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CASE REPORT

Peripheral nerve sheath tumor invading the nasal cavities of a 6-year-old female Pointer dog

Alessandra Sfacteria*, Laura Perillo, Francesco Macrì, Giovanni Lanteri, Claudia Rifici and Giuseppe Mazzullo

Department of Veterinary Sciences, University of Messina, Messina, Italy

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A mass in the nasal planum of a 6-year-old female Pointer dog underwent fine needle aspiration. Cytology smears resulted in a generic diagnosis of a spindle cell tumor. The owner refused any additional diagnostic procedures or therapeutic treatment and, over a few months, the tumor extended into the nasal cavities causing severe dyspnea. Euthanasia and subsequent necropsy were performed with tissue samples collected and fixed in 10% buffered formalin and routinely processed. Due to the size and the polymorphous pattern of the mass, a tissue microarray was self-made by means of a biopsy punch of about 2 mm diameter with minor modification from a recently published method (Choi et al. 2012) and 5-μm sections were stained for histochemical (Hematoxylin&Eosin, Toluidine Blue, PAS) and immunohistochemical visual examination. For immunohistochemistry, the labeled avidin–biotin (LAB) method was used. Specifically, slides were steamed in 0.01 mol/L sodium citrate buffer, pH 6, in a microwave oven. Endogenous peroxidase activity was quenched by 0.3% hydrogen peroxide in methanol, while non-specific binding of immunoglobulins (IgGs) and tissue proteins were blocked by incubation with 2.5% bovine serum albumin (BSA). Slides were then incubated overnight at 4 °C with anti-Vimentin (mouse monoclonal, clone VIM3B4, Santa Cruz Biotechnology, Dallas, TX, USA), anti-glial fibrillary acidic protein (GFAP rabbit polyclonal, clone R40, Gene Tex, Irvine, CA, USA), anti-S-100 (mouse monoclonal, clone SB6, Santa Cruz Biotechnology, Dallas, TX, USA), and anti-PECAM (goat polyclonal, clone M20, Santa Cruz Biotechnology, Dallas, TX, USA) primary antibodies (Abs) followed by incubation at room temperature with biotinylated IgGs (Biospa, Milan, Italy; Vector Laboratories, Burlingame, CA, USA) and by an avidin peroxidase complex (Biospa, Milan, Italy). The reaction was developed with the DAB peroxidase (HRP) substrate kit, 3,3′-diaminobenzidine (Vector Laboratories, Burlingame, CA, USA) and counterstained with hematoxylin. Negative controls were also performed by omission of primary Abs, substitution of primary Abs with normal IgGs and substitution of primary Abs with non-reactive antibodies of the same species and immunoglobulin class. The immunohistochemical stain was interpreted by assessing the intensity of labeling. Cytoplasmic and/or membrane immunoreactivity was considered positive.

At necropsy, the external examination of the dog showed tumor growth so extensive as to deform the normal nasal profile, the left nasal cavity and part of the oral cavity. A necrotic ulcerative area on the top of the left nostril was also detectable. In the oral cavity, a pedunculated proliferation involving the oral mucosa, and originating close to the left maxillary premolar, was observed. An extra nodular lesion originated from the gums and protruded into the mouth. Moreover, a remarkable and extensive deformation of the entire palatine area, swelling of soft tissues and protuberance of the left lip were present. After skin and soft tissue removal, the nasal structures appeared to be completely and bilaterally invaded by the tumor. The neoplastic tissue was lardaceous, pinkish-white with shades of gray and hard-elastic in consistency. At the cutting section, confluent nodular structures, with irregular yet sharp boundaries were detectable. The nasal cavities were severely compromised, showing a reduction in size, particularly on the left side. In the intraoral region, the tumor infiltrated gingival tissues and bone structures in an irregular manner. Histologically, the neoplastic tissue appeared mainly composed of thin and stretched spindle cells, characterized by a poorly defined and weakly eosinophilic cytoplasm, intermingled with shorter and scant spindle cells. Cells were embedded in an abundant fibromixoid matrix. In some areas, the proliferation was arranged in interlacing bundles, streams, and whorls around nerve trunks of different size in an ‘onion skin-like’ appearance. Cuffings of inflammatory cells, mainly macrophages and mast cells, were scattered throughout the lesion (Figure 1). In other fields, parallel nuclear palisades and streams of spindle wavy cells characterized the cell proliferation. The main pattern was of a tumor without impressive signs of malignancy, despite the aggressive and infiltrative behavior. Only after a deeper examination of the whole mass, focal areas of necrosis and cells bearing large atypical nuclei were detectable. Immunohistochemistry demonstrated the neoplastic cells positive for GFAP (Figure 2), Vimentin (Figure 3), and S-100

*Corresponding author. Email: asfacteria@unime.it

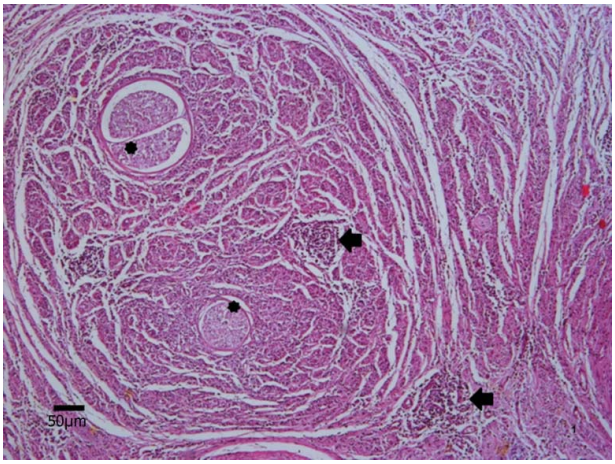

Figure 1. Mass in the nasal cavities from a 6-year-old female Pointer dog. Histopathological examination showed a cell proliferation arranged in interlacing bundles, streams and whorls around nerve trunks of different size in an 'onion skin-like' appearance (asterisk). Cuffings of inflammatory cells, mainly constituted by macrophages and mast cells, were scattered throughout the lesion (arrow) (PAS, magnification 10×).

(Figure 4). PECAM-1 (except for endothelial cells; not shown) was negative, therefore excluding the diagnosis of perivascular tumors. Histopathological and immunohistochemical results were strongly suggestive of a diagnosis of a peripheral nerve sheath tumor (PNST).

Occurrence of tumors in the nasal structures (nasal planum, nasal cavities, and paranasal sinuses) is usually sporadic in animal species, although in canine breeds it is of growing importance, being a common cause of chronic nasal disease (Tasker et al. 1999; Meler et al. 2008; Lobetti 2009; Sapierzynski & Zmudzka 2009; Pietra et al. 2010). The dolichocephalic breeds or dogs living in urban environments are predisposed to the development of nasal tumors. Most of them arise from nasal epithelium and are malignant, with the highest incidence rate for

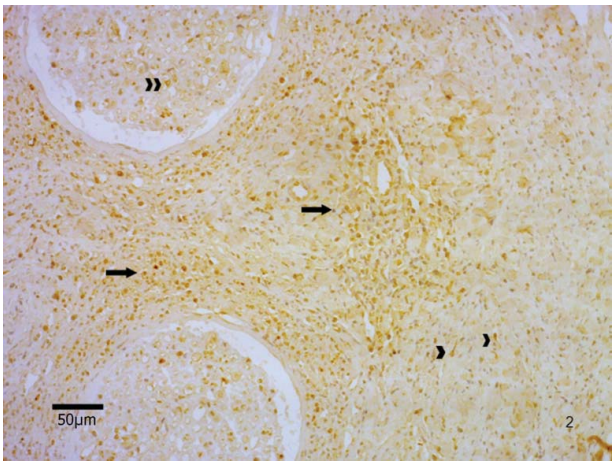

Figure 2. Mass in the nasal cavities from a 6-year-old female Pointer dog. Immunohistochemical examination showed a cytoplasmic positivity for GFAP inside nerve trunks (double arrow head) and in cells grouped around vessels and nerve trunks (arrow). Some positive spindle cells are clearly visible scattered in the tissue (arrow head) (IHC for GFAP, DAB stain, magnification 20×).

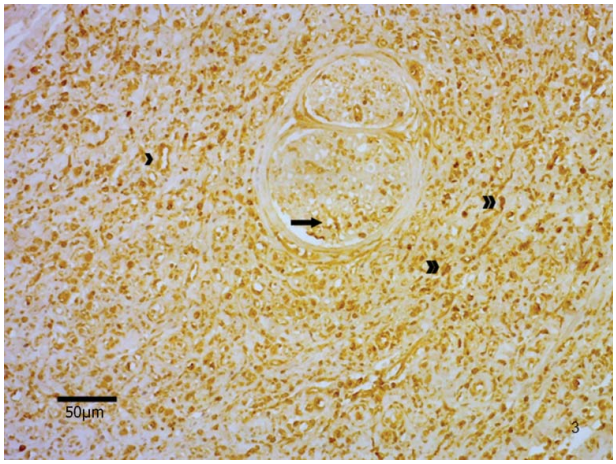

Figure 3. Mass in the nasal cavities from a 6-year-old female Pointer dog. Immunohistochemical examination showed diffuse cytoplasmic positivity for Vimentin inside nerve trunks (arrow), vessels (arrow head) and neoplastic cells (double arrow head) (IHC for Vimentin, DAB stain, magnification 20×).

adenocarcinoma, followed by transitional cell carcinoma and squamous cell carcinoma. Among the mesenchymal tumors, chondrosarcoma is the most reported (Ogilvie & LaRue 1992; Wilson & Dungworth 2002). Rarely reported tumors are melanoma (Hicks & Fidel 2006), olfactory neuroblastoma (Brosinski et al. 2012), neuroendocrine carcinoma (Sako et al. 2005; Ninomiya et al. 2008; Koehler et al. 2012), and lymphosarcoma (Robertson 1998). Nasal tumors are locally aggressive with a tendency to infiltrate the underlying tissues, to extend into the forebrain or to destroy the septum causing a bilateral involvement. The clinical course is usually slow and insidious, with long-term symptoms (2−7 months), except for adenocarcinomas that have a very rapid onset. In humans nasal PNSTs are well described yet rare pathologies, in veterinary medicine no cases have been described so far, even if their occurrence is hypothesized (Wilson &

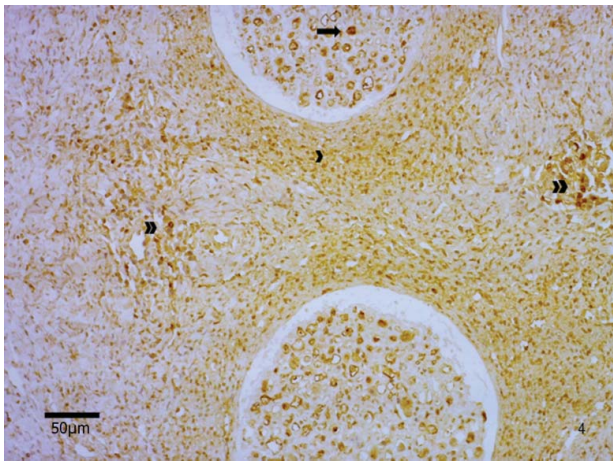

Figure 4. Mass in the nasal cavities from a 6-year-old female Pointer dog. Immunohistochemical examination showed intense cytoplasmic positivity for S-100 inside nerve trunks (arrow). Cuffings of cells around nerves (arrow head) and cells scattered in the mass (double arrow head) were from moderately to intensely stained (IHC for S-100, DAB stain, magnification 20×).

Dungworth 2002). The aim of this paper was to expand the knowledge about nasal tumors by describing the pathological findings observed in a dog affected by a PNST with prominent features of neurofibroma.

In humans, PNSTs include, among others, schwannomas and neurofibromas that are further subclassified according to their growth patterns (schwannoma: localized or plexiform; neurofibroma: localized, plexiform, or diffuse) and histopathologic features (e.g., classic, collagenous, cellular, and pigmented). A localized schwannoma or neurofibroma is a single, well-demarcated, expansile tumor, whereas a plexiform variant is composed of multiple nodular masses. Schwannomas include the concurrent presence of highly and poorly cellular areas of fusiform neoplastic Schwann cells in a stroma that is either collagenous or scant, or myxoid and abundant (designated Antoni A areas and Antoni B areas, respectively). Other features are nuclear palisading, the formation of Verocay bodies, and hyalinized microvessels. Nerve fibers are absent within the tumor, but are often present at the tumor margin. Neurofibroma displays a mixture of cell types, including Schwann cells, axonal processes, perineurial cells, endoneurial fibroblasts, and mast cells that are embedded in abundant collagenous extracellular myxoid matrix and wavy collagen fibers. Within the mass, nerve fibers can be identified. The spindle-shaped cells may exhibit nuclear palisading (Gottfried et al. 2006). Diffuse neurofibroma has infiltrative growth, but other features of malignancy are absent (Fletcher 2000). Because of its infiltrative nature, diffuse neurofibroma may recur, but metastases have not been reported. However, diffuse neurofibroma must be distinguished from malignant PNST. In animals, PNSTs are most often reported in dogs and cattle (Bundza et al. 1986; Johnson et al. 1988; Summers et al. 1995; Zachary 2007), infrequently in cats and horses (Goldschmidt & Hendrick 2002; Quinn et al. 2005; Sturgeon et al. 2008), and rarely in other species, such as goats (Veazey et al. 1993; Ramirez et al. 2007), pigs (Tanimoto & Ohtsuki 1993), birds (Bossart 1983; Ono et al. 2004), and fish (Marino et al. 2008, Marino et al. 2010). In veterinary medicine, many authors have so far considered schwannoma and neurofibroma as a unique entity, suggesting they be named together with the general term of peripheral nerve sheath tumor (PNST), both benign and malignant (MPNST), because of the presence of a mixed cell population and/or lack of cellular differentiation on histopathology. However, Schoniger and Summers (2009) debated on whether this classification is mainly due to a lack of diagnostic criteria for their subclassification, and demonstrated the existence of neurofibroma and several subtypes in dogs, horses, and chicken, like those tumors that occur in humans. Furthermore, these studies showed that similarities between neurofibroma in animals and humans are not restricted to microscopic features, but that they also exist in regard to tumor location and patient's age (Schoniger & Summers 2009). After publication of the report by Schoniger and Summers (2009), a real neurofibroma in the neck of a dog was described (Fattahian et al. 2012). In humans, PNST are usually benign neoplasm. Malignancy is based on histologic findings of anaplasia, abundant mitoses, necrosis, and/or biologic behavior of invasion of adjacent tissues or rare metastasis (Skovronsky & Oberholtzer 2004). The biological behavior of canine PNSTs is more aggressive than that of the human counterpart, so canine PNSTs are generally considered as MPNSTs (Summers et al. 1995; Dennis et al. 2011). Immunohistochemical staining is often helpful in the diagnosis of PNST as it allows identification of the neoplastic cell type through intermediate filament identification (Moore et al. 1989). No one specific immunohistochemical marker is able to define a PNST and a panel of markers has to be employed. PNSTs, as mesenchymal tumors, are positive for Vimentin; S-100 immunoreactivity is restricted to a subpopulation of the tumor cells, because this marker only labels the neoplastic Schwann cells but not the remaining tumor cells; there may be a variable expression of GFAP, NGFR (nerve growth factor receptor), and NSE (neuron-specific enolase) (Chijiwa et al. 2004). Calretinin has proved to be a cross-reactive and useful marker in the differential diagnosis of PNSTs, being positive in schwannomas but not in neurofibromas (Fine et al. 2004). Concerning the localization, PNSTs are rare in the dog and have been mainly reported in subcutaneous tissues and brachial plexuses (Koestner & Higgins 2002). Other localizations in the dog include spleen (Bergmann et al. 2009), vagina (Sontas et al. 2010), spinal cord (Tavasoly & Malmasy 2009), diaphragm (Anderson et al. 1999), and eye (Sato et al. 2005). To the best of our knowledge, primary PNSTs have not been described previously in the canine nasal cavities. Although rare, PNSTs arising in the nasal cavity are a well-known entity in man. Neurofibroma, in particular, may occur singly or as a part of the syndrome of neurofibromatosis (both type I and type II neurofibromatosis) (Chua et al. 2006). This case report showed the histological features of a PNST, with prominent features of the diffuse neurofibroma. The tumor was well differentiated, histologically similar to the PNSTs described in other localizations and had highly infiltrative and destructive behavior despite lacking of common features of malignancy, except for scant areas of necrosis and hemorrhage. The case seemed worth describing for the unusual site of development, not reported so far, and to bring valuable information to the state of knowledge in the field of PNSTs and respiratory tract diseases in dogs.

Disclosure statement

No potential conflict of interest was reported by the authors.

References

Anderson GM, Dallaire A, Miller LM, Miller CW. 1999. Peripheral nerve sheath tumor of the diaphragm with osseous differentiation in a one-year-old dog. J Am Anim Hosp Assoc. 35:319–322.

Bergmann W, Burgener IA, Roccabianca P, Rytz U, Welle M. 2009. Primary splenic peripheral nerve sheath tumour in a dog. J Comp Pathol. 141:195–198.

Bossart GD. 1983. Neurofibromas in a macaw (*Ara chloroptera*): morphologic and immunocytochemical diagnosis. Vet Pathol. 20:773–776.

Brosinski K, Janik D, Polkinghorne A, Von Bomhard W, Schmahl W. 2012. Olfactory neuroblastoma in dogs and cats – a histological and immunohistochemical analysis. J Comp Pathol. 146:152–159.

Bundza A, Dukes TW, Stead RH. 1986. Peripheral nerve sheath neoplasms in Canadian slaughter cattle. Can Vet J. 27:268–271.

Chijiwa K, Uchida K, Tateyama S. 2004. Immunohistochemical evaluation of canine peripheral nerve sheath tumors and other soft tissue sarcomas. Vet Pathol. 41:307–318.

Choi CH, Kim KH, Song JY, Choi SJ, Kim L, Park IS, Han JY, Kim JM, Chu YC. 2012. Construction of high-density tissue microarrays at low cost by using self-made manual microarray kits and recipient paraffin blocks. Korean J Pathol. 46:562–568.

Chua CN, Alhady M, Ngo CT, Swethadri GK, Singh A, Tan S. 2006. Solitary nasal neurofibroma presenting as compressive optic neuropathy. Eye (Lond). 20:1406–1408.

Dennis MM, McSporran KD, Bacon NJ, Schulman FY, Foster RA, Powers BE. 2011. Prognostic factors for cutaneous and subcutaneous soft tissue sarcomas in dogs. Vet Pathol. 48:73–84.

Fattahian H, Mortazavi P, Moosavian H, Mohyeddin H, Moridpour R. 2012. Immunohistochemical study of a canine neurofibroma. S Afr Vet Assoc. 83:4.

Fine SW, McClain SA, Li M. 2004. Immunohistochemical staining for calretinin is useful for differentiating schwannomas from neurofibromas. Am J Clin Pathol. 122:552–559.

Fletcher CD. 2000. Peripheral neuroectodermal tumors. 2nd ed. In: Christopher DMF, editor. London: Churchill Livingstone; GBA0–W8671.

Goldschmidt MH, Hendrick MJ. 2002. Tumors of the skin and soft tissues. In: Meuten DJ, editor. Tumors in domestic animals. Ames (IA): Iowa State Press.

Gottfried ON, Viskochil DH, Fults DW, Couldwell WT. 2006. Molecular, genetic, and cellular pathogenesis of neurofibromas and surgical implications. Neurosurgery. 58:1–16; discussion 11–16.

Hicks DG, Fidel JL. 2006. Intranasal malignant melanoma in a dog. J Am Anim Hosp Assoc. 42:472–476.

Johnson RC, Anderson WI, Luther PB, Ryan AM. 1988. Multicentric schwannoma in a mature Holstein cow. Vet Rec. 123:649–650.

Koehler JW, Weiss RC, Aubry OA, Smith AN, Hathcock JT, Brawner WR Jr. 2012. Nasal tumor with widespread cutaneous metastases in a Golden Retriever. Vet Pathol. 49:870–875.

Koestner A, Higgins RJ. 2002. Tumors of the nervous system. In: Meuten DJ, editor. Tumors in domestic animals. Ames (IA): Iowa State Press-Blackwell Publishing; p. 697–738.

Lobetti RG. 2009. A retrospective study of chronic nasal disease in 75 dogs. J S Afr Vet Assoc. 80:224–228.

Marino F, Germana A, Panebianco A. 2008. A case of schwannoma in farmed seabream *Sparus aurata*. Dis Aquat Organ. 82:249–252.

Marino F, Macri D, Lanteri G, Manganaro M, Monaco S, Germana A. 2010. Neurofibroma in a striped mullet: histochemical and immunohistochemical study. J Aquat Anim Health. 22:92–94.

Meler E, Dunn M, Lecuyer M. 2008. A retrospective study of canine persistent nasal disease: 80 cases (1998–2003). Can Vet J. 49:71–76.

Moore AS, Madewell BR, Lund JK. 1989. Immunohistochemical evaluation of intermediate filament expression in canine and feline neoplasms. Am J Vet Res. 50:88–92.

Ninomiya F, Suzuki S, Tanaka H, Hayashi S, Ozaki K, Narama I. 2008. Nasal and paranasal adenocarcinomas with neuroendocrine differentiation in dogs. Vet Pathol. 45:181–187.

Ogilvie GK, LaRue SM. 1992. Canine and feline nasal and paranasal sinus tumors. Vet Clin North Am Small Anim Pract. 22:1133–1144.

Ono M, Tsukamoto K, Tanimura N, Haritani M, Kimura KM, Suzuki G, Okuda Y, Sato S. 2004. An epizootic of subcutaneous tumors associated with subgroup A avian leukosis/sarcoma virus in young layer chickens. Avian Dis. 48:940–946.

Pietra M, Spinella G, Pasquali F, Romagnoli N, Bettini G, Spadari A. 2010. Clinical findings, rhinoscopy and histological evaluation of 54 dogs with chronic nasal disease. J Vet Sci. 11:249–255.

Quinn GC, Fews D, Scase TJ, Pearson GR. 2005. Malignant peripheral nerve sheath tumour of the heart in a horse. Vet Rec. 157:847–849.

Ramirez GA, Herraez P, Rodriguez E, Godhino A, Andrada M, de los Monteros AE. 2007. Malignant peripheral nerve sheath tumour (malignant schwannoma) in the diaphragm of a goat. J Comp Pathol. 137:137–141.

Robertson HM. 1998. What is your diagnosis? Nasal lymphoblastic lymphosarcoma causing epistaxis in a dog. J Am Vet Med Assoc. 212:1871–1872.

Sako T, Shimoyama Y, Akihara Y, Ohmachi T, Yamashita K, Kadosawa T, Nakade T, Uchida E, Okamoto M, Hirayama K, et al. 2005. Neuroendocrine carcinoma in the nasal cavity of ten dogs. J Comp Pathol. 133:155–163.

Sapierzynski R, Zmudzka M. 2009. Endoscopy and histopathology in the examination of the nasal cavity in dogs. Pol J Vet Sci. 12:195–201.

Sato T, Yamamoto A, Shibuya H, Sudo H, Shirai W, Amemori T. 2005. Intraocular peripheral nerve sheath tumor in a dog. Vet Ophthalmol. 8:283–286.

Schoniger S, Summers BA. 2009. Localized, plexiform, diffuse, and other variants of neurofibroma in 12 dogs, 2 horses, and a chicken. Vet Pathol. 46:904–915.

Skovronsky DM, Oberholtzer JC. 2004. Pathologic classification of peripheral nerve tumors. Neurosurg Clin N Am. 15:157–166.

Sontas BH, Altun ED, Guvenc K, Arun SS, Ekici H. 2010. Vaginal neurofibroma in a hysterectomized poodle dog. Reprod Domest Anim. 45(6):1130–1133.

Sturgeon BPR, Milne EM, Smith KC. 2008. Benign peripheral nerve sheath tumor of the perianal region in a young pony. J Vet Diagn Invest. 20:93–96.

Summers BA, Cummings JF, deLahunta A. 1995. Veterinary neuropathology. St. Louis (MO): Mosby-Yearbook Inc.

Tanimoto T, Ohtsuki Y. 1993. Cutaneous plexiform schwannoma in a pig. J Comp Pathol. 109:231–240.

Tasker S, Knottenbelt CM, Munro EA, Stonehewer J, Simpson JW, Mackin AJ. 1999. Aetiology and diagnosis of persistent nasal disease in the dog: a retrospective study of 42 cases. J Small Anim Pract. 40:473–478.

Tavasoly A, Malmasy A. 2009. Occurrence of neurofibroma in the spinal cord of a German shepherd dog. J Comp Pathol. 141:310–310.

Veazey RS, Angel KL, Snider TG, Lopez MK, Taylor HW. 1993. Malignant schwannoma in a goat. J Vet Diagn Invest. 5:454–458.

Wilson DW, Dungworth DL. 2002. Tumors of the respiratory tract. In: Meuten DJ, editor. Tumors in domestic animals. 4th ed. Ames (IA): Iowa State Press-Blackwell Publishing; p. 365–399.

Zachary J. 2007. Nervous system. In: McGavin MD, Zachary JF, editors. Pathological basis of veterinary disease. 4th ed. St. Louis (MO): Mosby Elsevier; p. 833–972.