canal tumours seem to have a better prognosis than cats with spinal lymphoma (4). Cats with spinal meningioma can have a good prognosis after surgical excision. The median survival time was 180 days with one cat still alive 1,400 days after surgery (4). One cat with chondrosarcoma survived for 365 days postoperatively in spite of incomplete excision, and one cat with osteosarcoma lived for 1,705 days after surgery with incomplete excision (4).

Adjunctive treatment

Surgical resection is considered by some authors to be rarely complete for spinal tumours and therefore ancillary therapies such as chemotherapy and radiotherapy should be performed (10). In a retrospective analysis of 20 dogs with vertebral osteosarcoma or fibrosarcoma (17), all died because of their disease – 15 because of local failure and five from metastasis. These dogs had been treated with surgery ($n = 4$), radiation and chemotherapy ($n = 6$), surgery and chemotherapy ($n = 2$) or surgery, radiation, and chemotherapy ($n = 8$). Eight dogs improved neurologically after the treatment, seven remained the same, and five deteriorated. Median survival for dogs with osteosarcoma was 135 days and for dogs with fibrosarcoma it was 113 days. There was no statistical difference between the survival times of dogs with primary and metastatic disease (median 120 days and 135 days, respectively).

The data suggested that early diagnosis with minimal to no neurological deficits seemed to provide better survival and that multimodality treatment showed a trend toward improved outcome (17).

Prognosis

Dogs with spinal cord tumours may have a better prognosis when treated with surgery and postoperative irradiation. In a retrospective analysis of nine dogs (six meningiomas, one ependymoma, one neuroepithelioma, and one nerve sheath tumour), all dogs improved neurologically and the median survival time was 17 months with a range of 6.5 to 70 months (18). Five dogs were euthanased owing to recurrence of tumour or neurological signs. Dogs with meningioma had a median survival time of at least 12 months (range 8 to 25 months) and the dog with ependymoma died 70 months postoperatively of an unrelated cause (18).

Cells in the spinal cord are usually resistant to radiation because of their poor ability to replicate, but detrimental side effects may be seen after approximately two years (5). Radiation damage primarily occurs in the white matter and occurs through demyelination and malacia. Cells affected by radiation are oligodendrocytes, endothelial cells, astrocytes, and microglial cells (19).

Spinal lymphoma in cats

Lymphoma in cats has been treated with chemotherapy (3, 14); however, the best treatment regimen for spinal lymphoma remains to be evaluated. Because cats with spinal lymphoma usually have multicentric disease, chemotherapy is indicated (14). The role of surgery appears to be limited because the lymphoma often extends over several vertebral bodies and decompressive surgery may destabilise the vertebral column (14). Irradiation has been used to treat spinal lymphoma in cats in conjunction with chemotherapy (3). Rapid reduction in tumour mass can occur within hours of delivering a single large dose of radiation (3). Therapy should be started immediately after the diagnosis to avoid progression of spinal cord damage (3, 14). Chemotherapy should be considered even in cats with severe neurological deficits because complete remission can still be achieved (14). The prognosis for cats with spinal lymphoma appears to be worse than that for cats with other forms of lymphoma as the prevalence and duration of complete remission were lower (14). Most cats will succumb to their disease within five months (3, 14).

Vertebral neoplasia

The current recommendation for dogs with vertebral neoplasms is to perform decompression, or stabilization, or both if the dog is rapidly declining neurologically, is non-ambulatory, or has intractable pain (17). In this study, surgical treatment was intralesional, without curative intent and usually included decompression laminectomy. Stabilisation was deemed necessary in three dogs and was achieved with dynamic compression plate or Steinmann pins in combination with polymethylmethacrylate (17). Complete removal of affected vertebrae (spondylectomy or vertebrectomy) may be attempted in selected cases, but almost invariably results in an incomplete resection of the tumour and requires surgical stabilisation (17). In one case report, a fibrosarcoma of the fifth lumbar vertebra of a three-year-old mixed breed dog was treated by vertebrectomy and replacement with a cortical femoral allograft. Stabilisation of the spine was provided with two limited-contact dynamic compression plates and adjuvant therapy consisted of antitumour vaccination. There was no evidence of tumour recurrence 13 months postoperatively and the patient was still doing well 26 months postoperatively, although faecal and urinary continence was never recovered (20). If the vertebral neoplasm is a myeloma then chemotherapy is indicated (10), which emphasises the need to biopsy.

Peripheral nerve neoplasia

Surgery has been the treatment of choice for dogs with peripheral nerve sheath tumours. Local resection, amputation, laminectomy, or a combination of these procedures, may be required (12). The type of surgery attempted is dictated by the location of the tumour. The tumour can be located distal to the plexus (peripheral), within the plexus, or involve the vertebral canal (root) (12). A tumour that invades the spinal canal requires a hemilaminectomy. Peripheral tumours that are very large may be best treated with amputation in order to achieve complete resection, or may be treated with marginal resection followed with adjuvant radiation therapy in order to avoid amputation. Other factors to consider when deciding between resection and amputation, especially for tumours that are within the plexus or involving a root, are the degree of neuralgic impairment preoperatively and the extensiveness of the tumour.

Resection of the tumour does not improve the neuralgic function of the limb but can improve the pain that the tumour causes to the dogs. If the degree of neuralgical impairment is too severe preoperatively, or if the tumour is so extensive as to require multiple nerve root resection and greatly compromise limb function, then amputation is the treatment of choice.

The prognosis for dogs with peripheral nerve sheath tumours is guarded to poor and appears to be related to the location of the tumour. The relapse-free interval was significantly longer for the peripheral group than for the plexus and root groups. There appeared to be a trend for a longer relapse-free interval for the plexus group (median 7.5 months, range 0 to 43 months) compared with the root group (median 1 month, range 0 to 14 months). Multiple nerve involvement did not seem to affect survival times compared with single nerve involvement. Sixty-five per cent of dogs demonstrated an improvement in their presenting clinical signs or cessation of progression of their clinical signs of at least two months following the surgery (12). Although complete versus incomplete surgical excision was not compared, because metastases are rare (12), it appears that complete surgical excision must be performed and can prove to be curative. Adjunctive chemotherapy or radiotherapy remains to be evaluated (12). Two cats that underwent surgical excision of a nerve sheath tumour were the subject of a case report (4). One had an incomplete excision and a survival time of 70 days and the other cat had a complete excision and was still alive at 2,190 days postoperatively (4).

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