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Paradoxical vestibular disease with trigeminal nerve-sheath tumor in a dog

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ABSTRACT

A thirteen-year old spayed female poodle was referred because of atrophy of temporal and masseter muscles on the left and head tilt and episodical circling to the right side. Additionally, decreased facial sensation, absent menace reaction, palpebral and corneal reflexes on the left side, as well as ipsilateral hemiparesis and tongue palsy were noticed. Generalised vestibular ataxia and hypermetria in the front limbs were present. Based on the clinical signs, the presumptive anatomical localization of the lesion was the cerebellopontine angle including parts of the caudal brainstem with involvement of the trigeminal, facial and hypoglossal nerves. Involvement of either flocculonodular lobe or the caudal cerebellar peduncle on the left side causing paradoxical vestibular disease was suspected. On magnetic resonance imaging a large enhancing lesion in the area of the left cerebellopontine angle involving the trigeminal nerve and compressing cerebellum and brainstem was seen. Because of the poor prognosis the dog was euthanized on the owner's request. This space occupying lesion could be identified as a trigeminal neurofibrosarcoma/schwannoma on post mortem histopathological examination.

Key words: paradoxical vestibular disease – nerve-sheath tumor – magnetic resonance imaging – trigeminal nerve.

Paradoxes Vestibulärsyndrom bei einem Hund mit Trigeminus Neurofibrosarkom/ Schwannom

Ein 13-jähriger kastrierter Pudel wurde mit folgenden Symptomen überwiesen: einer Atrophie der Temporalis- und Massetermuskulatur auf der linken Seite, Kopfschiefhaltung und episodischem Kreisen zur rechten Seite. Zusätzlich wurde eine herabgesetzte Sensibilität im Gesichtsbereich, abwesender Drohreflex sowie Palpebral- und Kornealreflex auf der linken Seite als auch eine ipsilaterale Hemiparese und Zungenlähmung festgestellt. Eine generalisierte vestibuläre Ataxie und Hypermetrie der Vordergliedmasse war vorhanden. Anhand der klinischen Symptome war die voraussichtliche anatomische Lokalisation der Läsion der cerebelopontine Winkel einschliesslich von Teilen des kaudalen Hirnstamms mit Einbezug der Nerven trigeminus, fazialis und hypoglossus.
Es wurde vermutet, dass Beteiligung des Lobus flocculonodularis oder des kaudalen cerebellären Pedunkel der linken Seite eine paradoxe Erkrankung des Vestibulärsystems verursache. Mittels Magnetresonanztomographie wurde eine große Läsion in der Gegend des linken cerebello-pontinen Winkels unter Einbezug des N. trigeminus gesehen, welche Kleinhirn und Hirnstamm komprimiert. Aufgrund der schlechten Prognose wurde der Hund auf Wunsch des Besitzers euthanasiert. Die Raumforderung wurde in der histopathologischen Untersuchung als Trigeminus Neurofibrosarkom/Schwannom diagnostiziert.

Schlüsselwörter: paradoxes Vestibulärsyndrom – Schwannom – Neurofibrom – Magnetresonanztomographie – Nervus trigeminus.

Introduction

Although peripheral nerve tumors represent 26.6% of canine nervous system neoplasia (Hayes et al., 1975), cranial nerve-sheath tumors are relatively uncommon in veterinary medicine. In dogs schwannomas and/or neurofibromas of the trigeminal nerve are more frequently reported in comparison with tumors of other cranial nerves in dogs (St Clair und Safanie, 1957; Pumarola et al., 1996; Bagley et al., 1998; Saunders et al., 1998). The true incidence of trigeminal nerve-sheath tumors in human and veterinary medicine is unknown.

Infiltrating trigeminal neoplasias can involve either a part or the entire nerve and are usually reflected by masticatory weakness and unilateral muscle atrophy (Oliver et al., 1997 (A)). Additionally, ipsilateral clinical signs such as reduced facial and corneal sensation and rubbing of the face have been reported (Bagley et al., 1998). In contrast to neoplasias, idiopathic inflammatory conditions usually lead to bilateral involvement of the trigeminal nerves and therefore dogs may be presented with a dropped jaw and inability to close the mouth (Oliver et al., 1997). Nevertheless, multicentric fibrosarcomas of multiple cranial nerve roots with bilateral neurological deficits have been reported in dogs (Zachary et al., 1986). Interestingly, a bilateral trigeminal neurofibrosarcoma was diagnosed also in a human patient presented with bilateral clinical signs (Liwnicz 1979). Extension of the tumor along the nerve or predominantly intracranial growth can cause secondary compression of the brainstem resulting in ipsilateral hemiparesis and/or additional cranial nerve deficits (Fankhauser und Vandevelde, 1981; Vandevelde et al., 1977).

In this report, a poodle with trigeminal nerve-sheath tumor and secondary invasion of the central nervous system is described. Clinical signs, including all features of paradoxical vestibular disease, as well as magnetic resonance imaging (MRI) of the brain and histopathological characteristics are discussed.

Signalment, history and clinical examination

A thirteen-year-old, female spayed poodle had been examined by a local veterinarian because of a history of acute sneezing. Rhinoscopy was performed and neither a foreign body nor a mass was found. Bacteriological examination of material from the nasal cavity revealed Escherichia coli. The dog was discharged and treated with Amoxycillin/Clavulanic acid (Synulox®, Gräub) 12.5 mg/kg bodyweight (BW) BID. One month later, the dog had additionally developed atrophy of temporal and masseter muscles on the left side. The same therapy was continued. After one month no improvement was noticed. Based on the clinical signs, a lesion of trigeminal nerve was suspected and skull radiographs were performed, but no abnormalities were found. After another three months a head tilt and episodical circling to the right was noticed by the owner. Otitis media/interna was suspected by the local veterinarian and treatment with Cefalexin (Cefaseptin®, Chassot) 20 mg/kg BW BID was initiated. Two months later no improvement was noticed and the dog was referred to the small animal clinic of University of Bern.

The clinical examination revealed periodontal disease with halitosis and a severe keratoconjunctivitis on the left side. Significant temporal and masseter, as well as facial muscle atrophy was noticed on the left side. On thoracic auscultation a holosystolic murmur was best heard in the area of the 5th intercostal space. The dog seemed to be slightly disoriented, showed compulsive walking and had a head tilt to the right side. A mild generalised vestibular ataxia including drifting to the right side and marked hypermetria in the front limbs were noticed. The dog showed a hemiparesis on the left side and had proprioceptive positioning deficits (e.g. overknuckling) in the left rear extremity. All spinal reflexes and superficial as well as deep pain sensation were normal.

The cranial nerve examination revealed multiple abnormalities: menace reaction was absent on the left and decreased on the right side; palpebral and corneal reflexes as well as facial sensation were absent on the left side. The left nostril was small and paretic. Additionally, the strength of the tongue retraction was decreased. Based on the clinical signs the presumptive anatomical localization of the lesion was the caudal brainstem involving the cerebellopontine angle, the left trigeminal, facial and hypoglossal nuclei and/or nerves. Abnormalities in posture, gait and postural reactions could fit with paradoxical vestibular disease (Palmer et al., 1974) involving the flocculonodular lobe or the caudal cerebellar peduncle on the left side. Disorientation and compulsive walking were the signs of forebrain disease, which could have been secondary due to a brainstem or multifocal lesion. Possible differential diagnoses were a space occupying lesion such as neoplasia or meningoencephalitis. An atrioventricular valve insufficiency was also suspected but was not further investigated.

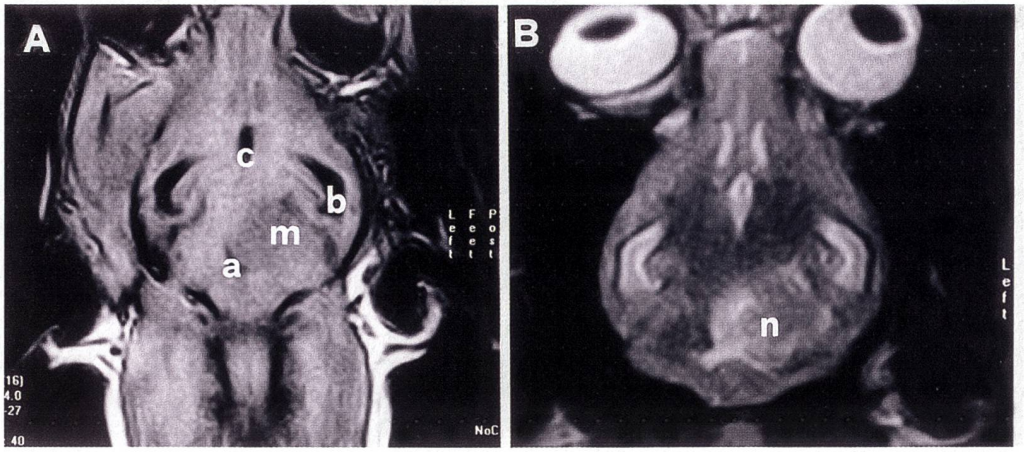

Figure 1: Dorsal plane T1-weighted (A) and T2-weighted image (B) at the level of the fourth ventricle. On the left side of the posterior fossa there is a hypointense circular mass (m) displacing the fourth ventricle (a) to the right side. Lateral (b) and third (c) ventricles are visible. Atrophy of the left masticatory muscles is obvious (A). On the T2-weighted sequence (B) the lesion presents as slightly hyperintense and inhomogeneous mass (n).

Clinicopathological findings and follow-up

Hematologic abnormalities included lymphopenia (670 cells/µl; reference range (RR): 1,000–4,800 cells/µl). Abnormalities in serum biochemistry were hypercholesterolaemia (10,04 mmol/l; RR: 3,24–6,48 mmol/l) and hyperglobulinaemia (43,9 g/L; RR: 31–35 g/l). Urinalysis revealed no abnormalities. Latero-lateral thoracic radiographs of both sides revealed no abnormalities. The results of the occipital CSF examination were normal.

T1-(35/12), T2-weighted (3500/80), IRSE (inversion recovery spin-echo: TR 2176ms, TI 1600ms, TE 120ms) and T1 weighted contrast-enhanced (Gadodiamide 0.1 mmol/kg BW, Omniscan™, Nycomed) sequences using a lowfield MRI-system (0.23T: Picker Outlook) in transverse, dorsal and sagittal planes were performed.

On T1-pre-contrast images a slightly hypointense space occupying lesion in the posterior fossa displacing the fourth ventricle to the right side was seen (Figure 1, A). On IRSE and T2-weighted images the lesion presented as a inhomogeneous hyperintense mass (Figure 1, B). The left foramen ovale was enlarged and atrophy of the left sided masticatory muscles was evident in all sequences. The extraaxial lesion showed a uniform and intense contrast enhancement and had a semicyclic, well defined border towards the brain tissue (Figure 2, A, B, C). It originated in the area of the cerebello-pontine angle thus displacing and compressing cerebellum and caudal brainstem/medulla oblongata. It extended through the base of the skull ventrally, divided into two branches (maxillary and mandibular nerves) projecting lateral to the pharynx (Figure 2, D). Lateral and third ventricles were moderately enlarged, the fourth ventricle seemed to be patent but was displaced to the right side (Figure 2, A–D).

Our presumptive diagnosis included an infiltrative schwannoma/neurofibroma of the trigeminal nerve with secondary invasion of the caudal medulla oblongata and cerebellopontine angle. Because of unfavourable prognosis, the owner preferred not to attempt any therapy and the dog was euthanized after two weeks by the referring veterinarian.

Pathological findings

On macroscopic examination, besides ventricular dilation, a pale firm tumor was present in the left ponto-cerebellar angle. It was very large and markedly compressed the left side of the cerebellum (Figure 3, A), caudal cerebellar peduncle and medulla oblongata. Histologically, $^3/_4$ of the features of the tumor were those of a classical neurofibrosarcoma/schwannoma. Briefly, the tumor cells had dark elongated or light oval nuclei, embedded as interwoven bands in a stroma of collagenous connective tissue (Figure 3, B). Whorl formation could be observed. The dark type of nuclei sometimes was located in a palisading pattern around homogeneous eosinophilic, elongated tissue strips (Verocay bodies) or they formed so called pseudomeissnerian corpuscles, both formations found in schwannomas. $^1/_4$ of the tumor at the medial periphery was almost devoid of connective tissue, therefore the impression was less orderly. In this part of the tumor microcavitation and multinucleated giant cells occurred (Figure 3, C). Mitotic figures were very numerous in all tumor sections. In spite of obvious malignancy the growth pattern seemed expansive rather than invasive.

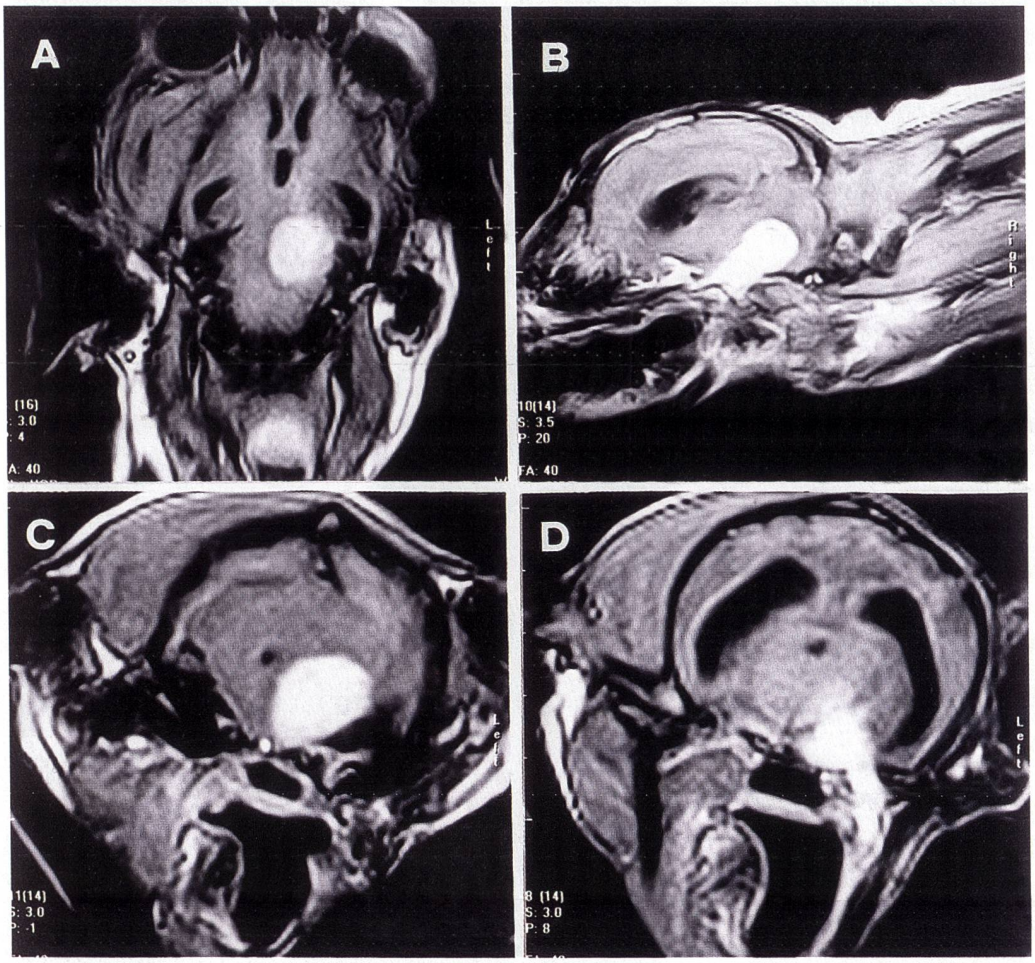

Figure 2: Post contrast T1-weighted sequences: dorsal (A), sagital (B), and transverse plane (C,D). There is a uniform and intense contrast enhancement. The mass has well defined borders (A,B,C), originates in the area of the cerebello-pontine angle displacing the compressed brainstem, fourth ventricle and cerebellum (B,C) and extends cranioventrally through the trigeminal canal into the pharyngeal soft tissues (B,D). The lateral ventricles are enlarged.

Discussion

Trigeminal nerve-sheath tumors have been described in several case reports in veterinary literature (St Clair und Safanie, 1957; Pumarola et al., 1996; Bagley et al., 1998; Saunders et al., 1998) and clinical features were extensively studied in dogs (Bagley et al., 1998) and humans (Birch, 1993; Urich, 1993). The three main trigeminal branches, including the ophthalmic, maxillary and the mandibular nerve may be involved selectively or all together (Evans und Kitchell, 1993). It is well established in veterinary literature that unilateral atrophy of the muscles of mastication is a consistent clinical sign in dogs with trigeminal nerve-sheath tumors reflecting mandibular branch involvement (St Clair und Safanie, 1957; Pumarola et al., 1996; Bagley et al., 1998; Saunders et al., 1998). In contrary, masticatory muscle weakness is less commonly observed in humans with the same condition. However, complains of diffuse pain or altered sensation of the face are usually reported by people with trigeminal nerve lesions suggesting maxillary or ophthalmic branch involvement (Urich, 1993; Maroun et al., 1986; McCormick et al., 1988). These clinical differences most likely do not reflect the varying anatomical locations of the tumor but rather suggest, that sensory signs are more difficult to detect in small animals. Such manifestations may be undetected until significant atrophy of the masticatory muscles is clinically relevant. Our dog showed no signs of facial pain or dysesthesia (rubbing of the face) at presentation, although, sneezing episode could have been a sign of abnormal sensation. However, altered sensation expressed by decreased reaction to facial skin stimulation has been described in dogs with trigeminal nerve-sheath tumors (Pumarola et al., 1996; Bagley et al., 1998).

Involvement of additional cranial nerves or signs of brainstem, cerebellar or forebrain lesion in dogs with trigeminal nerve-sheath tumors are not often reported (Bagley et al., 1998). If they occur, they usually reflect the expansive or infiltrative nature of the space occupying process to adjacent brain structures. We found that the tumor location of our dog at the left ponto-cerebellar angle and the se-

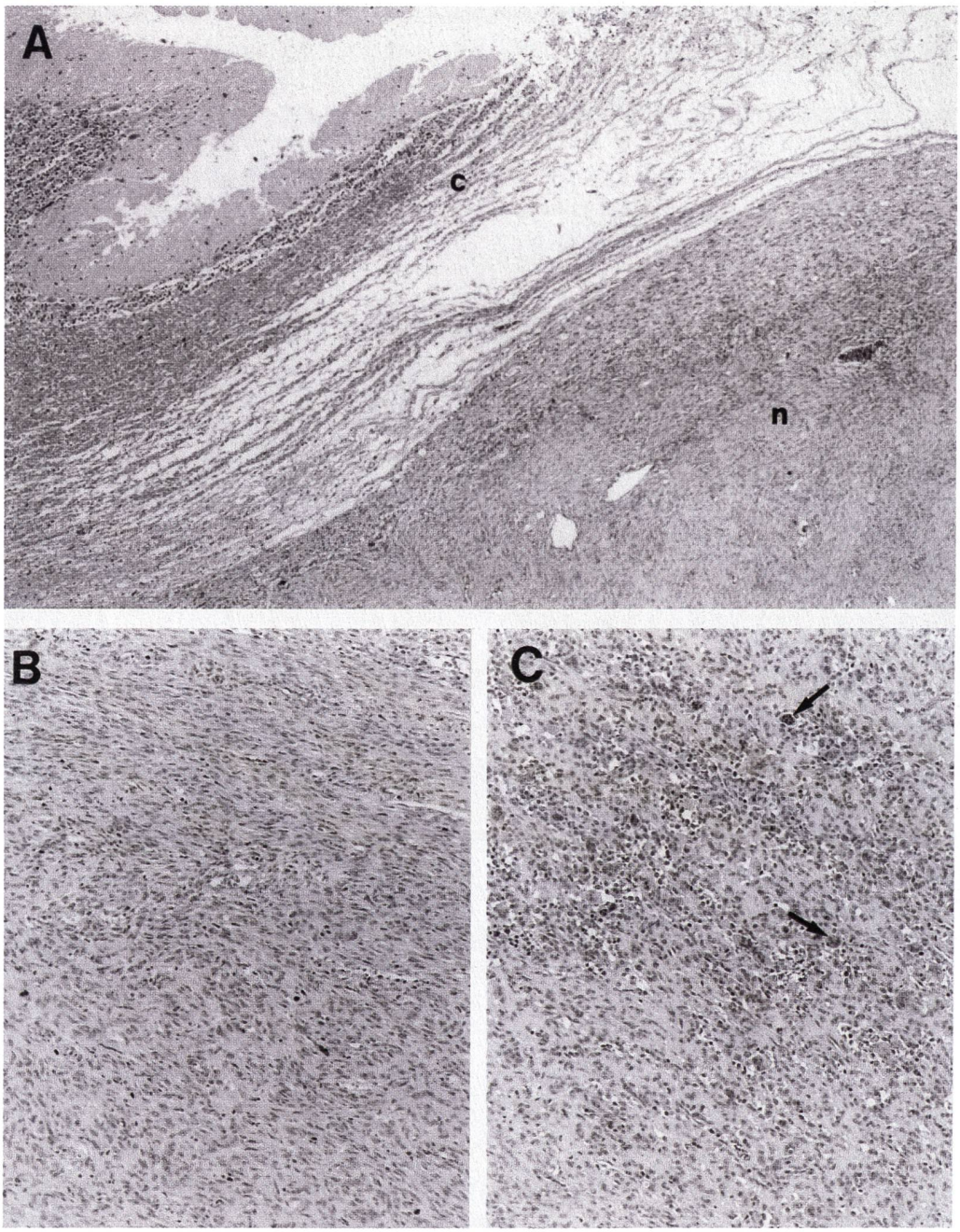

Figure 3: Brain of the patient at the cerebello-pontine level (A,B,C). Tumor (n) markedly compresses the left side of the cerebellum (c) causing severe tissue atrophy (A). HE, 10X. Centre of trigeminal tumor of the patient. Tumor cells with dark elongated or light oval nuclei, embedded as interwoven bands in a stroma of collagenous connective tissue (B). HE, 25X. Medial periphery of trigeminal tumor of the patient. Part of the neoplasia with less connective tissue and less orderly structure as in B (C). Multinucleated giant cells are visible (arrows). HE, 25X.

condary compression of the left cerebellar hemisphere including the caudal cerebellar peduncle, corresponded very well with the clinical manifestation of a "classical" paradoxical vestibular syndrome (Palmer et al., 1974; De Lahunta, 1983; Oliver et al., 1997 (B)). If the growth of the intracranial mass is slowly progressive, impairment of cerebrospinal fluid flow may result and lead to secondary hydrocephalus (Oliver et al., 1997 (A)). Although the enlargement of the ventricular system in our dog was noticed on MRI and confirmed at necropsy, the histopathology revealed no secondary structural parenchymal changes, especially of the forebrain. Furthermore, the mesencephalic aqueduct and fourth ventricle were patent. We concluded from these observations, that changes in mental status and behaviour were most probably caused by direct impairment of the reticular formation at the brainstem level.

High soft tissue contrast, the absence of beam hardening artefacts caused by bone in computed tomography (CT) and the possibility of imaging in any desired plane makes MRI the method of choice in imaging of lesions located in the poste-

rior fossa (Rigamonti et al., 1987). In the present case the extraaxial location of the well delineated expansive lesion in the cerebello-pontine angle region, extension through the enlarged trigeminal canal and the muscle atrophy of masticatory muscles allowed the diagnosis of a tumor involving the trigeminal nerve. Nerve sheath tumors (schwannomas or neurofibromas) are described in human and veterinary literature to be moderately hypo- to isodense on T1 and moderately hyper-, occasionally isointense on T2. Most of them show a uniform contrast enhancement (Bagley et al., 1998; Saunders et al., 1998, Kippenes et al., 1999; Majoie et al., 1999; Platt et al., 1999). In Schwannomas, additional but uncommon MRI features may include intratumoral haemorrhage, low signal intensity in the T2-weighted image and multicystic appearance with rim enhancement (Majoie et al., 1999).

Histological features of the tumor in our case were those of a classical neurofibrosarcoma/schwannoma, except that the medial periphery was almost devoid of connective tissue. Different classifications have been used for the tumors of nerve-sheath origin (Lantos et al., 1997). The term peripheral nerve-sheath tumor has been proposed, although histologically these neoplasms are heterogeneous. Because of presumed origin from Schwann cells and similar biological behaviour, the term peripheral nerve-sheath tumor is widely accepted for these neoplasias and also used by different authors (Braund, 1984; Bradley et al., 1982). In spite of obvious malignancy the growth pattern of the tumor in our case seemed expansive rather than invasive. Slow expansion would correspond with the gradual deterioration of the clinical signs over the seven month period.

In general, the prognosis for cases with nontreated trigeminal nerve-sheath tumors is guarded to poor. The survival time of such dogs, as described by Bagley (1998), ranged from 5 to 21 months. It seems that the best treatment of the nerve-sheath tumors is the aggressive surgical resection of the mass at an early stage of disease. In fact, the survival time of cases treated by total resection was longer than in dogs with subtotal resection (Bagley et al., 1998). In addition, other factors such as location, direction of growth and invasiveness of the neoplasia are also important considerations for the prognosis. The success rate of postsurgical chemo- and/or radiation therapy needs to be determined yet. It is reported, that postsurgical radiotherapy may control the growth of such nerve-sheath tumors for only a short period of time (McChesney, 1989). To the best of our knowledge, this is the first clinical report of a dog with a paradoxical vestibular syndrome and additional cerebellar signs originating from a trigeminal nerve-sheath tumor. Our case clearly shows that prognosis for nontreated trigeminal nerve-sheath tumors is poor, especially if they are affecting intracranial structures.

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