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Original Article

Compartmental resection of peripheral nerve tumours with limb preservation in 16 dogs (1995–2011)

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ABSTRACT

Peripheral nerve tumours (PNTs) affecting the limbs may lead to chronic pain, lameness and/or monoparesis that is refractory to medical treatment. The most common radical therapy for PNTs has been surgical excision with limb amputation. However, compartmental resection with preservation of the limb has been performed by the authors with favourable clinical results and therefore this bi-institutional retrospective study was undertaken to assess limb function, survival and recurrence.

Sixteen dogs that had been diagnosed with PNTs between 1995 and 2011 met the inclusion criteria for this study. In the majority of the cases, good to excellent limb function was achieved. The overall median survival time (MST) was 1303 days (42.8 months; range, 14 days–4639 days, [0.5–152.4 months]), with two dogs still alive at time of evaluation. Non-infiltrated margins were the best prognostic indicator; dogs with non-infiltrated margins had a MST of 2227 days ($P < 0.001$) compared to dogs with infiltrated margins (MST of 487 days). The 1-year calculated survival rate was 68.8% and the 2- and 3-year calculated survival rates were 62.5%. Surgical treatment with tumour removal and limb spare for proximal and distal PNTs can be successful. Compartmental excision can lead to good limb function, producing survival comparable to limb amputation, and should therefore be considered as an alternative to limb amputation in canine PNTs.

Introduction

Peripheral nerve tumours (PNTs) in dogs are malignant mesenchymal tumours that originate from nerve tissue and grow proximally and distally along the affected nerve. The brachial and lumbosacral plexus are common sites for PNTs. They lead to chronic pain, lameness, monoparesis, and muscle atrophy, refractory to medical treatment (Carmichael and Griffiths, 1981; Wheeler et al., 1986; Sharp, 1989; Targett et al., 1993, Brehm et al., 1995; Jones et al., 1995).

Local control is the hallmark of treatment of PNTs because distant metastasis of PNTs in dogs is rare (Sharp, 1989). The most common therapy for PNTs has been surgical excision of the tumour, combined with limb amputation (Wheeler et al., 1986; Brehm et al., 1995; Sharp and Wheeler, 2005; Caplan, 2012). Complete excision can be challenging because of the proximal extension of the tumour into the vertebral canal. Dogs with nerve tumours affecting a nerve distal to a plexus have a better prognosis than dogs with tumours affecting the plexus itself or invading the vertebral canal (Sharp, 1989; Brehm et al., 1995). Survival times for dogs following surgical excision of PNTs have been reported to range from 2 months to 2 years (Brehm et al., 1995; Sharp and Wheeler, 2005; Caplan, 2012).

In human medicine, surgical excision consists of removal of the affected nerve with a proximal and distal margin and limb amputation is performed only in rare cases. Status of surgical margins is an important prognostic factor in humans (Wong et al., 1998; Anghileri et al., 2006; Zou et al., 2009).

The purpose of this study was to retrospectively assess the efficacy of compartmental resection of PNTs with preservation of the limb in relation to survival rate, limb function, histological completeness of resection and disease free period.

Materials and methods

Dogs and study design

The inclusion criteria for this bi-institutional retrospective study were dogs with a PNT affecting limb function that were treated with compartmental resection and limb preservation. Dogs were excluded if clinical information, imaging, surgical findings, histopathology or follow-up was not available for review. The study was

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Table 1
Postoperative limb function according to lameness grade.[a]

Limb function (owner assessed)	Lameness grade (Arnoczky&Tarvin)	Description
Good	Grade 0	No lameness
Good	Grade 1	Minimally impaired locomotion
Reasonable	Grade 2	Impaired locomotion, still weight bearing
Poor	Grade 3	Lameness, infrequent non-weight bearing
Poor	Grade 4	Non-weight bearing lameness

[a] Descriptive lameness grading schedule by Arnoczky and Tavin was applied to the lameness assessment by the owners, ranging from no visible lameness (grade 0) to non-weight bearing lameness (grade 4).
Modified after Arnoczky and Tarvin (1981).

approved by the Internal Ethical Review Committee of the Advancement in Veterinary Research (AVR) Council, Department of Clinical Sciences of Companion Animals, Utrecht University.

Medical records were reviewed for signalment, presenting complaints, clinical signs, preoperative lameness grade (Table 1), imaging findings, tumour location and histological diagnosis and margin assessment.

Imaging and surgery

Imaging was performed by (or a combination of) ultrasonography, radiography, computed tomography (CT), and magnetic resonance imaging (MRI). Images were reviewed by board-certified veterinary radiologists. The long and short axis of the tumour were measured. Dogs were graded and staged using the TNM scheme (Liptak and Forrest, 2013).

Surgery was performed by board-certified surgeons. The PNT was followed in proximal and distal direction until the nerve tissue was considered normal on macroscopic inspection. The nerve was then infiltrated with local anaesthetic (lidocaine 2 mg/kg, 20 mg/mL) and sharply transected. The distal nerve margin was marked using surgical ink or sutures and the excised nerve was fixed in formalin.

Histopathology

Histological diagnosis on haematoxylin and eosin (HE) staining was performed by a board-certified pathologist according to the canine PNT literature (Koestner and Higgins, 2002; Cantile and Youssef, 2016) or comparative literature (Patnaik et al., 2002; Chijiwa et al., 2004; Rodriquez et al., 2012; Suzuki et al., 2014). Microscopic evaluation of margins consisted of evaluation of qualitative margin assessment on fascial planes and tumour borders as previously described (Bostock and Dye, 1980; Kuntz et al., 1997; Kawaguchi et al., 2004). Absence of tumour cells at the surgical margin was categorised as non-infiltrated margins, tumour cells at or within the proximity of several cell layers at the surgical margin, without the presence of fascial plane were categorised as infiltrated margins.

Follow up

Follow up data on limb use, disease free interval and survival was acquired by a telephone questionnaire administered to owners and veterinarians. Owners and veterinarians were asked to grade pre-operative, post-operative and current limb function. Limb function after surgery was classified as decreased, stable, or improved compared with pre-operative limb function. Current limb function was classified as poor, reasonable, or good (Table 1).

Statistics

Survival time (MST) was defined as the period between the date of surgery and the date of death. Dogs that died of unrelated causes or that were still alive at the end of the data accrual period, were censored for survival. Disease free interval (DFI) was defined as the period between the date of surgery and the last available date of remission or the date of recurrence of clinical signs.

Survival curves were drawn by the Kaplan–Meier method. The variables tumour location, histological margins, and post-operative limb function were evaluated for predicting death using the log-rank test. Correlations between tumour location, histological margins and post-operative limb function were evaluated using chi-square tests. Differences were considered to be significant at $P < 0.05$. Statistical analysis of data was performed with SPSS 22.0 computer software.

Results

Case information

Eleven male (six castrated and five intact) and five female (three spayed and two intact) dogs of various breeds with a male to female ratio of 2.2:1 were included (Tables 2 and 3). The median age was 8 years (range, 2–13 years), and median bodyweight was 30 kg (range, 5.8–51.1 kg).

The most common clinical signs included monoparesis ($n = 15$) and muscle atrophy ($n = 15$). Dogs presented with an acute (case 16) or chronic history of progressive lameness ($n = 10$), lumbosacral pain ($n = 10$), or cervical pain (case 2). In 14 dogs, the median duration of clinical signs prior to diagnosis was 3.5 months (range, 1–12 months); in two dogs time of onset of clinical signs was unknown.

Imaging results

Thirteen dogs staged negative for pulmonary metastatic disease based on thoracic radiographs and/or CT. Diagnostic imaging of the mass was performed by MRI ($n = 7$), contrast-enhanced CT ($n = 3$), ultrasound ($n = 2$) or a combination of imaging modalities ($n = 4$; Tables 2 and 3). Local lymph node enlargement was not evident in any of the dogs. Tumour dimensions (long and short axes) ranged from 0.5 to 14 cm (Table 3). Three dogs were determined to have stage 3 sarcoma in the tumor/regional nodes/metastasis (TNM) schedule (cases 1, 7 and 14); two of those three dogs had non-infiltrated margins (cases 1 and 7). Nine dogs had spinal canal involvement on imaging. Spinal cord invasion was an intra-operative, and in some cases, a histological diagnosis.

Surgical technique

The affected nerve segment was resected en bloc, attempting to achieve 2–3 cm of grossly normal nerve proximally and distally. In six dogs, the tumour extended into the spinal canal requiring foraminotomy, hemilaminectomy or dorsal laminectomy. In three dogs with lumbosacral plexus involvement the affected nerve root was removed (Tables 2–4).

Histopathology

The histopathological ($n = 16$) and immunohistochemical ($n = 5$) diagnosis was sarcoma. Peripheral nerve sheath tumours (PNSTs) were identified in 14 cases, and in two cases a neuroectodermal tumour (case 1) and a myxosarcoma (case 13) were located within the nervous tissue. Histopathological evaluation of the surgical margins showed complete resection in nine dogs and incomplete resection in seven dogs. In four dogs (cases 2, 3, 12 and 14), proximal margins were infiltrated, in three dogs (cases 6, 10 and 15) distal margins were infiltrated. Four of nine dogs with spinal canal involvement had non-infiltrated margins on the proximal and distal sides.

Post-operative limb function

Post-operative limb function was considered stable in 2/16 dogs and improved in 14/16 dogs (Table 2). Good limb usage and function was achieved eventually in 10/16 dogs; three dogs had

Table 2
Individual dog characteristics.

Dog no.	Sex	Age (years)	Weight (kg)	Breed	Location	Imaging	Thoracic staging	Tumor-related death (yes/No)	Non-infiltrated margins	Pre-operative grade lameness[a]	Post op change in limb use	Post-operative limb use	Survival (days)
1	F	10	38	Rhodesian ridgeback	L7	MRI	CT	No	Yes	4	Improved	Reasonable (brace)	487
2	MC	13	26.7	American Staffordshire terrier	C1–C2	MRI		Yes	No	Neck pain[b]	Improved	Good	378
3	MC	9	51.1	New foundland	C7–T1	CT	CT	Yes	No	4	Stable	Poor	117
4	M	6	29.1	Flat-coated retriever	Sciatic N.	CT, US	CT	NA	Yes	3	Improved	Reasonable (brace)	1877
5	MC	8	8.5	Jack Russell terrier	Sciatic N.	MRI		NA	Yes	4	Improved	Good	1209
6	FS	9	5.8	Coton du Tulear	C7–C8	CT, MRI	RX, CT	No	No	4	Stable	Poor	1039
7	M	7	23	Mixed breed	Tibial N.	US		NA	Yes	3	Improved	Good	2227
8	M	12	30	Nova Scotia duck tolling retriever	L7	MRI, CT	CT	No	Yes	3	Improved	Good	1303
9	MC	8	39.9	Golden retriever	S1	MRI	RX	No	Yes	3	Improved	Good	2911
10	MC	7	45	Labrador retriever	C6	MRI	CT	Yes	No	3	Improved	Good	365
11	M	8	50	Russian terrier	Radial N.	MRI	CT	Yes	Yes	3	Improved	Good	14
12	M	3	37.9	Golden retriever	S1	CT	CT	Yes	No	3	Improved	Good	113
13	F	2	12	English Cocker spaniel	Tibial N.	US	RX	No	Yes	3	Improved	Good	4639
14	FS	7	33.5	Bouvier des Flanders	C6	CT	CT	Yes	No	3	Improved	Poor	62
15	FS	9	24.5	Labrador tretriever	Median N.	MRI, US	RX	Yes	No	3	Improved	Reasonable	306

MRI, magnetic resonance; CT, computedomography; US, ultrasound; RX, radiography.
[a] Table 1.
[b] This dog had severe neck pain only.

Table 3
Individual tumour and staging characteristics.[a]

Dog no.	Non-infiltrated margins	Histological diagnosis	Length × median diameter (cm)	IHC	Staining	MI	Grade	Tumour status	Nodal status	Distant metastases status	Stage
1	Yes	PNT neuroectodermal	6 × 1.5	S100	+/−		3	T2b	N0	M0	3
2	No	PNST myxoid metaplasia	0.5 × 0.5	S100	+++	<9	1	T1b	N0	M0	1
3	No	PNST				<9	2		N0	M0	
4	Yes	PNST	14 × 1	S100, vimentin, CD18	S100 −, Vimentin + +, CD18 −	≫9	2	T2b	N0	M0	1
5	Yes	PNST myxoid metaplasia	10 × 1.5			>9	2	T2b	N0	M0	1
6	No	PNST	7 × 0.5			<9	1	T2b	N0	M0	1
7	Yes	PNST	3.5 × 1	S100	+	>9	3	T1b	N0	M0	3
8	Yes	PNST	1 × 0.5			<9	1	T1b	N0	M0	1
9	Yes	PNST	1 × 0.5			<9	1	T1b	N0	M0	1
10	No	PNST	6 × 2.5				1	T2b	N0	M0	1
11	Yes	PNST					1		N0	M0	
12	No	PNST	2 × 0.4				1	T1b	N0	M0	1
13	Yes	PNT Myxoma	5 × 0.5	alcian blue/ LFB	++/++	<9	1	T1b	N0	M0	1
14	No	PNST	1.5 × 0.7			>9	3	T1b	N0	M0	3
15	No	PNST chondroid metaplasia	7 × 1.5			>9	2	T2b	N0	M0	1
16	Yes	PNST	6 × 1.5			>9	3		N0	M0	

[a] Immunohistochemical (IHC) stains used in the individual tumours included: S100 protein staining, used to identify cells derived from the neural crest; Vimentin as a marker for mesenchymal origin of cells, CD 18 as a marker for leucocytes and hemopoietic neoplasm and in particular histiocytic neoplasms; Luxol fast blue (LFB) as a stain form myelin and Alcian blue as a stain for acidic polysaccharides in order to identify mucinous tumours such as myxomas. The World Health Organization TNM schedule for tumours of the central nervous system was adapted to the cases, as described by Louis et al. (2007).

Table 4
Distribution of the peripheral nerve tumours and recurrence rate per section.

Location	*n*	Spinal canal	Recurrence
Cervical nerve roots (C1–C5)	1	1/1	1
Brachial plexus (C6–T2)	5	2/5	2
Radial nerve	1	1/1	
Median nerve	1		1
Lumbosacral plexus (T5–S2)	4	4/4	1
Sciatic nerve	2	1/2	
Tibial nerve	2		

reasonable limb use (lameness grade 2); and three dogs had poor limb use (lameness grade 3 and 4). All dogs with lameness grades 3 and 4 had infiltrated margins in the brachial plexus segment (Table 2).

Survival and prognostic factors

The median overall survival time (MST) was estimated at 1303 days (42.8 months; range, 14 days–4639 days, [0.5–152.4 months]; Fig. 1). The 1-, 2-, and 3-year calculated survival rate were 68.8%, 62.5%, and 62.5% respectively. Six dogs died of tumour-related causes. Five of these dogs were euthanased due to recurrence of clinical signs and confirmed or presumptive tumour recurrence. One dog died 14 days post operatively and was classified as a tumour-related death. Seven dogs died due to non-tumour related causes.

Only surgical margins were significantly prognostic for survival. Dogs with clean surgical margins had significantly ($P = 0.014$) longer estimated MST (2227 days; 73.2 months) than those with dirty margins (MST 487 days, [16.0 months]; Table 5 and Fig. 2). Infiltrated margins were found in three of six cases with mitotic indices (MI) <9 and in two of six cases with MI >9. Margin status was not associated with MI.

Recurrence

Five dogs that showed initial improvement developed recurrence of clinical signs. All of these dogs had surgical margins that showed incomplete resection (cases 2, 10, 12, 14, 15). The diagnosis of recurrence was based on clinical signs ($n = 5$), advanced imaging with MRI or CT ($n = 2$), ultrasound ($n = 1$) and/or post-mortem examination ($n = 2$). MST and DFI of the five dogs that were diagnosed with recurrence were 275 days (9.0 months; range, 51–377 days [1.7–12.4 months]) and 304 days (10.0 months; range, 62–378 days [2.0–12.4 months]), respectively; all were euthanased within 1 month of onset of recurrence.

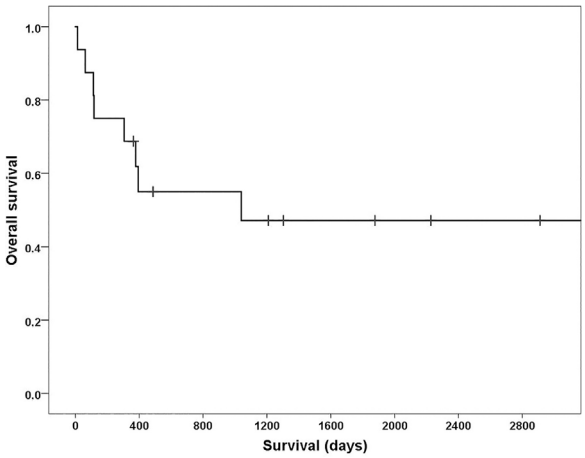

Fig. 1. Overall survival for 16 dogs with local compartmental resection of a peripheral nerve tumour (PNT) without limb amputation.

Table 5
Survival in days of dogs with peripheral nerve tumours.

Margins	*n*	Mean survival	Median survival	Survival range
Overall	16	1703	1303	14–4639
Infiltrated	7	809	487*	62–1039
Non-infiltrated	9	2457	2227*	14–4639

* $P = 0.014$.

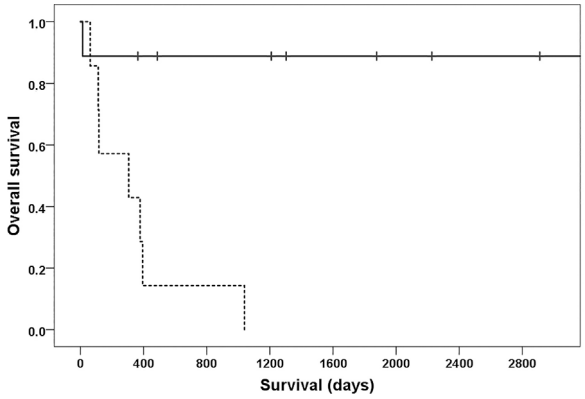

Fig. 2. Overall survival for dogs with a peripheral nerve tumour (PNT) with non-infiltrated resection margins ($n = 9$; solid line) and infiltrated margins ($n = 7$; dashed line). The survival rate of the two groups differed significantly (log-rank test; $P = 0.014$).

Discussion

This study describes 16 dogs with PNT that were treated with compartmental tumour resection and limb sparing. Local tumour resection and limb salvage with long term follow up for canine PNT has only been reported as a single case report (Simpson et al., 2006). Our study population is comparable to previous reports of PNTs. Six dogs in this study were retrievers and previous studies have reported 4/10 (Jones et al., 1995), 2/6 (Wheeler et al., 1986) and 10/51 (Brehm et al., 1995) dogs with PNT were retrievers. Although this may reflect the general popularity of this breed, a true propensity of retrievers for this disease is supported by recent findings stating that Golden retrievers are more prone to develop soft tissue sarcomas (Boerkamp et al., 2014).

Besides non-specific progressive lameness, other clinical signs associated with PNTs include paresis, (isolated) muscle atrophy and pain in the affected limb. Diagnosis of PNTs relies heavily on additional tests, including electromyography or advanced imaging (Wheeler et al., 1986; Rapoport et al., 1988; Sharp, 1989; Targett et al., 1993; Brehm et al., 1995; Jones et al., 1995; Platt et al., 1999; Rudich et al., 2004; Rose et al., 2005; Kraft et al., 2007; le Chevoir et al., 2012).

In five of nine dogs with PNTs involving the spinal canal, surgical margins with complete resection were achieved and these dogs had an excellent long-term survival. In the other four cases with incomplete resection, this resulted in tumour recurrence and euthanasia. It has been reported that spinal canal involvement is a poor prognostic indicator (Sharp, 1989; Brehm et al., 1995). However, spinal canal involvement may not equate to spinal cord invasion. Also, advanced diagnostic imaging cannot always differentiate between spinal canal involvement and spinal cord invasion, as in our cases, where spinal cord involvement was an intraoperative diagnosis. Based on our study, PNT with spinal canal

involvement may still warrant surgical exploration to determine if marginal or even wide excision may be possible.

Dogs in this study that had non-infiltrated surgical margins had a statistically significant survival advantage. The five dogs in this study that were euthanased due to their disease all had margins with incomplete resection and eventually evidence of tumour recurrence. This suggests that dogs with a completely clean resection that survive the surgical intervention and live for 1 year will likely experience a long-term survival. The predictive value of clean margins for the prediction of long term outcome in canine neoplasia have been emphasised by several studies (Bostock and Dye, 1980; Kuntz et al., 1997; Scarpa et al., 2012; Kry and Boston, 2014). In our study, non-infiltrated margins were associated with local control and long term favourable outcome. Mitotic index was not associated with margin status, and thus not with survival. MI has been associated with margin status and metastatic rates in canine soft tissue sarcomas (Bostock and Dye, 1980; Kuntz et al., 1997); however, metastatic rates are considered low in PNT (Sharp, 1989). Therefore, the relevance of MI in PNTs is unknown.

Five of six dogs that died of tumour-related causes had surgical margins with incomplete resection and developed recurrence. Margin status in canine PNT is an important prognostic indicator for disease free interval and survival, as it is in human PNT (Wong et al., 1998; Anghileri et al., 2006; Zou et al., 2009). Adjuvant radiation therapy may be beneficial in dogs, but this is not well described in the veterinary literature for this specific pathology (McKnight et al., 2000; Kung et al., 2014). In humans, disease free- and overall survival can be improved when using neoadjuvant or adjuvant radiation therapy (Wong et al., 1998; Anghileri et al., 2006).

Two dogs with PNTs were diagnosed with an atypical tumour type residing within the perineurium, invading the nerves. The atypical tumours, a myxomatous and neuroectodermal (small cell) variant, have been described in dogs and humans within the range of PNT neoplasms (Chijiwa et al., 2004; Rodrigues et al., 2012), but they have not been described in the 2007 WHO classification of tumours of the central nervous system (Louis et al., 2007). 'Divergent differentiation' has been suggested as an explanation for epithelial tissue within a PNT and remarkable metaplasia is seen within up to 10% of human PNTs (Patnaik et al., 2002; Rodriguez et al., 2012). Myxoid, osseous, epithelioid, melanotic and chondroid metaplasia have been reported and can be extensive (Pumarola et al., 1996; Patnaik et al., 2002). The presence of divergent differentiation is explained by the origin of the neuronal crest stem cells, from which Schwann cells also arise, and is associated with a poor outcome (Patnaik et al., 2002). The neuroectodermal tumour found in our study had a remarkable resemblance with human small cell malignant peripheral nerve sheath tumours (Rodriguez et al., 2012). For the 14/16 cases thatwere originally diagnosed as true peripheral nerve sheath tumours based upon HE staining, the majority were graded as low/grade 1 according to soft tissue sarcoma grading schemes (Koestner and Higgins, 2002; Liptak and Forrest, 2013; Cantile and Youssef, 2016). Immunohistochemistry may give more insight in the origin of the neoplasm, and according to basic oncological principles, may predict biological behaviour and outcome. However, immunohistochemical staining cannot consistently differentiate between fibrosarcomas and PNSTs (Meyer and Klopfleisch, 2014). S100 staining, which was chosen as preferred staining for Schwann cells in general (Hendrick et al., 1998; Suzuki et al., 2014), cannot accurately identify tumours of PNST origin (Rodriguez et al., 2012). The divergent theory is supported by the demonstration of different forms of metaplasia when immunohistochemistry is used to differentiate canine PNTs that originate within the peripheral nerves from other soft tissue sarcomas (Patnaik et al., 2002). A novel histological classification scheme for canine nerve tumours may contribute to the prognostic value of histopathology in these tumours.

Two dogs showed no improvement after radial nerve tumour resection and in both there were multiple roots from which the affected nerve originated. Involvement and/or removal of the radial nerve can lead to impaired limb function (Wheeler et al., 1986; Sharp, 1989; Brehm et al., 1995; Caplan, 2012; Liptak and Forrest, 2013). However, impairment may be moderate, which was the case in one dog for which a brace to support limb function was made. Tumour removal appeared to decrease pain in our dogs and this is likely the reason for improvement in 14 of 16 dogs post-operatively.

The biggest challenge for complete resection depends largely on the proximity of the tumour to the spinal cord or cauda equina (Knecht and Greene, 1977; Bradley et al., 1982; Sharp, 1988; Bailey, 1990; Simpson et al., 2006; Harcourt-Brown et al., 2009; Caplan, 2012; Liptak and Forrest, 2013). Removal of the limb does not necessarily improve proximal resection with spinal canal involvement. It could also be argued that the additional morbidity of limb amputation might not be warranted as these dogs, since they are likely to have a worse prognosis for local control. In contrast, for distal resection of the PNT, the distal margin can more often be reliably achieved by limb amputation. However, in general this margin was not challenging because it required following the affected nerve(s) distally and then cutting the nerve 2–3 cm from the gross tumour. The compartmental resection was achieved because the tumour was encapsulated within the perineurium and that was an adequate barrier to invasion by the tumour into the surrounding limb muscle (Kawaguchi et al., 2004). If the tumour does not remain within the perineurium, it behaves more as a soft tissue sarcoma and compartmental resection is not usually recommended for this type of tumour, as the pseudocapsule of most soft tissue sarcomas is not to be considered a safe margin (Liptak and Forrest, 2013).

The overall MST in this study was 1303 days (42.8 months); in nine of 16 cases, clean surgical margins were achieved with no subsequent recurrence of signs or tumour. Our survival rates were comparable or longer than previous reports of canine PNT where local resection was combined with limb amputation (Brehm et al., 1995; Sharp, 1989; Sharp and Wheeler, 2005; Caplan, 2012; Liptak and Forrest, 2013). Thus, compartmental resection of PNTs does not appear to have a negative impact on survival or the ability to achieve surgical margins with complete resection.

The limitations of this study are its retrospective nature, which inevitably means that not all information was available for all cases, and that an unintended case selection may have taken place, which may have influenced outcome. Also, case numbers were low, which affected statistical analysis. Follow up information on limb use was obtained from both written medical histories and telephone questionnaires and we chose a simplified 4-point lameness score and a 3-point progression score. Time between surgery and telephone follow up ranged from months to many years; not all dogs returned at the 6-week postoperative appointment and only few came back afterwards.

Conclusions

Compartmental resection of canine PNT with limb sparing yielded a good prognosis for local control and limb function. Surgical margin histopathology can be used as a guide to prognosis for local control and long-term outcome.

Conflict of interest statement

None of the authors has any other financial or personal relationships that could inappropriately influence or bias the content of the paper.

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