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Veterinary Made Easy!
Mini Series

Session 3: Intracranial neurologic disorders (forebrain, cerebellar and vestibular disease)

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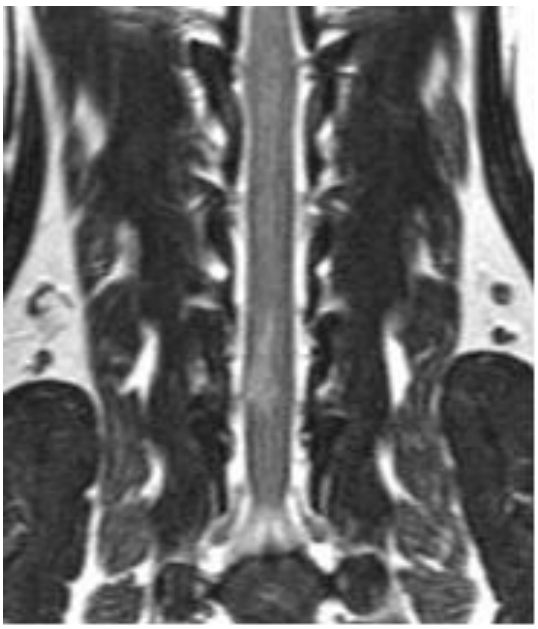

INTRACRANIAL DISORDERS

The learning outcomes of the third module of the CPD solution Neurology mini-series are become better able at: 1. Performing and interpreting the neurologic examination in dogs and cats with intracranial disease 2. Achieving a neuroanatomic diagnosis 3. Developing a systematic approach to the patient with intracranial disease including establishing a differential diagnosis list, diagnostic investigations, treatment options and prognosis 4. Understanding common intracranial neurologic conditions.

Based on the neurologic examination findings the clinician can develop a neuroanatomic localisation.

Neurologic signs of forebrain dysfunction include: • Mental status: Normal, obtunded, demented, stupor (less likely) • Behavior: Normal, hemi-inattention, wandering, vocalizing • Seizures: Present or absent • Posture: Normal, head turn (ipsilateral to the side of unilateral/lateralised lesions), pleurothotonus (ipsilateral to the side of unilateral/lateralised lesions), head-pressing • Gait: Normal, circling (ipsilateral to the side of unilateral/lateralised lesions), movements with lack of purpose • Cranial nerve evaluation: Normal, decreased or absent menace response, decreased or absent nasal/facial sensation • Postural reactions: postural reaction deficits (contralateral to the side of unilateral/lateralised lesions) • Motor function: normal to hemi-tetraparesis • Spinal reflexes: Intact • Spinal hyperesthesia: Present or absent, especially in the cervical spine • Pain perception: Usually normal; may see mild contralateral sensory loss, particularly on the face • Micturition: May show inappropriate urination and/or defecation Lesions of the forebrain often cause behavioural change, altered mental status (e.g. obtundation), seizure activity, compulsive walking in circles (usually in the direction of the lesion), and head pressing. Decreased menace response and decreased facial sensation may also be detected. Hemi-inattention syndrome," or "hemineglect syndrome," refers to a phenomenon in which a patient with a lateralised or unilateral structural forebrain lesion ignores input from onehalf of his or her environment. Since most sensory stimuli are interpreted primarily in the cerebral hemisphere contralateral to the stimulus side, the side that the patient ignores is contralateral to the side of the lesion. These patients may eat from only one-half of the food bowl, turn the opposite direction when called by name (i.e. when called from the ignored side), and ignore or have difficulty localizing nociceptive stimuli when applied contralateral to the side of the brain lesion. Patients with diencephalic lesions may also exhibit sings of endocrine dysfunction (e.g. PU/PD), abnormal eating patterns, and problems with temperature regulation.

Neurologic signs of brain stem dysfunction include:

• Mental status: obtunded, stupor, coma • Posture: normal, head tilt (ipsilateral/contralateral), wide-base stance; recumbent patients may manifest decerebrate or decerebellate rigidity • Gait: normal, spastic paresis • Cranial nerves: abnormalities in cranial nerves III to XII may occur uni or bilaterally, central vestibular signs can occur • Postural reactions: postural reaction deficits in four limbs or ipsilateral to the side of unilateral/lateralised lesions • Spinal reflexes: Normal to increased • Spinal hyperaesthesia: absent or can have cervical hyperaesthesia

Lesions from the midbrain through the medulla are more likely to produce severe disturbances of consciousness (stupor, coma) due to impairment of the ARAS

Neurologic signs of unilateral vestibular dysfunction include • Head tilt • Asymmetric ataxia • Falling, rolling • Nystagmus • Positional ventrolateral strabismus In dogs with peripheral vestibular disease the nystagmus is generally horizontal or rotatory and not altered with position of head, there are no postural reaction deficits and facial paralysis and/or Horner's signs can occur In dogs with central vestibular disease the nystagmus can be in any direction, it can change direction when the position of the head is altered, there are postural reaction deficits and cranial nerves V, VI, IX, X can be affected

Neurologic signs of cerebellar dysfunction include: • Mental status: normal • Posture: head tilt (ipsilateral/contralateral), wide-base stance • Gait: spastic ataxia, dysmetria, intention tremor, and no obvious signs of weakness • Cranial nerves: nystagmus may occur but is usually more of a tremor of the globe than the slow-quick (jerk) movements • associated with vestibular disease • Postural reactions: postural reaction deficits in four limbs or ipsilateral to the side of unilateral/lateralised lesions • Spinal reflexes: Normal to increased The cerebellum coordinates movements. It controls the rate and range of movements without actually initiating motor activity. Head intention tremors are uncoordinated movements that become much worse as the animal initiates an activity, such as eating or drinking. Acute injury to the cerebellum can cause a decerebellate posture, typically extensor hypertonus in the thoracic limbs, flexion in the pelvic limbs, and opisthotonos. Lesions of the flocculonodular lobes of the cerebellum produce signs similar to those of vestibular disease.

By combining the information obtained from a thorough medical history, the general physical examination and the neuroanatomic diagnosis, the clinician can develop a differential diagnosis list and subsequently select appropriate diagnostic investigations. Selected intracranial diseases that commonly occur in dogs and/or cats are presented in order according to the acronym VITAMIN D.

Vascular

Cerebrovascular accidents (ischemic, haemorrhagic) Cerebrovascular accidents (Wessmann 2009). Cerebrovascular accident (CVA), also termed stroke, results from any pathological process of the blood vessels supplying the brain and is characterised by nonprogressive (or rapidly progressive) intracranial neurological signs with peracute (6 hours) to acute (24 hours) onset and duration of at least 24 hours (Victor and Ropper 2001). When the neurological signs last less than 24 hours, the event is referred to as a transient ischaemic attack (TIA) (Victor and Ropper 2001). TIAs may precede a CVA. Cerebrovascular diseases and CVA can be broadly classified as: • ischemic (resulting from occlusion of a cerebral blood vessel by a thrombus or embolism, causing ischaemic necrosis or infarction) and • haemorrhagic (resulting from rupture of an intracranial blood vessel wall, causing bleeding into or around the brain) (Wessmann 2009; Garosi 2010). Ischaemic CVA can be classified by the territory that the affected blood vessel supplies, the size of the vessel (e.g., territorial infarct with large arterial vessel disease; and lacunar infarct with small perforating arterial vessel disease), the age of the infarct (e.g. recent, organising), the presence of secondary haemorrhage, the pathogenesis of the stroke (e.g. thrombotic, embolic, haemodynamic) and the suspected underlying aetiology. Haemorrhagic CVA can be classified according to the anatomical site of the haemorrhage (e.g. epidural, subdural; subarachnoid; intraparenchymal; intraventricular), size of the lesion (e.g. small, large), age of the lesion or the suspected underlying aetiology (Wessmann 2009). Several disorders can predispose to ischemic or haemorrhagic CVA including: Ischemic CVA • Embolus (septic, fat, air, parasites (e.g. Dirofilaria immitis), primary or secondary neoplasia, fibrocartilaginous) • Systemic hypertension (generally associated with chronic renal disease, hyperadrenocorticism or pheochromocytoma) • Hypercoagulable state • Increased blood viscosity (e.g. polycytemia vera, multiple myeloma) • Cardiac disease • Hyperlipoproteinemia in Miniature Schnauzers • Atherosclerosis associated with primary hypothyroidism, diabetes mellitus, hyperadrenocorticism, or hereditary hypercholesterolaemia

Haemorrhagic CVA • Neoplasia (e.g. intravascular lymphoma, hemangiosacoma, oligodendrogliomas, • glioblastomas, ependymomas, haemangioendotheliomas) • Coagulopathy (associated with von Willebrand's disease, Angiostrongylus vasorum

infection, or neoplasia) • Congenital or acquired vascular malformations • Cerebral amyloid angiopathy • Necrotizing vasculitis The most commonly reported concurrent medical conditions in dogs with ischemic CVA include hyperadrenocorticism, chronic renal disease, hypothyroidism, and hypertension (Garosi 2005). Reported concurrent medical conditions in dogs with haemorrhagic CVA include Angiostrongylus vasorum infection, primary or secondary brain tumours, hypertension, hyperadrenocorticism, chronic renal disease, and hypothyroidism (Lawrie 2012). A concurrent medical condition has not been identified in about 50% and 66% of dogs with ischemic and haemorrhagic strokes, respectively (Garosi 2005; Lawrie 2012).

Reports of ischemic or haemorrhagic strokes in cats are limited (Cherubini 2007; Altay 2011). Reported concurrent medical conditions include hyperthyroidism, hypertrophic cardiomyopathy, hepatic and renal disease (Altay 2011). Clinical signs Neurological signs in animals with CVA have typically a peracute (6 hours) to acute (24 hours) onset and are nonprogressive or rapidly progressive. Progression of neurological signs for 24 to 72 hours can occur due to worsening cerebral oedema and haemorrhage. Once the highest degree of neurological dysfunction is reached, neurological signs plateau and then gradually improve in most cases, except fatal CVA. In animals with ischemic CVA neurological signs commonly refer to a focal and unilateral intracranial anatomic neurolocalization (Garosi 2010). In animals with haemorrhagic strokes neurological signs may be less focal than with ischemic CVA as the haemorrhage usually involves the territory of more than one artery and increase in intracranial pressure can cause signs consistent with a multifocal intracranial anatomic localization. In animals with CVA affecting the forebrain seizures can occur soon after the CVA or several weeks later and are often recurrent (Garosi 2005; Lawrie 2012). CVA can recur and relapses are most frequent in dogs where an underlying cause is identified but it is difficult to treat (Garosi, 2005). Diagnostic investigations Ocular fundus examination should be performed in all animals with suspected CVA as it may reveal tortuous retinal vessels (suggestive of systemic hypertension), haemorrhage (suggestive of coagulopathy or systemic hypertension), or papilloedema (suggestive of increased ICP) (Garosi 2010). Imaging studies of the brain such as computed tomography (CT) and conventional and functional MRI are necessary to diagnose CVA and exclude other intracranial diseases, to differentiate between ischaemic and haemorrhagic CVA, and to determine the location and extent of the lesion. CT is very sensitive at detecting acute haemorrhage which appears hyperdense, but it may not detect acute ischemia in the brain (Garosi 2010). Conventional MRI can detect both ischemic and haemorrhagic CVA. Functional MRI including diffusion and perfusion weighted images and magnetic resonance angiography improve the sensitivity and specificity of the diagnosis of peracute and acute CVA (Garosi 2010). Once an MR imaging diagnosis of CVA has been achieved, further diagnostic investigations are aimed at identifying the underlying cause of ischemic or haemorrhagic CVA. These include:

Diagnostic investigations to identify the underlying aetiology of ischemic CVA – Serial blood pressure measurements – Complete blood count – Serum biochemistry profile – Urinalysis – Urine protein/creatinine ratio – Serum antithrombin III activity – D-dimers – Endocrine testing for hyperadrenocorticism, thyroid diseases, and pheochromocytoma – Thoracic radiographs – Abdominal ultrasound – Echocardiography and electrocardiography.

Diagnostic investigations to identify the underlying aetiology of haemorrhagic CVA – Serial blood pressure measurements – Complete blood count – Serum biochemistry profile – Buccal mucosa bleeding time

– Prothrombin time (PT) – Activated partial thromboplastin time (APTT) – Thoracic radiographs – Abdominal ultrasound – Faecal analysis to investigate parasitic infestation (such as A. vasorum)

Treatment

Treatment of CVA focuses on prevention of secondary brain damage or complications, such as increased ICP or epileptic seizures, and on the underlying disease. Prognosis Prognosis depends on the severity of the neurological dysfunction, occurrence of complications, and the underlying cause, if identified. Most dogs recover within weeks after the onset of ischemic CVA with only supportive care.

Inflammatory/ infectious Inflammatory disease of the CNS can be classified as infectious (when caused by a known or suspected infectious agent) or non-infectious when the underlying aetiology is unknown and an immune-mediated process is suspected. Inflammatory disease of the CNS may affect the brain parenchyma (encephalitis), the meninges (meningitis) and the spinal cord (myelitis). Clinical signs Signs of systemic involvement may (e.g. certain viral diseases or mycotic disorders) or may not (e.g. cerebral abscess, neurotropic infections, non-infectious encephalitis) be present. Ophthalmologic examination may reveal fundic changes or uveitis. Neurological signs in animals with inflammatory CNS disease often have an acute onset, are progressive and reflect multifocal or diffuse involvement of the CNS. However focal neurological deficits can also occur (e.g. cerebral abscess, fungal granuloma). Diagnostic investigations Haematology may sometimes provide evidence of systemic infection (e.g., alterations in white blood cell count), and serum biochemistry may reveal changes consistent with involvement of other organs. Cerebrospinal fluid analysis often reveals pleocytosis and increased protein concentration. The type of pleocytosis may be suggestive of a particular aetiology or disease group. CSF may be normal when the CNS inflammation does not involve the meninges or the ependymal lining of the ventricular system or if the animal has been treated with antiinflammatory medications (particularly corticosteroids) prior to CSF collection. Additional tests on CSF (such as polymerase chain reaction (PCR), antibody or antigen titers, immunofluorescence and culture can help to reach an aetiologic diagnosis. Sometimes certain microorganism can be visualised on CFS cytology. Inflammatory CNS disease can cause increased intracranial pressure and CSF collection may be contraindicated due to the risk of cerebral herniation and death. Anytime increased intracranial pressure is suspected, MRI of the brain should be performed before considering CSF collection. MRI of the brain can reveal changes suggestive of inflammatory CNS disease such as multifocal, diffuse or sometimes focal lesions within the brain parenchyma that typically appear hyperintense on T2-weighted and FLAIR images, iso to hypointense on T1-weighted images, and show variable contrast enhancement sometimes with meningeal involvement following administration of contrast medium. Treatment Treatment of CNS infections depends on the identification of the aetiologic agent and selection of the appropriate antimicrobial agent. Treatment of viral CNS infections is mostly supportive and symptomatic. Treatment of non-infectious inflammatory CNS disorders involves immune-suppressive medications.

Prognosis

Prognosis is variable and dependent on the underlying aetiology, extent and severity of the CNS inflammation and associated neurological deficits, and promptness of diagnosis and treatment.

Granulomatous meningoencephalomyelitis

Granulomatous meningoencephalomyelitis (GME) is an inflammatory disorder of the brain whose aetiopathogenesis remains unknown. Autoimmune, infectious, neoplastic, genetic and even toxic aetiologies have been proposed (Schatzberg 2010). Most likely GME is a nonspecific immunologic response associated with multiple environmental triggers (including pathogens and vaccinations) as well as genetic factors (Schatzberg 2010). Typically, GME presents as an acute-onset, progressive, neurologic disease that may be fatal if left untreated. Young to middle-aged dogs, females and toy and terrier breeds are overrepresented; however, dogs of any age, gender and breed may be affected (Schatzberg 2010).

Clinical signs

Clinical manifestation and lesion topography of GME can vary. Three basic forms of the disease have been reported, ocular, focal and disseminated or generalised. The disseminated form is the most common (Schatzberg 2010). The focal form of GME should be differentiated from CNS malignant histiocytosis and primary CNS lymphosarcoma.

Diagnostic investigations

Haematology, serum biochemistry and urinalysis may be normal or reveal aspecific changes. On MRI, lesions are typically hyperintense on T2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences, iso- to hypointense on T1-weighted images, and variably contrast-enhancing, ranging from none to intense contrast uptake. In the disseminated form of GME these lesions typically have an infiltrative appearance with irregular margins and are multifocal. Although GME has a predilection for white matter, it is not associated with distinct topography on MRI, as NME and NLE are, and MRI lesions often are distributed throughout both gray and white matter (Higginbotham 2007; Schatzberg 2010). Vasogenic edema is commonly present in the white matter and appears hyperintense to cerebral parenchyma on T2-weighted images. Meningeal enhancement may or may not be observed. A focal space occupying mass or abnormalities involving the optic nerves may be observed in animals with the focal or ocular forms, respectively. CSF analysis can reveal mild to severe mononuclear (and less commonly, mixed) pleocytosis and elevation of total protein concentration; however, CSF can occasionally be normal. As the MRI and CSF findings are not specific for GME, the antemortem diagnosis of this disease is also based on exclusion of infectious or neoplastic CNS disorders by means of various tests including serology, CSF PCR, thoracic and abdominal imaging. Definitive diagnosis requires histological evaluation of the brain through biopsy or post mortem. Histologically, GME is characterized by large perivascular cuffs of mononuclear cells sometimes distributed in a whorled pattern, within the neuroparenchyma and meninges. Unlike NME and NLE, tissue necrosis and secondary cavitation are lacking (Higginbotham 2007).

Treatment and prognosis

Immunosuppression is the mainstay of therapy for GME as well as other MUE (meningoencephalitis of unknown aetiology). Gold standard treatment protocols have yet to be established due to the lack of blinded, controlled, randomized, prospective studies comparing different standardised treatment protocols in dogs with GME or MUE (Granger 2010). In clinical practice corticosteroids (prednisone or dexamethasone) treatment is commonly initiated when GME is suspected based on clinical and diagnostic investigation findings. The dosage of corticosteroid and whether and when additional immunomodulatory agents are started depend on the clinician preference, index of suspicion of GME (or other MUE) and the severity of neurological dysfunction. Antinflammatory dosage of corticosteroids (e.g. prednisolone 0.5 mg/kg to 1.0 mg/kg once daily) and antibiotic therapy and are often administered while awaiting serology and PCR results for regional infectious diseases. However, if the index of suspicion of GME (or other MUE) is high and neurological dysfunction is severe, immunosuppressive dosage of prednisolone (1 to 2 mg/kg every 12 hours) alone or in combination with another immunomodulatory medication may be started immediately. Prednisolone protocol can vary depending on clinician preference, severity of neurological dysfunction, response to treatment, development of steroid-related adverse effects, pet-owner financial and personal situation and availability of other immunomodulatory medications. The aim of long-term prednisolone treatment is to find the lowest dose to control signs in each dog. Adverse effects associated with long-term, highdose corticosteroid therapy include polyuria–polydipsia, polyphagia, weight gain, hepatotoxicity, gastrointestinal ulceration, pancreatitis, and iatrogenic hyperadrenocorticism.

Reported adjunctive immunomodulatory medications include cytosine arabinoside, procarbazine, cyclosporine, lomustine, leflunomide, and mycophenolate mofetil.

Cytosine arabinoside is commonly administered at 50 mg/m2 subcutaneously twice daily for 2 consecutive days or intravenously as constant rate infusion at 200 mg/m2 over 24-48 hours. This treatment cycle is repeated every 3 weeks for three cycles. Subsequently, the interval between treatment cycles is increased by 1 week and the dog receives three treatment cycles at the new treatment interval. After three treatments, the interval between treatment cycles is extended by another week. The new interval is maintained for three treatment cycles. Treatment cycle intervals are gradually extended. Concurrently, the dose of prednisone is gradually tapered to a low dosage administered every other day. Adverse effects are dose-dependent and include myelosuppression, vomiting, diarrhea, and hair loss (Scott-Moncrieff 1991). Haematology should be performed prior to each treatment course and 10 to 14 days after the first course of cytosine arabinoside. A fair long-term prognosis has been reported in dogs with GME treated with combined prednisone and cytosine arabinoside therapy.

Repeating MRI and CSF can help establish the safest way to taper off treatment in individual patients.

Neoplastic

Neoplasia of the nervous system can be classified as primary and secondary. Primary nervous system tumours originate from neuroectodermal, ectodermal, and/or mesodermal cells normally present in, or associated with brain, spinal cord or peripheral nerves. Secondary tumours affecting the nervous system may originate from hematogenous metastasis of a primary tumour in another organ or from structures surrounding the neuroparenchyma, such as the nose, ear, calvaria, pituitary gland, or vertebrae and may affect the neural tissue by infiltration or compression. Dissemination or metastasis of CNS tumours is rare, but may occur via the CSF pathways, especially if tumours are located close to the subarachnoid space or ventricular cavities (e.g., choroid plexus tumours or ependymoma), or via a hematogenous route, such as the dural sinus, with subsequent development of distant metastasis, usually in the lung (Vite 2005). This section will focus on intracranial neoplasia.

Intracranial neoplasia Brain tumours exert their pathologic effects both by directly encroaching upon and/or invading brain tissue and by secondary effects such as peritumoural oedema, inflammation, obstructive hydrocephalus, and haemorrhage.

Canine and feline intracranial neoplasias are listed below Primary Meningioma Astrocytoma (glioblastoma multiforme) Oligodendroglioma Gliomatosis cerebri Ependymoma Choroid plexus tumours Primitive neuroectodermal tumours (neuroblastomas, medulloblastoma, gangliocytomas) Primary CNS lymphomas Primary CNS histiocytic sarcoma (malignant histiocytosis) Secondary Hemangiosarcoma Lymphoma Pituitary Tumours Carcinomas/ Adenocarcinomas (mammary, prostatic, pancreatic, pulmonary) Nasal tumours (eg, adenocarcinoma, squamous cell carcinoma, chondrosarcoma, neuroesthesioblastoma) Histiocytic sarcoma Calvarial osteosarcoma and multilobulated tumour of bone (multilobulated osteochondrosarcoma) Malignant melanoma Others

Incidence An accurate estimate of the incidence of intracranial neoplasia in animals is unknown. One study reported a rate of 14.5 and 3.5 per 100,000 dogs and cats, respectively (Vandevelde 1984). In other studies, the incidence of intracranial neoplasia was 2.8% and 2.2% in dogs and cats, respectively (Zaki 1976; Zaki 1977). The most commonly reported primary brain tumour in dogs and cats is meningioma (Troxel 2003; Snyder 2006). The second most common primary brain tumours in dogs and cats are astrocytoma and oligodendroglioma (Snyder 2006; Troxel 2003). The most common secondary tumour is hemangiosarcoma in dogs and lymphoma in cats (Snyder 1998; Troxel 2003, Tomek 2006). Pituitary tumours are the second most common secondary tumour in dogs and cats (Snyder 1998; Troxel 2003). The golden retriever and boxer have been reported at increased risk to develop intracranial tumours (primary and secondary) (Snyder 2006; Struges 2008). Menigiomas have been most commonly reported in dolicocephalic dog breeds, especially German Shepherds, Golden Retrievers and Labrador Retrievers as well as in the boxer (Snyder 2006; Struges 2008). Glial tumours (astrocytomas and oligodendrogliomas) have been reported in the boxer, Boston terrier, and other brachycephalic breeds with higer frequency than in other canine breeds (Snyder 2006). In addition to the golden retriever and boxer, also the Labrador retriever and German shepherd dog are most commonly affected by secondary intracranial tumours (Snyder 2008). The reported mean age of dogsand cats with primary brain tumours is 9.5 and 11.3 years, respectively (Bagley 1999; Troxel 2003; Snyder 2006). Dogs and cats with meningioma are significantly older at diagnosis than those with other primary brain tumours (Troxel 2003; Snyder 2006). The mean age of dogs with

secondary brain tumours is 9.6 years (Snyder 2008). The mean age of cats with secondary brain tumours is the same as for primary brain tumours (Troxel 2003). No gender predisposition for different intracranial tumour types has been consistently reported. Clinical signs Clinical signs commonly reflect the location and the secondary effects of the tumour. Onset of signs is generally chronic and progressive however acute onset or deterioration can occur with haemorrhage, obstructive hydrocephalus, or sudden exhaustion of cerebral compensatory mechanism resulting in severely increased ICP. Seizures and altered mentation have been reported as the most common presenting signs in dogs and cats with primary and secondary intracranial neoplasia (Troxel 2003; Snyder 2006; Schwartz 2011). Frequency of seizures in animals with intracranial neoplasia varies among studies ranging from 45% (Bagley1999) to 62% (Schwartz 2011) in dogs and being nearly 23% in cats (Troxel 2003; Tomek 2006). Seizures can occur as single events, cluster seizures or less commonly as status epilepticus (Schwartz 2011, Tomek 2006). Seizures can be the only clinical abnormality when the neoplasia is focally affecting the so called “clinically silent regions”, such as olfactory, frontal, and pyriform lobes. Diagnostic in vestigations The diagnostic investigation of animals with suspected intracranial neoplasia includes haematology, serum biochemistry profile, urinalysis, thoracic radiography and abdominal ultrasonography to investigate concurrent extracranial disease including primary and metastatic neoplasia. Thoracic radiographic abnormalities such as metastatic lesions or concurrent disease (e.g. pneumonia, megaesophagus, heart failure) have been detected in approximately 20% of dogs with primary intracranial neoplasia and in 54% of dogs with secondary intracranial neoplasia (Snyder 2006; Snyder 2008). Neoplasia unrelated to the primary intracranial tumour, mostly involving the thoraciac or abdominal cavity, has been detected at necropsy in 23% (38/170) of dogs in one study (Snyder 2006). Fine needle aspirate or true cut biopsy of any accessible extraneural masses may help to reach a definitive diagnosis of primary or metastatic neoplasia related or unrelated to the primary intracranial tumour. MRI or CT of the brain can help to support the antemortem diagnosis of intracranial neoplasia and particularly MRI can often provide a relatively accurate presumptive diagnosis. Meningioma has been correctly dignosed based on MRI findings in 100% of dogs and 95% of cats with histologically confirmed intracranial tumours (Polizopoulou 2004; Troxel 2004). The MR imaging features of primary and common secondary canine and feline intracranial neoplasia have been described and are summarised in table 5.14 (Troxel 2004; Hecht 2010; Palus 2011; Ródenas 2011; Wisner 2011; Young 2011; Martin-Vaquero 2012; Westworth 2008). Some nonneoplastic intracranial lesions can present with imaging features similar to intracranial neoplasias.

Definitive antemortem diagnosis of intracranial neoplasia requires histological examination following stereotactic or surgical brain biopsy. However, cerebrospinal fluid cytology may sometimes allow a diagnosis of lymphoma (Troxel 2003; Palus 2011). Unless neoplastic cells are detected, CSF analysis provides limited information in the diagnosis of primary intracranial neoplasia. As intracranial tumours may cause an increased ICP, CSF collection should be performed only if considered safe following brain MRI of CT. In animals with primary intracranial neoplasia, CSF analysis may be normal, reveal increased protein concentration alone or in association with pleocytosis. In one study on canine primary intracranial neoplasia, CSF pleocytosis occurred in 58% of dogs and was most commonly mixed (Snyder 2006). Neutrophilic pleocytosis has been reported in 19% to 25% of dogs with intracranial meningiomas (Bailey 1986; Dickinson 2006).

Treatment and survival times

Treatment of intracranial neoplasia can be divided into palliative and definitive. The aim of palliative treatment is to alleviate clinical signs by minimising the secondary effects of the intracranial neoplasia (mainly vasogenic oedema). Prednisone (0.5 to 1.0 mg/kg/day orally) may be effective at reducing endothelial permeability, vasogenic oedema, and CSF production. If improvement is observed, the dosage may be gradually reduced to the lowest effective dosage to control neurologic signs. In animals with suspected or confirmed increased ICP, administration of intravenous corticosteroids, mannitol or hypertonic saline (see section on increased ICP and traumatic brain injury) can be also effective in rapidly reducing vasogenic oedema, decrease CSF production and stabilizing the endothelial membrane. Antiseizure treatment should be instituted in all animals with seizures caused by intracranial neoplasia. The choice of the antiseizure medication is affected by many variables including severity and frequency of seizures, presence and degree of neurological deficits (e.g. decreased mental status and ataxia), hepatic and renal function, interaction with other medications (e.g. chemotherapeutic agents), owner life style and costs. Phenobarbitone is commonly used in animals with normal hepatic function and with normal to mildly obtunded mental status. Loading may be necessary when rapid achievement of target levels is required, however this could affect monitoring of neurological status by causing or worsening sedation and ataxia. Alternatively, levetiracetam may be used to control seizures at least initially. Potassium bromide or phenobarbitone at maintenance dosage may be started at the same time of Levetiracetam to provide longer term seizure control while avoiding the undesiderable effects of loading. In animals with persistent sedation following administration of phenobarbitone or potassium bromide or in those with moderately to severely obtunded mental status prior to antiseizure treatment, it may be preferable to use levetiracetam or zonisamide. These newer antiseizure medications may also be preferable in animals needing lifelong corticosteroid administration as side effects of phenobarbital and potassium bromide (e.g., polyuria, polydipsia, and polyphagia) are likely to be compounded by concurrent steroid use. In animals with hydrocephalus of the lateral ventricles related to obstruction of and/ or overproductions of CSF (e.g. with a choroid plexus tumour), ventriculoperitoneal shunting can help control intracranial pressure and improve clinical signs (see Hydrocephalus section) (de Stefani 2011). Median survival for dogs receiving palliative pharmacological treatment for brain tumours varies among studies ranging from 0.5 to 7 months (Heidner 1991; Rossmeisl 2009). Dogs with mild neurologic dysfunction due to forebrain meningiomas have the longest survival time (Rossmeisl 2009). Survival times are influenced by tumour type and location, severity of neurological signs, response to treatment and the pet-owner's willingness to continue therapy. Definitive treatment consists of surgical removal/ debulking, radiation therapy, and chemotherapy, alone or in combination. Definitive treatment is commonly combined with palliative pharmacological treatment. Benefits of surgical treatment include removal of neoplastic tissue, decompression of the neuroparenchyma, decrease of ICP and provision of a sample for histologic diagnosis. Surgery is generally aimed at solitary noninvasive tumours located on or near the brain surface. A careful and complete surgical resection, an intensive anesthetic monitoring and postoperative care are essential for a favourable outcome. Surgical approaches to the brain and technical details on intracranial surgery have been described and are beyond the scope of this text (Glass 2000; Bagley 2003; Forterre 2006, 2009; Barreau 2010; Meij 2002; Uriarte 2011). Most data on outcome and survival following intracranial surgery involve meningiomas in both dogs and cats and are described in the section on treatment and survival times of meningiomas. Information on microsurgical transsphenoidal hypophysectomy is presented in the the section on treatment of pituitary tumours.

Radiation therapy may be performed following incomplete surgical resection or as sole treatment when the intracranial tumour is not surgically accessible or surgery is not considered the best therapeutic option. Radiation therapy protocols vary, but most involve administration of a total radiation dose of 46 to 48 Gy in 2.0 to 4.0 Gy fractions daily or every other day. The acute adverse effects of radiation include cerebral oedema and, possibly, a temporary increase in seizure activity. Brain oedema generally responds to corticosteroid therapy. Late effects of radiation can be seen months to years after therapy and are due to brain necrosis. Clinical signs of late radiation damage are often similar to the initially presenting neurologic signs, and differentiation between radiation-induced damage and tumour recurrence can be challenging. Late effects of radiation cannot be effectively treated (Brearley 1999). The median survival time for dogs with brain tumours treated with radiation therapy alone ranges from 4.7 months to 23.3 months (Heidner 1991; Turrel 1984; Brearley 1999; Spugnini 2000; Bley 2005) and has been reported to be over 43.6 months in dogs with pituitary tumours (Bley 2005; Kent 2007). This great difference in survival times is most likely due to differences in radiation therapy protocols, tumour types, size and location, and severity of neurological signs. Stereotactic radiosurgery has been used to deliver a single fraction (10 to 15 Gy) of radiation to canine intracranial tumours (Lester 2001). The median survival time of 3 dogs with intracranial tumours (2 meningiomas and 1oligodendroglioma) treated with stereotactic radiosurgery is 14.2 months (Lester 2001). There is limited information on the use of chemotherapy for primary brain tumours in dogs and cats.

Degenerative Cerebellar cortical abiotrophy This group of diseases specifically refers to the degeneration of normal neuronal cell populations within the cerebellar cortex after birth. Additionally, deep cerebellar nuclei and the terminal fields of cerebellar projections may be affected. Many of these diseases are inherited; most are suspected to be autosomal recessive. The aetiology for this group of disorders is unknown. Lack of a metabolic component necessary for cellular survival may be involved. Some of these abiotrophies may represent inappropriate programmed cell death of cerebellar neurons (apoptosis). Cerebellar cortical abiotrophy has been primarily reported in dogs, with only sporadic feline reports. The onset and rate of the progression of clinical signs varies with the breed affected. Most breeds show an onset of clinical signs when the animal is 3–12 wks old. The course of the disease can be rapid (several weeks) or slowly progressive (several years). In certain cases, the clinical signs will plateau, and the animal will remain stable. In some breeds (like the Gordon Setter), clinical manifestations of cerebellar dysfunction occur near or during adulthood. Clinical signs of cerebellar abiotrophy are consistent with the cerebellar syndrome and may include dysmetria/hypermetria, intention tremors, nystagmus, poor menace responses with normal vision, opisthotonus. Neurodiagnostics have generally not been beneficial in the antemortem diagnosis of this condition; however, in several breeds there are gross structural abnormalities of the cerebellum (hypoplasia and focal signal changes) that may be detectable with magnetic resonance imaging (Dewey and Da Costa 2015).

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