DIAGNOSIS OF BRAIN TUMORS IN DOGS AND CATS: A REVIEW OF THE LITERATURE

Diagnose van hersentumoren bij hond en kat: een literatuuroverzicht

[1]S. Van Meervenne, [2]H. Van Bree, [1]L. Van Ham

[1]Vakgroep Geneeskunde en Klinische Biologie van de Kleine Huisdieren, Faculteit Diergeneeskunde, UGent, Salisburylaan 133, B-9820 Merelbeke
[2]Vakgroep Medische beeldvorming, Faculteit Diergeneeskunde, UGent, Salisburylaan 133, B-9820 Merelbeke
Sofie.VanMeervenne@UGent.be

ABSTRACT

Primary brain tumors are the most common intracranial tumors in the dog. An incidence of 14.5 in 100 000 for dogs and 3.5 in 100 000 for cats has been suggested. At present the prevalence is estimated to be higher because of better diagnostic methods. These methods will be discussed in the present article. On the basis of the signalment, history and a complete physical and neurological examination, the presence of a brain lesion can be suspected. Cerebrospinal fluid analysis and X-ray examinations can be suggestive of a brain neoplasia, but computed tomography and magnetic resonance imaging are necessary to confirm the presence of an intracranial mass. The use of ultrasonography and scintigraphy are rather anecdotal diagnostic procedures, not commonly used in small animal neurology. A crucial step in obtaining a definitive diagnosis is the taking of a biopsy sample of the intracranial mass, preferably by a stereotactic CT-guided method.

SAMENVATTING

Primaire hersentumoren zijn de meest voorkomende hersentumoren bij de hond. De prevalentie van hersentumoren werd een twintigtal jaar geleden geschat op 14,5 op 100 000 honden en 3,5 op 100 000 katten. Omwille van de betere diagnostische middelen waarover dierenartsen heden ten dage beschikken, is het heel waarschijnlijk dat deze cijfers nu hoger liggen. In dit artikel worden de mogelijke diagnostische technieken besproken. Op basis van het signalement, de anamnese en een algemeen klinisch en neurologisch onderzoek kan men een hersenletsel vermoeden. Onderzoek van cerebrospinaal vocht en radiografieën van de kop kunnen een indicatie geven, maar computer tomografisch en nucleair magnetisch resonantieonderzoek van de hersenen zijn nodig om de aanwezigheid van een intracraniale massa te bevestigen. Sporadisch worden echografie en scintigrafie beschreven voor de diagnose van hersentumoren, maar deze technieken worden niet routinematig gebruikt. Essentieel voor het verkrijgen van een definitieve diagnose is echter de bioptname van het letsel, bij voorkeur door middel van een stereotactische CT-geleide methode.

INTRODUCTION

Vandevelde (1984) has suggested an incidence of brain tumors of approximately 14.5 in 100 000 dogs and 3.5 in 100 000 cats. By comparison, 4 to 5 humans suffer from intracranial tumors in a population of 100 000 individuals (Morrison, 1998b).

Primary brain tumors are the most common intracranial tumors in the dog. Secondary involvement of the brain via metastasis or by direct extension from extraneural sites appears to be less common. However, the cranial vault is uncommonly evaluated as a metastatic site in most dogs and cats. Therefore, the exact incidence of intracranial metastasis is not known (Moore *et al.*, 1996).

Meningioma is the most common primary brain tumor in dogs and cats. Meningioma is a benign, primary tumor of the meninges that may arise from any of the

meningial constituents, such as arachnoid cells, fibroblasts, or blood vessels. It is a slow-growing tumor that frequently displaces brain tissue, and it is described as an irregular, firm, lobulated, well-circumscribed, grey-white mass (Lawson *et al*., 1984). Meningioma is an extra-axial (situated outside the parenchyma) tumor, mostly situated in the rostral (bulbus olfactorius and frontal lobes of the cerebrum) or caudal fossa (medulla oblongata, pons and cerebellum). In cats, a large percentage of the patients with meningioma have multiple masses (Jeffery *et al*., 1992).

A second group of brain tumors is constituted of gliomas, which arise from cells of the brain parenchyma. These cells can be subdivided into astrocytes, oligodendrocytes, ependymal cells, and choroid plexus cells, which give rise to three types of primary brain tumours. Astrocytomas are neuro-ectodermal tumors arising from astrocytes. Astrocytes are the largest and most numerous neuroglial cells in the brain and spinal cord. Astrocytomas are intra-axial tumors, commonly located in the pyriform area of the temporal lobe, in other regions of the cerebral hemispheres, the thalamus, hypothalamus or midbrain. They are solid grey-white tumors which are poorly demarcated from the surrounding parenchyma. Astrocytomas do not penetrate the ventricular system or metastasize (Hoerlein, 1971). Oligodendrogliomas are tumors arising from oligodendrocytes, which are neuroglial cells of the central nervous system whose function is to myelinate central nervous system (CNS) axons. Oligodendrogliomas are also intra-axial tumors. They are most often located in the cerebral hemispheres and seem to originate from white matter. Oligodendrogliomas are often red, red-pink or grey in color and often erode through the ventricular or meningeal surfaces (Hoerlein, 1971). Choroid plexus papillomas are neoplasms of the choroid plexus, a collection of blood vessels of the pia mater, which develops in the third, fourth and lateral ventricles. They are well circumscribed with a grey-white to red, granular to papillomatous appearance. On rare occasions they are invasive and metastasize along cerebrospinal fluid pathways (Hoerlein, 1971).

Pituitary tumors are a third group of primary brain tumors. They are located in the sella turcica and cause typical clinical signs such as Cushings disease in dogs and acromegaly in cats (Jeffery *et al.,* 1992).

Other primary tumors involving the brain – all of which are uncommon – include lymphosarcoma, germ cell tumors, dermoid and epidermoid cysts, and craniopharyngiomas (Bagley, 1995).

On the basis of signalment, history and the results of complete physical and neurological examinations, it is possible to localize a problem to the brain and, in some cases, to determine the approximate intracranial location. In order to eliminate categories of disease other than neoplasia, it is essential to add more specific diagnostic techniques, which will be discussed in this article.

DIAGNOSTIC METHODS IN BRAIN NEOPLASIA

Signalment, history and clinical signs

Brain tumors occur most frequently in dogs more than 5 years old, with greatest incidence between 6 and 11 years of age, although they may occur at any age. Glial cell tumors and pituitary tumors occur commonly in brachycephalic breeds, whereas meningiomas occur most frequently in dolichocephalic breeds (LeCouteur, 1999).

Breeds of dogs commonly affected include the Boxer, Doberman Pinscher, Golden Retriever, Boston Terrier and English Bulldog. In several studies, mixed breed dogs are also commonly affected and can represent up to 20% of cases (Morrison, 1998b). Moore *et al.* (1996) adds Scottish Terriers and Old English Sheepdogs to this list. Gender predisposition is not well established.

In cats, meningioma and CNS lymphoma are the most frequently diagnosed brain tumors.

The nature and course of neurological signs resulting from a brain tumor depend on the tumor type, neuroanatomic location, degree of parenchymal compression, growth rate, inflammatory response, and presence of brain herniation. The typically slow growth of brain tumors permits CNS compensation. Clinical signs may be extremely subtle until such time as decompensation occurs, or until tumor growth leads to secondary effects such as hemorrhage, peritumor edema, acquired hydrocephalus, or brain herniation (LeCouteur, 1999). The brain responds to disease in a limited number of ways, regardless of the underlying primary disease process. Rapidly growing tumors are usually associated with acute onset of neurologic dysfunction.

The most frequently observed clinical sign associated with brain neoplasm in a dog or a cat is seizures. Other signs are behavioral changes, circling, blindness, head tilt, pacing, altered states of consciousness, or associated locomotion disturbances. Infrequent clinical signs included weight loss, head pressing and

ptyalism. Should a neoplasm involve the brain stem, cranial nerve deficits may be seen (Bagley *et al.,* 1999; Moore *et al.*, 1996; Morrison, 1998b). These clinical signs are by no means pathognomonic for a brain tumor as they can occur in any brain disorder. Therefore additional examinations are necessary to obtain a definitive diagnosis.

Cerebrospinal fluid analysis

Cerebrospinal fluid (CSF) collection is always performed on a patient under general anesthesia. Atlantooccipital puncture is preferred in patients with lesions above the foramen magnum. Samples without blood contamination provide the most reliable results. In samples contaminated with blood in excess of 500 RBC/µl, the total WBC count and total protein values are corrected using blood counts for comparison (Bailey and Higgins, 1986).

Analysis of CSF should include examination of the physical characteristics of the fluid (color, turbidity), the protein concentration, the total nucleated cell count, the cytological examination, titers for antibodies against infectious organisms and culturing. This procedure should be done as soon as possible after puncture. Delayed processing of samples may result in the preparation of slides that are inadequate for interpretation due to disrupted cell structure (Cellio, 2001). Elevation of CSF pressure is a nonspecific abnormality found in many pathologic conditions. The measurement of CSF pressure adds technical difficulty to the collection procedure and increases the risk both of iatrogenic hemorrhage in the sample and of trauma to the CNS parenchyma (Cook and DeNicola, 1988).

In a study of Bailey and Higgins (1986), the results of cisternal CSF analyses of 77 dogs with brain tumors were examined retrospectively. For all 77 tumors, the most common abnormality was an increased total protein content (69.4%); the least common abnormality was an increased total WBC count (41.3%). Considering the five types of primary brain tumors, the CSF associated with primary brain tumors in the dog was best described as having a total WBC count <50 cells/µl with an increased total protein content and/or an increased pressure. The reference values of the total WBC count and the total protein content vary depending on the laboratory.

Tumor cells are rarely found in CSF samples. Neoplastic cells are most likely to be identified when sedimentation techniques are used for analysis (Cellio, 2001). Results of cisternal CSF analyses of dogs with primary brain tumors varied from case to case, but nearly 10% were normal. Normal CSF were encountered most often with deeply seated parenchymal tumors (astrocytomas and oligodendrogliomas).

Rand *et al.* (1994) describes the CSF data from 12 cats with CNS neoplasia. The majority of the cats had a mild increase in CSF protein concentration, an increased percentage of neutrophils or lymphocytes, and a normal total white cell count.

Neoplasia of the brain is a condition often associated with an increased intracranial pressure (ICP). When ICP is already higher than normal, the removal of CSF increases the existing pressure gradient between the cranial and the spinal compartments. This further predisposes the affected individual to brain herniation. Recognition of factors or procedures that potentiate the risk of brain herniation is important because the process is difficult to reverse and always has a grave prognosis (Kornegay *et al*., 1983; Cellio, 2001).

X-ray examination

In a study by Lawson *et al*. (1982), radiography of the calvarium was performed in 10 cats with cerebral meningioma. Three projections of the calvarium were obtained in most cats, including lateral, ventrodorsal and modified occipital. The most common finding, hyperostosis of the calvarium adjacent to the meningioma, was present in all but one cat.

Tumor density, resulting from partial calcification of the tumor, was apparent in varying degrees in all cases. Enlargement of the middle meningeal artery, resulting from enlargement of the vessel that feeds the tumor, was noted in three cats. Invasion of the meningioma, with bone destruction and pressure erosion of the calvarium was seen in only one cat.

Computed Tomography (CT)

Technical details

Computed tomography (CT) is a frequently used technique to detect and localize intracranial processes in small animals. The biggest asset of CT scanning is the fact that it is a noninvasive technique with superior soft tissue differentiation, and without superposition (Hathcock and Stickle, 1993). The differentiation of densities is a hundred times more precise than in the classical radiography (Delisle and Devauchelle, 1991). Computed tomography offers essential information for surgical biopsy or the removal of brain tumors: ac-

curate definition, localization and determination of accessibility. The information contained in CT scans also enables appropriate selection of animals for radiation therapy (LeCouteur *et al.*, 1983).

The ability to image in cross-section makes it possible to build up a three-dimensional picture. Modern CT scanners allow a choice of reconstruction algorithms to provide the optimal image, depending on the area or tissue of greatest interest. Because most algorithms are based on human calibration phantoms, the optimal reconstruction for small animals can often only be established on a trial-and-error base (Gielen *et al.,* 2003).

One of the most important indications to perform a CT scan is a *space-occupying* process, suspected after a neurological examination. A single lesion seen on a CT scan is most likely a brain tumor. Dogs showing multifocal neurological involvement are suspected of having an infectious or inflammatory disease process. Another indication is an anomaly of the ventricular system, for instance a congenital or acquired hydrocephalus. CT scanning is valuable in the assessment of head trauma, both for the accurate determination of the presence of skull fractures and for the assessment of intracranial hemorrhage (Jeffery *et al.*, 1992).

Lesions on CT scans are described as hyper-, iso- or hypodens, depending on their density relative to the surrounding tissues. Hypodensity of the parenchymal tissue is generally associated with edema, malacia, radiolucent fluid or fatty substances. Hyperdensity can be associated with inflammatory or neoplastic conditions, acute hemorrhage or calcification (Fike *et al*., 1981; Jeffery *et al*., 1992).

The entire CT scan must be carefully examined, with the following criteria being systematically evaluated: localization, orientation, mass effect, peritumoral edema, hydrocephalus, calcification, bone erosion or hyperostosis, pre-contrast density, size, shape, contrast-enhancement characteristics (degree, homogeneity, ring enhancement) and type of margination. Mass effect is defined as the displacement of the falx cerbri and/or the ventricular system. Peritumoral edema is defined as a hypodense area peripheral to the tumor (Turrel *et al*., 1986).

The CT scanning characteristics alone cannot be diagnostic of a particular lesion. The definitive diagnosis must rest on histopathological examination of sampled tissues (Jeffery *et al*., 1992).

Characteristics of brain tumors on CT images

The characteristics of the different types of brain tumors in dogs are summarized in Table 1.

On CT images, the height of the pituitary can be measured from the image of the spatial series that contains the largest cross section of the pituitary gland. On the same image, the edges of the brain are traced and the enclosed area is calculated by the computer. From the height of the pituitary and the area of the brain, the pituitary height/brain area [P/B] ratio can be calculated. The P/B ratio provides a valuable tool for the distinction between enlarged and normal-sized pituitary glands.

On routine contrast-enhanced CT images, microadenomas of the pituitary gland often are indistinguishable from nontumorous pituitary tissue because of isoattenuation. Therefore, dynamic CT examination of the pituitary is necessary. Dynamic contrast-enhanced CT includes a series of scans (dynamic series) of identical slice thickness at the same slice position through the center of the pituitary gland during and after IV injection of contrast medium. The pituitary gland appeared to be abnormal using dynamic CT in 45 of 55 dogs (82%) with pituitary-dependent hyperadrenocorticism (van der Vlught-Meijer *et al.,* 2003).

Other less frequently described intracranial tumors may show similar characteristics to the five primary brain tumors mentioned in Table 1, rendering definitive diagnosis difficult.

One case report of a primitive neuroectodermal tumor was observed as a hyperdense, well circumscribed mass with some peritumoral edema and mild contrast enhancement (Turrel *et al*., 1986).

Ependymomas have several presentations on CT images. According to Fike *et al*. (1981), ependymomas show essentially the same CT patterns as malignant astrocytomas. Turrel *et al*. (1986) described two ependymomas, one as a hyperdens mass causing a moderate mass effect and having minimal contrast enhancement with poorly defined tumor margins; the other ependymoma was described as having prominent peritumoral edema, moderate hydrocephalus and marked mass effect. It showed homogeneous contrast enhancement and well-defined tumor margins.

Neoplastic reticulosis is isodense on native CT images and has no mass effect or peritumoral edema. The tumor enhances uniformly and is well marginated (Turrel *et al*., 1986).

Table 1. Characteristics of primary brain tumors in dogs on CT images.

Characteristic	Meningioma	Astrocytoma	Oligodendroglioma	Choroid plexus papilloma	Pituitary tumor
Pre-contrast density	iso- or hyperdens	iso- or hyperdens	hypodens	hyperdens	iso- (or hyper)dens
Localization	rostral and caudal fossa	pros-, di-, mesenchephalon	prosenchephalon		sella turcica
Orientation	periphery of the theca				
Mass effect	possible	prominent	marked	absent to minimal	mild
Peritumoral edema	possible	marked	moderate	minimal	mild
Hydrocephalus		very rare		controversial	
Calcification	occasionally				occasionally
Hyperostosis	especially in cats				
Type of margination	well-defined	poorly-defined	poorly-defined	well-defined	
Size		usually large	large	usually small	
Shape	irregular, lobulated				
Contrast enhancement	marked	marked	mild	marked	minimal to marked
Post-contrast homogeneity	homogeneous		heterogeneous	homogeneous	homogeneous
Post-contrast type of margination				well-defined	well-defined
References	Turrel *et al.* (1986)	Fike *et al.* (1981)	LeCouteur *et al.* (1981)	LeCouteur *et al.* (1981)	Turrel *et al.* (1986)
	Gordon *et al.* (1994)	LeCouteur *et al.* (1981)	Turrel *et al.* (1986)	Turrel *et al.* (1986)	
		Turrel *et al.* (1986)		Jeffery *et al.* (1992)	

Magnetic resonance imaging (MRI)

Technical details

Magnetic resonance imaging (MRI), a non-invasive technique that provides accurate, detailed, anatomic images, has had a major impact in the diagnosis of human disease, and is starting to become more available in veterinary medicine.

Unlike in CT scanning, beam-hardening artifacts originating from thick compact bone do not occur in MRI. This makes MRI especially useful for imaging the middle and caudal fossae. Although cortical bone

cannot be critically assessed, and lesions causing bony lysis or calcification are better documented with CT, lesions affecting bone marrow are readily identified (Thomson *et al.*, 1993).

One main advantage of MRI versus CT is its higher sensitivity for subtle changes in soft tissue chemical properties, which means that infarcts and edema can be detected in an earlier stage. With MRI there is an ability to acquire images in any plane desired. Especially when repeated examinations are anticipated, the absence of ionizing radiation is an advantage over CT. The limitations are the higher cost and the limited availability. Metallic objects in the scan fields can cause severe distortion artifacts and MRI is more sensitive to motion artifacts. Special precautions have to be taken with metallic implants, as they can shift or heat during the process (Braund, 1994).

Relaxation is the process by which excited nuclei return to their original energy state. The relaxation characteristics of individual tissues determine signal intensity and contrast. The relaxation of hydrogen nuclei can be studied in two planes (transverse and longitudinal) with respect to the strong magnetic field created by the magnet. The longitudinal relaxation of hydrogen nuclei occurs relative to the main, external magnetic field. Relaxation in the longitudinal plane is characterized by a time constant, T1. Transverse relaxation occurs when hydrogen nuclei dephase or return their spins to a random state. Relaxation in the transverse plane is characterized by a time constant T2. Relaxation times vary for individual tissues of the body. The timing of radiofrequency (RF) pulse sequences can be adjusted to make T1-weighted (T1WI), T2-weighted (T2WI) or proton density (PDWI) images. On T1-weighted images, tissues with a short T1-time (fat, gadolinium contrast medium and proteinaceous fluid) have high signal intensity and are white, while tissues with long T1 times (other fluids, edema, air, bone and fast-flowing blood) have low signal intensity and appear dark. The converse is true with T2-weighting: tissues with long T2 times (fluid, edema) have high signal intensity and those with short T2 times (soft tissue, air, bone, and fast-flowing blood) have low signal intensity. In summary, T1WI provide good anatomic detail, while T2WI reflect pathological changes in tissues. PDWI measure the contribution of hydrogen nuclei (protons) to the MR signal rather than T1 or T2 effects. Protons in the liquid state add more to the MR image than those bound to solid tissues such as bone, fat and ligaments. Therefore, tissues containing abundant protons in the liquid state are intense on PDWI. Fluid appears dark, fat appears white, and grey matter appears brighter than white matter (Morrison, 1998a).

The T1-value of neoplasms is often prolonged due both to an increase in water content and a decreased degree of tissue organization. Therefore, the surrounding normal parenchyma appears whiter than the tumor in T1WI. In contrast, tumors generally appear whiter on T2WI. Peritumoral edema results in a distinct rim of hypointensity at the tumor/edema interface, apparently because of iron within macrophages at this level. Tumors may be better identified through the use of paramagnetic contrast agents such as gadolinium-diethylenetriaminepentacetic (Gd-DTPA). Maximal enhancement is noted in the first ten minutes with most tumors, with gradual subsequent wash-out of signal. Some presumably benign tumors (e.g. meningiomas) enhance uniformly, whereas malignant gliomas enhance peripherally (ring pattern) or heterogeneously (Thomson *et al.*, 1993).

MRI features evaluated for intracranial tumors include physical features such as intra-axial or extra-axial origin, anatomic site, shape, presence of mass effect, presence of ventricular enlargement and growth pattern. Growth pattern refers to growth of the tumor relative to the surrounding tissues, including physical displacement or replacement (i.e. invasion) by the mass or smaller tumor extensions into adjacent regions. Features more specific to MRI included signal intensity, gadolinium enhancement pattern and edema. Tumor signal intensity was described as hypointense, isointense, hyperintense or mixed compared to normal-appearing cortical gray matter (Thomas *et al*., 1996; Kraft *et al*., 1997).

Characteristics of brain tumors on MRI images

Although various types of brain tumors have been characterized by MRI, the degree of correlation between MRI and histologic findings has not been clarified (Thomas *et al*., 1996).

Tables 2 and 3 contain the characteristics of different tumor types of MRI images in dogs and cats, respectively.

In humans, the dural tail is a sign seen on contrast enhanced T1-weighted magnetic resonance images. This finding is considered specific for meningioma. The dural tail is a linear enhancement of thickened dura mater adjacent to an extra-axial mass seen on Gd-DTPA enhanced T1WI. A number of criteria for diagnosing a dural tail have been described: it should be continuous with the associated extra-axial mass, it

Table 2. Characteristics of brain tumors in dogs on MRI images.

Characteristic	Meningioma	Astrocytoma	Oligodendroglioma	Choroid plexus papilloma	Pituitary tumor
T1WI	iso- or hypointense	Iso- (benign) or hypointense	hypointense	hyperintense or mixed hyper/iso	hypointense
T2WI	iso- or hyperintense	hyperintense	hyperintense	hyperintense or mixed hyper/iso	iso-, hyperintense or mixed
PDWI	iso- or hyperintense	hyperintense	isointense	hyperintense or mixed hyper/iso	iso-, hyperintense or mixed
Localization	rostral and caudal fossa	pros-, di-, mesenchephalon	prosenchephalon	interventricular foramen or cerebellopontine angle	sella turcica
Orientation	broad based along falx/dura				
Mass effect	mild		marked	marked	
Edema	absent to marked	mild or marked (higher-grade)	mild or absent	mild or absent	absent or mild
Hydrocephalus	rare	occasionally	occasionally	frequently	occasionally
Calcification		occasionally		rare	
Hemorrhage		occasionally	occasionally	multifocal (50%)	occasionally
Type of margination	smooth to irregular	poorly defined		irregular	poorly defined
Contrast enhancement	marked	variably intense		marked	mild to marked
Post-contrast homogeneity	uniform (non-uniform)	non-uniform		uniform	uniform
Ring enhancement	occasionally	occasionally	frequently		
References	Hathcock, 1996 Thomas *et al*., 1996 Kraft *et al.*, 1997	Kraft *et al.*, 1997	Kraft *et al.*, 1997	Thomas *et al.*, 1996 Kraft *et al.*, 1997	Thomas *et al.*, 1996 Kraft *et al*., 1997

Table 3. Characteristics of brain tumors in cats on MRI images.

Characteristic	Meningioma	Lymphoma	Gliomas	Pituitary tumor
T1WI	iso- or hypointense, homogeneous	iso- or hypointense, homogeneous	hypointense	isointense, heterogeneous
T2WI	hyperintense, heterogeneous	hyperintense, heterogeneous	hyperintense	hypointense, heterogeneous
PDWI	hyperintense	hyperintense, heterogeneous		
Localization	extra-axial	extra- or intra-axial	intra-axial	sella turcica
Orientation	broad based			
Mass effect	frequently	frequently	occasionally	
Edema	mild	moderate to marked	mild to moderate	absent
Hydrocephalus	frequently	rare	occasionally	absent
Calcification	occasionally	absent	absent	absent
Hemorrhage	occasionally	absent	absent	absent
Type of margination	regular, distinct			regular, distinct
Contrast enhancement	marked	marked	variably intense	moderate
Post-contrast homogeneity	homo-or heterogeneous	heterogeneous		heterogeneous
Ring enhancement	rare	absent	frequently	frequently
Reference	Troxel *et al.,* 2004	Troxel *et al.,* 2004	Troxel *et al.,* 2004	Troxel *et al.,* 2004

should enhance to an equal or greater degree than the associated mass and it should be seen in at least two contiguous slices or in two imaging planes to preclude confusion with vascular structures. Trauma, surgery, hemorrhage, infection and metastasis have all been reported to cause meningeal enhancement following contrast medium administration (Graham *et al.*, 1998). MR examinations of 18 dogs and 4 cats for which a definitive diagnosis was available were reviewed in an article by Graham *et al*. (1998). Seventeen of the 22 patients had an intracranial neoplasm, 10 of which were meningiomas, and the other 5 patients had inflammatory CNS disease. The dural tail sign appears to occur relatively commonly with canine and feline meningioma, although the rate of detection varied from 40 to 80%.

The only ependymoma described after MRI analysis was a thin-walled non-enhancing proteinaceous cyst effacing the frontal horn of a lateral ventricle without evidence of edema. This mass was hyperintense on PDWI and T2WI, and isointense on T1WI (Kraft *et al.,* 1997).

Ultrasonography of the brain

Ultrasonography of the brain is an easy, safe, less expensive procedure which provides a rapid, repeatable, non-invasive method for evaluating the brain (Spaulding and Sharp, 1990).

The brain can be imaged through craniotomy defects, open fontanelles or some larger neural foramina. Some animals have sufficiently thin bone in the tem-

poral region to allow transcranial imaging without a craniotomy defect (Braund, 1994).

The most common application for brain ultrasonography is to determine the size of lateral ventricles in small breed dogs with suspected hydrocephalus. The second most common application is to evaluate the brain in animals with suspected intracranial neoplasia. Most neoplasms appear hyperechoic. A technique for ultrasound-guided biopsy has been developed for use in dogs (Thomas *et al*., 1993). Intraoperative ultrasonography may be used to guide surgical biopsy or the excision of intracranial masses (Gallagher *et al.*, 1995). After radiation or chemotherapy, the size of a biopsied mass may be monitored by ultrasonography. The site of a surgically excised mass can be checked over time to assess tumor growth. No adverse effects or contraindications are known in diagnostic imaging of the brain using ultrasound (Tucker and Gavin, 1996).

Scintigraphy

Nuclear medicine (gamma scintigraphy) has been used for diagnostic brain imaging in veterinary patients for over 20 years. Brain scintigraphy yields both anatomic and functional information (Tucker and Gavin, 1996).

When combined with historical information, neurological evaluation, and appropriate laboratory tests, brain scintigraphy can help localize lesions and suggest a diagnosis. However, planar brain scintigraphy is primarily a test of the functional integrity of the blood-brain barrier rather than a morphologic imaging technique such as computed tomography or magnetic resonance imaging (Dykes *et al.*, 1994).

The diagnostic strength of brain scintigraphy is the ability to confirm the presence of suspected intracranial lesions. Similar to other advanced imaging modalities, brain scintigraphy is not specific in determining the exact etiologic origin of a lesion, but may yield a characteristic pattern or location of activity that supports a specific disease diagnosis (Tucker and Gavin, 1996).

Scintigraphy of the brain is indicated when there is suspected intracranial disease, and when CT or MRI is either unavailable or cost-prohibitive.

The main limitation of planar scintigraphy is the low sensitivity for early intracranial or spinal cord disease that is obscured by the superimposition of overlying structures. Newer, tomographic, scintigraphy techniques show promise for increasing the sensitivity of scintigraphy procedures (Braund, 1994). Single photon emission computed tomography (SPECT) and positron emission tomography (PET) are nuclear medicine procedures that produce tomographic images of the brain with superior spatial and contrast resolution, in addition to providing more precise localization of the lesion.

A retrospective study from Dykes *et al.* (1994) showed that focal brain scintigrams had 75% sensitivity and 90% specificity for any focal brain disease. The sensitivity and specificity of a focal scintigraphic lesion for a brain tumor was 72% and 82%, respectively.

Brain biopsy

Technical details

Many intracranial diseases can be accurately and reliably located with advanced imaging techniques such as CT and MRI. However, a definitive diagnosis can only be reached by obtaining a tissue sample for histopathological examination.

A variety of techniques have been reported in the medical neurosurgical literature: open surgical (Niebauer *et al.*, 1991), free-hand needle (Marshall *et al.*, 1974), stereotactic (Heath *et al.*, 1961), ultrasound-guided (Thomas *et al.*, 1993), CT-guided (Harari *et al.*, 1993) and MRI-guided (Bradbord *et al.*, 1987; Maciunas and Galloway, 1989) brain biopsy. In veterinary medicine the free-hand needle technique and the stereotactic brain biopsy have been described.

CT-guided free-hand needle biopsy

As part of an animal model project evaluating the selective radiation therapy of brain tumors in dogs, Harari *et al.* (1993) examined a contrast-enhanced, CT-guided, free-hand needle biopsy in eight dogs with intracranial mass lesions. In three of eight dogs, a histologic biopsy diagnosis of neoplasia was obtained. In two of these patients, the diagnosis was confirmed by necropsy. Seven of eight dogs had mild, transient complications after biopsy.

The results of this study indicate that the needle biopsy was safe, but it provided a low diagnostic yield. The reasons for the poor success rate could have been the misinterpretation of contrast-enhanced CT images, the movement of the biopsy needle after imaging and before sampling, technical errors in using the biopsy needle, normal cellular foci within the tumor, the easier aspiration of normal peritumor cells than of neoplastic cells, inadequate sample size, and

inexperience in evaluating needle biopsy samples of brain tissue.

In human medicine the results are more promising. In an article by Duquesnel *et al.* (1995), the results of CT-guided needle biopsy of intracranial tumors in 118 human patients were evaluated. For superficial and large tumors (larger than 2 cm in diameter) it is a simple, fast and effective procedure. In this study the pathological diagnosis was obtained in 89% of the cases. This technique is less expensive but theoretically more likely to induce complications than a stereotactic method. During the procedure the normal brain tissue overlying the lesion can be traumatiszed and the lack of a fixation device risks a leucotomy effect. These possible complications depend on the size and location of the tumor.

Stereotactic CT-guided brain biopsy (SCTGBB)

Another technique for brain biopsy is the stereotactic CT-guided biopsy of intracranial lesions. Several human instruments have been modified to make it compatible with CT-target localization in the dog.

Moissonnier *et al.* (2000, 2002) presents a modified Laitinen's stereo stereoadapter initially designed for human patients. The procedure involves four steps. With practice, the entire procedure (skin incision to the end of suture) can be carried out within 1 hour.

Two points are critical for the success of the procedure. Correct positioning of the head in the device is of particular importance because it has to be performed twice. The choice of the craniotomy site is a second crucial step in terms of limiting trauma during the passage through healthy brain tissue. A brain lesion exceeding 6 mm in diameter can be sampled with this device (Moissonnier *et al.*, 2000).

Hemorrhage, temporary neurological deficits and death were the complications encountered in the present study. Mortality (2 of 23 dogs) and morbidity (6 of 23 dogs) rates are high when compared to those described in the human literature. The differences in morbidity can be related to epidemiological and technical considerations. The diagnosis of brain tumors in animals usually occurs late on in the progression of the disease. Furthermore, SCTGBB is carried out in the dog without precise evaluation of the tumour vascularization, which could enhance the safety and accuracy of the procedure. For financial reasons, it was not possible to check for post-biopsy hemorrhage by CT immediately postoperative. Two patients (8%) had lethal complications related to the biopsy of highly vascularized brainstem tumors.

SCTGBB was satisfactory in obtaining a brain tumor sample in 95% of the cases. The accuracy of brain biopsy depends on the experience of the clinicians performing the biopsy, the characteristics of the mass (size, location, definition, texture) and the device used. The authors consider that the early cytological assessment of the brain sample is important. This gives the surgeon the opportunity to perform another biopsy while the dog is still in the operating theatre. The cytological results correlated with the histopathological diagnosis in 69% of the present cases. Compared to other studies (Vernau *et al.*, 2001), this percentage is low, probably because the surgeon and not a cytopathologist evaluated the sample in this study (Moissonnier *et al.*, 2002).

Koblik *et al.* (1999a and b) describes the results of SCTGBB performed in 50 dogs using a modified Pelorus Mark III Stereotactic System (PMIIISS). The Pelorus Mark III Stereotactic System has been promoted for being relatively inexpensive, mechanically less complex, and easier to use than other commercial stereotactic systems. Several modifications needed to take place to get a good fixation of the dog's head in the device. The modified device could be attached and secured to the heads of dogs varying in size from 2 to 47 kg (Koblik *et al.*, 1999a).

The stereotactic brain biopsy diagnosis was compared with that from surgical resection or at necropsy. In 91% of 22 dogs, a correct diagnosis was achieved. In 5 of 41 dogs, postoperative complications such as epistaxis, seizures, intracranial hemorrhage and cerebellar herniation were detected.

It is recommended to obtain multiple tissue samples to prevent failed or inconclusive biopsies. Sampling errors can be caused by lesion heterogeneity and technical problems.

On the basis of these results, we can conclude that SCTGBB using a modified PMIIISS is a safe and effective method for obtaining tissue samples for the accurate neuropathologic diagnosis of brain lesions (Koblik *et al.*, 1999b).

CONCLUSION

On the basis of signalment, history and clinical signs it is possible to localize a problem to the brain. However, further diagnostic workup is essential for obtaining a diagnosis of neoplasia. Cerebrospinal fluid (CSF) analysis can be a valuable additional tool, though it will not always be conclusive. Some inflammatory processes in the brain can cause identical

changes in the CSF as a neoplastic lesion. On the other hand, the CSF of an animal with a brain tumor can be completely normal. Moreover, this procedure is not without risk. Computed Tomography and Magnetic Resonance Imaging confirm the suspicion of an intracranial mass. To obtain a definitive answer, with an exact histopathological diagnosis, a biopsy sample of the mass is crucial. Different procedures for obtaining a biopsy sample are described, including CT-guided free-hand needle biopsy and stereotactic CT-guided brain biopsy.

LITERATURE

Bagley R.S. (1995). Diseases of the brain. In: Wheeler S.J. (editor). *BSAVA Manual of small animal neurology, second edition*. BSAVA, Kingsley House, Church Lane, Shurdington, Cheltenham, Gloucestershire, 112-124.

Bagley R.S., Gavin P.R., Moore M.P., Silver G.M., Harrington M.L., Connors R.L. (1999). Clinical signs associated with brain tumors in dogs: 97 cases (1992-1997). *Journal of the American Veterinary Medical Association 215*, 818-819.

Bailey C.S. en Higgins R.J. (1986). Characteristics of cisternal cerebrospinal fluid associated with primary brain tumors in the dog: a retrospective study. *Journal of the American Veterinary Medical Association 188*, 414-417.

Braund K.G. (1994). *Clinical syndromes in veterinary neurology, second edition.* Mosby -Year Book, Inc. (editor), St. Louis, Missouri, 342-349.

Cellio B.C. (2001). Collecting, processing and preparing cerebrospinal fluid in dogs and cats. *Compendium on Continuing Education for the Practicing Veterinarian 23*, 786-792.

Cook JR, DeNicola DB (1988). Cerebrospinal fluid. *Veterinary Clinics of North America: Small Animal Practice 18*, 475-498.

Delisle F., Devauchelle P. (1991). Le "scanner" en médecine vétérinaire. *Pratique Medicale et Chirurgicale de l'Animal de Compagnie 26*, *supplement*, 12-19.

Duquesnel J., Turjman F., Hermier M., Bascoulergue Y., Jouvet A., Gervesy G., Tournut P. (1995). CT-guided needle biopsy of intracranial tumours: results in 118 consecutive patients. *Acta Neurochirurgica 63*, *supplement*, 16-19.

Dykes N.L., Warnick D.L., Summers B.A., Wallace R.J., Kallfelz F.A. (1994). Retrospective analysis of brain scintigraphy in 116 dogs and cats. *Veterinary Radiology & Ultrasound 35*, 56-65.

Fike J.R., LeCouteur R.A., Cann C.E., Pflugfelder C.M. (1981). Computerized tomography of brain tumors of the rostral and middle fossas in the dog. *American Journal of Veterinary Research 42*, 275-281.

Gallagher J.G., Penninck D., Boudrieau R.J., Schelling S.H., Berg J. (1995). Ultrasonography of the brain and vertebral canal in dogs and cats: 15 cases (1988-1993). *Journal of the American Veterinary Medical Association 207*, 1320-1324.

Gielen I., Van Caelenberg A., Van Bree H. (2003). Computed tomography in small animals. Part 1. Technical aspects. *Vlaams Diergeneeskundig Tijdschrift 72,* 158-167.

Gordon L.E., Thacher C., Matthiesen D.T., Joseph R.J. (1994). Results of craniotomy for the treatment of cerebral meningioma in 42 cats. *Veterinary Surgery 23*, 94-100.

Graham J.P., Newell S.M., Voges A.K., Roberts G.D., Harrison J.M. (1998). The dural tail sign in the diagnosis of meningiomas. *Veterinary Radiology & Ultrasound 39,* 297-302.

Harari J., Moore M.M., Leathers C.W., Roberts G.D., Gavin P.R. (1993). Computed tomographic-guided, free-hand needle biopsy of brain tumours in dogs. *Progress in Veterinary Neurology 4*, 41-44.

Hathcock J.T., Stickle R.L. (1993). Principles and concepts of computed tomography. *Veterinary Clinics of North America: Small Animal Practice 23*, 399-415.

Hoerlein B.F. (1971). *Canine neurology: diagnosis and treatment, second edition.* W.B. Saunders Company, Philadelphia, London, Toronto, 26-50.

Jeffery N. D., Thakkar C.H., Yarrow T.G. (1992). Introduction to computed tomography of the canine brain. *Journal of Small Animal Practice 33*, 2-10.

Koblik P.D., LeCouteur R.A., Higgins R.J., Fick J., Kortz G.D., Sturges B.K., Pascoe P.J. (1999a). Modification and application of a Pelorus Mark III stereotactic system for CT-guided brain biopsy in 50 dogs. *Veterinary Radiology & Ultrasound 40*, 424-433.

Koblik P.D., LeCouteur R.A., Higgins R.J., Bollen A.W., Vernau K.M., Kortz G.D., Ilkiw J.E. (1999b). CT-Guided brain biopsy using a modified Pelorus Mark III stereotactic system : experience with 50 dogs. *Veterinary Radiology & Ultrasound 40*, 434-440.

Kornegay J.N., Oliver J.E., Gorgacz E.J. (1983). Clinicopathologic features of brain herniation in animals. *Journal of the American Veterinary Medical Association 182*, 1111-1116.

Kraft S.L., Gavin P.R., DeHaan C., Moore M., Wendling L.R., Leathers C.W. (1997). Retrospective review of 50 canine intracranial tumors evaluated by magnetic resonance imaging. *Journal of Veterinary Internal Medicine 11*, 218-225.

Lawson D.C., Burk R.L., Prata R.G. (1984). Cerebral meningioma in the cat: diagnosis and surgical treatment of ten cases. *Journal of the American Animal Hospital Association 20*, 333-342.

LeCouteur R.A., Fike J.R., Cann C.E., Pedroia V.G. (1981). Computed tomography of brain tumors in the caudal fossa of the dog. *Veterinary Radiology 22*, 244-251.

LeCouteur R.A., Fike J.R., Cann C.E., Turrel J.M., Thompson J.E., Biggart J.F. (1983). X-ray computed tomography of brain tumors in cats. *Journal of the American Veterinary Medical Association 183*, 301-305.

LeCouteur R.A. (1999). Current concepts in the diagnosis and treatment of brain tumours in dogs and cats. *Journal of Small Animal Practice 40*, 411-416.

Moissonnier P., Bordeau W., Delisle F., Devauchelle P. (2000). Accuracy testing of a new stereotactic CT-guided brain biopsy device in the dog. *Research in Veterinary Science 68*, 243-247.

Moissonnier P., Blot S., Devauchelle P., Delisle F., Beuvon F., Boulha L., Colle M-A., Lefrancois T. (2002). Stereotactic CT-guided brain biopsy in the dog. *Journal of Small Animal Practice 43*, 115-123.

Moore M.P., Bagley R.S., Harrington M.L., Gavin P.R. (1996). Intracranial tumors. *Veterinary Clinics of North America: Small Animal Practice 26*, 759-777.

Morrison W.B. (1998a). Alternate imaging for the diagnosis of cancer. In: Morrison W.B. (editor). *Cancer in dogs and cats: medical and surgical management.* First edition, Williams & Wilkins, Baltimore, Maryland, 206-209.

Morrison W.B. (1998b). Cancer affecting the nervous system. In: Morrison W.B. (editor). *Cancer in dogs and cats: medical and surgical management.* First edition, Williams & Wilkins, Baltimore, Maryland, 655-665.

Rand J.S., Parent J., Percy D., Jacobs R. (1994). Clinical, cerebrospinal fluid, and histological data from thirty-four cats with primary noninflammatory disease of the central nervous system. *Canadian Veterinary Journal 35,* 257-292.

Spaulding K.A., Sharp N.J.H. (1990). Ultrasonographic imaging of the lateral cerebral ventricles in the dog. *Veterinary Radiology 31*, 59-64.

Thomas W.B., Sorjoren D.C., Hudson J.A., Cox N.R. (1993). Ultrasound-guided brain biopsy in dogs. *American Journal of Veterinary Research 54*, 1942-1947.

Thomas W.B., Wheeler S.J., Kramer R., Kornegay J.N. (1996). Magnetic resonance imaging features of primary brain tumors in dogs. *Veterinary Radiology & Ultrasound 37*, 20-27.

Thomson C.E., Kornegay J.N., Burn R.A., Drayer B.P., Hadley D.M., Levesque D.C., Gainsburg L.A., Lane S.B., Sharp N.J.H., Wheeler S.J. (1993). Magnetic resonance imaging - A general overview of principles and examples in veterinary neurodiagnosis. *Veterinary Radiology & Ultrasound 34*, 2-17.

Tucker R.L., Gavin P.R. (1996). Brain imaging. *Veterinary Clinics of North America: Small Animal Practice 26*, 735-750.

Turrel J.M., Fike J.R., LeCouteur R.A., Higgins R.J. (1986). Computed tomographic characteristics of primary brain tumors in 50 dogs. *Journal of the American Veterinary Medical Association 188*, 851-856.

Van der Vlught-Meijer R.H., Meij B.P., Van den Ingh T.S.G.A.M., Rijnberk A., Voorhout G. (2003). Dynamic Computed Tomography of the pituitary gland in dogs with pituitary-dependent hyperadrenocorticism. *Journal of Veterinary Internal Medicine 17*, 773-780.

Vandevelde M. (1984). Brain tumors in domestic animals: an overview. Proceedings, Conference on brain tumors in man and animals, research triangle park, North Carolina, September 5-6, 1984.

Vernau K.M., Higgins R.J., Bollen A.W., Jiminez D.F., Anderson J.V., Koblik P.D., LeCouteur R.A. (2001). Primary canine and feline nervous system tumors: intraoperative diagnosis using the smear technique. *Veterinary Pathology 38*, 47-57.