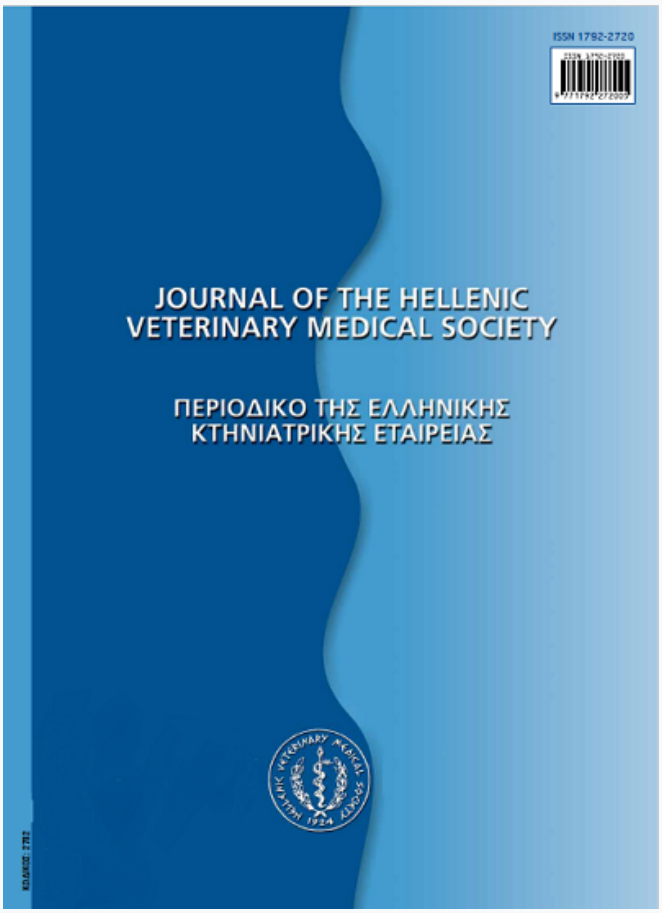
Journal of the Hellenic Veterinary Medical Society

Vol 64, No 3 (2013)



Canine primary encephalopathies: a retrospective study of 48 cases (2008-2012)

Z. S. POLIZOPOULOU (Ζ.Σ. ΠΟΛΥΖΟΠΟΥΛΟΥ), E. ELEKIDOU (Ε. ΕΛΕΚΙΔΟΥ), M. N. PATSIKAS (Μ.Ν. ΠΑΤΣΙΚΑΣ), G. BRELLOU (Γ. ΜΠΡΕΛΛΟΥ), N. SOUBASIS (Ν. ΣΟΥΜΠΑΣΗΣ)

doi: 10.12681/jhvms.15498

J HELLENIC VET MED SOC 2013, 64(3): 183-192
ΠΕΚΕ 2013, 64(3): 183-192

Research article
Ερευνητικό άρθρο

Canine primary encephalopathies: a retrospective study of 48 cases (2008-2012)

Polizopoulou Z.S.[1], Elekidou E.[2], Alamenou P.[2], Patsikas M.N.[2], Brellou G.[3], Soubasis N.[2]

[1]Diagnostic Laboratory, Faculty of Veterinary Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece

[2]Clinic of Companion Animals, Faculty of Veterinary Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece

[3]Laboratory of Pathology, Faculty of Veterinary Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece

Οργανικές εγκεφαλοπάθειες στο σκύλο: αναδρομική μελέτη 48 περιστατικών (2008-2012)

Πολυζοπούλου Ζ.Σ.[1], Ελεκίδου Ε.[2], Αλαμένου Π.[2], Πατσίκας Μ.Ν.[2], Μπρέλλου Γ.[3], Σούμπασης Ν.[2]

[1]Διαγνωστικό Εργαστήριο, Κτηνιατρική Σχολή, Αριστοτέλειο Πανεπιστήμιο Θεσσαλονίκης, Θεσσαλονίκη

[2]Κλινική Ζώων Συντροφιάς, Κτηνιατρική Σχολή, Αριστοτέλειο Πανεπιστήμιο Θεσσαλονίκης, Θεσσαλονίκη

[3]Εργαστήριο Παθολογικής Ανατομικής, Κτηνιατρική Σχολή, Αριστοτέλειο Πανεπιστήμιο Θεσσαλονίκης, Θεσσαλονίκη

ABSTRACT. A retrospective study was performed on 48 dogs with primary encephalopathies, admitted during a 5-year period (2008-2012). Their age ranged from 2 months to 19 years, the majority being older than 10 years. Genders were almost equally distributed and most animals were purebreds or crossbreds. Onset of neurological signs was acute (11/48), subacute (12/48) or chronic (24/48). Lesion localization was focal in 31 and multifocal in 17 dogs. The cerebrum and brainstem were the most common focal localizations, while cerebellar lesions were recorded only in 4 dogs. An aetiologic diagnosis was established in 29 dogs and included primary (8/29) or metastatic neoplasia (2/29), encephalitis of variable etiology (9/29), congenital or inherited diseases (6/29), senile cognitive dysfunction (3/29) and ischaemic encephalopathy (1/29). In the remaining 19 dogs, aetiology of intracranial dysfunction was not determined; however a tentative diagnosis was speculated in eight of these cases and included breed specific and viral encephalitis, neoplasia, ischaemic encephalopathy and inherited disease. Most dogs were euthanized due to the debilitating neurological signs (24/48) or died from complications of their illness (13/48). Six animals are still alive with symptomatic medical treatment and supportive nursing care and 5 were lost to follow up.

Keywords: brain tumour, cognitive dysfunction,, dog, encephalitis, inherited encephalopathy

Correspondence: Z.S. Polizopoulou,
Diagnostic Laboratory, Faculty of Veterinary Medicine,
Aristotle University of Thessaloniki, 11, Voutyra str., 54627 Thessaloniki, Greece.
E-mail: poliz@vet.auth.gr

Αλληλογραφία: Ζ.Σ. Πολυζοπούλου,
Διαγνωστικό Εργαστήριο, Κτηνιατρική Σχολή,
Αριστοτέλειο Πανεπιστήμιο Θεσσαλονίκης, Σταύρου Βουτυρά 11, 54627 Θεσσαλονίκη.
E-mail: poliz@vet.auth.gr

Date of initial submission: 20 March 2013
Date of revised submission: 28 May 2013
Date of acceptance: 29 May 2013

Ημερομηνία αρχικής υποβολής: 20 Μαρτίου 2013
Ημερομηνία αναθεωρημένης υποβολής: 28 Μαΐου 2013
Ημερομηνία αποδοχής: 29 Μαΐου 2013

ΠΕΡΙΛΗΨΗ. Η παρούσα αναδρομική μελέτη αφορά σε 48 περιστατικά σκύλων, με κλινική εικόνα οργανικής εγκεφαλοπάθειας, που είχαν προσκομιστεί στην Κλινική Ζώων Συντροφιάς της Κτηνιατρικής Σχολής Α.Π.Θ. στο διάστημα της τελευταίας πενταετίας (2008-2012). Οι περισσότεροι σκύλοι ήταν ενήλικοι, μάλιστα υπερήλικοι (ηλικίας άνω των 10 ετών), και ανήκαν σε καθαρόαιμες φυλές ή μιγάδες τους. Η εκδήλωση των νευρολογικών διαταραχών ήταν απότομη σε 11, υποξεία σε 12 και προοδευτική σε 24 ζώα. Η νευροανατομική εντόπιση των αλλοιώσεων ήταν εστιακή σε 31 σκύλους και στην πλειονότητά αφορούσε στα ημισφαίρια και στο στέλεχος του εγκεφάλου, ενώ μόνο σε 4 περιστατικά διαπιστώθηκε παρεγκεφαλιδικό σύνδρομο. Οι υπόλοιποι 17 σκύλοι εκδήλωσαν συμπτωματολογία διάχυτης εγκεφαλοπάθειας. Η αιτιολογική διάγνωση ήταν εφικτή σε 29 περιστατικά και περιλάμβανε τα νεοπλάσματα (πρωτογενή και μεταστατικά) του εγκεφάλου (10/29), την εγκεφαλίτιδα διάφορης αιτιολογίας (9/29), τα συγγενή και κληρονομικά νοσήματα (6/29) και τη ισχαιμική εγκεφαλοπάθεια (1/29). Στις λοιπές περιπτώσεις δεν προσδιορίστηκε το αίτιο της εγκεφαλοπάθειας, αν και σε 8 σκύλους υπήρξαν ενδείξεις της αιτιολογίας της. Οι περισσότεροι σκύλοι πέθαναν (13/48) από επιπλοκές της εγκεφαλοπάθειας ή τούς έγινε ευθανασία (24/48) λόγω της βαρύτητας της κλινικής τους εικόνας. Έξι από αυτούς ζουν μέχρι σήμερα με συμπτωματική και υποστηρικτική θεραπεία, ενώ για πέντε ζώα δεν είναι γνωστό κανένα νεότερο δεδομένο.

Λέξεις ευρετηρίασης: γνωστική δυσλειτουργία, εγκεφαλίτιδα, κληρονομικές εγκεφαλοπάθειες, νεοπλάσματα, σκύλος

INTRODUCTION

Encephalopathies are serious, life-threatening neurological disorders often encountered by veterinarians in clinical practice. They are manifested by severe clinical signs (paralysis, loss of vision, dysphagia, seizures, compulsive walking-circling), while frequent and often irreversible loss of cognitive function ultimately destroys the long-established bond between owners and their dogs (Chrisman, 1991). The initial clinical assessment is crucial in determining localization of the lesion and hypothesizing on its potential aetiology. The differential diagnosis is based on interpretation of current knowledge of disease characteristics coupled with information obtained from the patient's history, the clinical examination and the specific paraclinical tests. Often, this approach leads to an accurate final diagnosis, which indicates its importance in veterinary practice (Dewey and Bailey, 2008; Thomas, 2010a).

Objective of the present retrospective study is to describe clinical presentation, diagnostic approach, follow up and outcome in 48 dogs with signs of intracranial disease. All animals were brought for examination at the Clinic of Companion Animals of the Faculty of Veterinary Medicine of the University of Thessaloniki during the period 2008-2012.

MATERIALS AND METHODS

The study population included dogs with signs indicative of intracranial disease, which were admitted for examination at the Clinic of Companion Animals of the Faculty of Veterinary Medicine of the University of Thessaloniki during the period 2008-2012. Dogs suffering from head trauma, as well as those diagnosed (during the initial clinical and clinicopathological evaluation) with metabolic or toxic encephalopathies and/or idiopathic epilepsy were excluded from the study. After reviewing the respective records, 48 cases fulfilling above criteria were identified; of these, a final diagnosis was available in only 29 animals (Table 1, cases 1-29); in the remaining 19 animals, only a tentative diagnosis was available (Table 1, cases 30-48).

Data available for all dogs included information regarding their lifestyle, vaccination status, onset and progression of clinical signs, medical history and results of neuroanatomic lesion localization within the cranial vault (cerebrum, rostral or caudal brainstem, cerebellum).

In all dogs, the clinicopathological tests performed included a complete blood count, a blood serum biochemistry profile (total protein, albumin, glucose, cholesterol, triglyceride concentration, alkaline phosphatase activity, alanine aminotransferase, calcium, phosphorus, sodium, potassium concentration).

In some cases, analysis of cerebrospinal fluid samples concentration collected from the animal's *cisterna magna* had also been performed, which included macroscopic evaluation, total and differential cell counts and measurement of albumin concentration. Diagnostic imaging modalities, applied under general anesthesia in some of the patients, included computed tomography (CT), magnetic resonance imaging (MRI) and ultrasonography (US).

Follow-up of patients (where applicable) had been performed by sequential re-examinations, in order to evaluate the development of the problem and the efficiency of medical and/or supportive physical therapy. Physical treatment included standard supportive treatment for recumbent/severely paretic animals (assisted feeding and drinking, soft bedding, cleanliness), along with physical therapy (Drum, 2010). In dogs that died or were euthanized due to the severity of their disorder, data from post-mortem gross pathological examination and/or histopathological examination were also taken into account if available.

RESULTS

Of the animals in the study, 7 dogs were younger than one year; of the remaining 41 who were adults, most (27/41) were older than 10 years. Twenty-three dogs were males and 25 were females, whilst 24 animals were purebreds, 9 were crossbreds and 15 were mixed breed dogs.

Onset of neurological signs was reported to have been acute (within 24-48 hours) in 11 dogs, subacute (within 2-15 days) in 12 dogs and over a period of >15 days in 24 animals, whilst it was unknown in one dog. Moreover, 31 dogs presented signs compatible with a single or focal intracranial lesion, whilst in the remaining 17 diffuse neurological dysfunction was evident, suggesting multifocal brain involvement or secondary cerebral oedema (Table 1). In the 31 dogs with a single or focal intracranial lesion, lesions were neuroanatomically localized at the cerebrum (forebrain) in 15 animals, at the brainstem in 12 and at the cerebellum in 4 (Table 1). During the initial clinical assessment, various concurrent medical conditions were identified in 32 dogs (Table 1); in brief, 7 dogs had dermatological problems, 6 had cardiac disorders, 6 had mammary neoplasia, 5 had ophthalmologic abnormalities, 3 had gastrointestinal, 2 upper respiratory disease, 2 had mitral valve endocardiosis and 1 bilateral patellar subluxation.

A final diagnosis was reached in 29 cases. Of these, ten dogs were diagnosed with intracranial neoplasia, primary in eight animals and secondary or metastatic in two animals. Tumour detection was achieved by computed tomography in two animals, by magnetic resonance imaging in five animals and by histopathological examination of tissue samples collected post-mortem in three animals. Two of the primary neoplasms were classified histopathologically, one was an oligodendroglioma and the other a transitional meningioma (Table 1, cases 22 and 24, respectively). In the remaining dogs with primary brain tumours, which were euthanized or received a supportive welfare treatment, no post-mortem examination was performed. In the two dogs that had developed metastatic intracranial disease, the primary tumours were identified as adenocarcinomas originating from the liver and the nasal cavities, respectively. In the former animal, there was no evidence of liver disease during clinicopathological evaluation, whilst in the latter there was gross distortion of the facial bones and intermittent mucopurulent nasal discharge (Table 1, cases 20 and 21, respectively).

Moreover, in the other 19 dogs, the diagnosis was as follows; nine dogs were diagnosed with encephalitis of varying aetiology (viral or idiopathic), six with congenital or inherited disorders, three with senile cognition dysfunction and one with ischaemic encephalopathy (Table 1).

A final diagnosis was not established in 19 dogs, as their owners had declined to pursue diagnostic procedures in these animals. A tentative diagnosis was made in eight animals by deduction and integration of information collected from the history and the clinical findings. Potential diagnoses included breed-specific or infectious encephalitis, primary or metastatic neoplasia, ischaemic encephalopathy and genetic disorders.

Finally, follow-up details have been available for 41 animals. Of these, 24 dogs were euthanized due to debilitating neurological signs and poor prognosis of the main problem, 11 died from unrelated conditions or from consequences of the neurological problem, whilst six animals were still alive at the time of writing up this paper (Table 1).

Table 1. Details of 48 dogs with primary encephalopathy brought for examination at the Clinic of Companion Animals of the Faculty of Veterinary Medicine of the University of Thessaloniki during the period 2008 to 2012.

Case	Age[1]	Breed	S[2]	Reason for admission	Onset of signs[3]	Lesion localization	Differential diagnosis	Final diagnosis (diagnostic procedure by which achieved)[4]	Concurrent problem(s)	Treatment	Outcome[5]
1	0.7	Chihuahua	M	Visual dysfunction	Chronic (4 m)	Cerebrum	Hydrocephalus, cranial trauma	Hydrocephalus (MRI)	None	Medical	Stable after 1.5 y
2	0.4	Mongrel	F	Poor growth, seizures, behavioural change	Chronic (1 m)	Cerebrum	Hydrocephalus, storage disease, encephalitis	Hydrocephalus (gross pathology)	None	None	Euthanasia
3	0.2	Shih tzu	M	Dementia, circling, tetraparesis, divergent strabismus	Chronic (1 m)	Cerebrum	Hydrocephalus, cranial trauma	Hydrocephalus (US)	None	None	Euthanasia
4	0.3	Miniature Pinscher	F	Cognition dysfunction, hyperesthesia, disorientation, aggression, hypermetria	Chronic (2 m)	Diffuse (cerebrum, cerebellum)	Congenital malformation, storage disease	Hydrocephalus	Frontal bone malformation, blindness	Medical	Euthanasia
5	12	American Staffordshire terrier	F	Dysphonia, depression, facial asymmetry	Subacute (15 d)	Caudal brainstem	Encephalitis, brain tumour (primary or metastatic)	Nasal cavity tumour (histopathology)	Distortion of facial bones, keratoconjuctivitis sicca	Intensive care	Death at hospital
6	0.8	Rottweiler	M	Tetraparesis, hypermetria positional strabismus	Chronic (3.5 m)	Brainstem	Inherited encephalopathy	Neuronal vacuolation, spinocerebellar degeneration	Laryngeal paresis, multiple congenital ocular abnormalities	None	Euthanasia
7	15	Miniature pincher	M	Cognition dysfunction, pacing	Chronic (8 m)	Cerebrum	Encephalitis, brain tumour	Senile cognitive dysfunction (MRI)	Senile visual and hearing impairment	Medical	No improvement; death of unrelated cause
8	12	King Charles spaniel	F	Cognition dysfunction, compulsive walking	Chronic 12 m)	Cerebrum	Encephalitis, brain tumour, senile cognitive dysfunction	Senile cognitive dysfunction (MRI, CSF)	Mitral valve disease	Medical	No improvement; follow up lost
9	13	Poodle cross	M	Cognition dysfunction	Chronic (12 m)	Cerebrum	Encephalitis, brain tumour, senile cognitive dysfunction	Senile cognitive dysfunction (MRI)	Osteoarthritis of hip and knee joints, senile deafness	Medical	Progressive deterioration, euthanasia
10	0.5	Mongrel	M	Depression, myoclonus	Unknown	Diffuse (brainstem, C6-T2)	Encephalomyelitis	Distemper (histopathology)	None	None	Euthanasia
11	0.4	Mongrel	F	Seizures, myoclonus	Subacute (15 d)	Diffuse (cerebrum, caudal brainstem, C6-T2)	Encephalomyelitis	Distemper (histopathology)	Impetigo, digital hyperkeratosis	Medical	Euthanasia

12	12	Mongrel	F	Circling, head pressing, depression	Acute (1 d)	Cerebrum	Encephalitis, brain tumour, ischaemic encephalopathy	Encephalitis (histopathology)	None	None	Death after 1 d
13	0.4	Golden retriever	M	Seizures, myoclonus	Subacute (15 d)	Diffuse (cerebrum, spinal cord)	Encephalitis	Distemper (histopathology)	Enteritis	Medical	Death
14	12	Mongrel	F	Seizures, disorientation, compulsive walking, ataxia, myoclonus positional strabismus	Acute (3 d)	Diffuse (cerebrum, spinal cord)	Encephalomyelitis	Distemper (histopathology)	Mitral valve disease, mammary tumour, enteritis	Medical	Euthanasia
15	13	German shepherd	M	Left head tilt, ataxia, hypermetria	Chronic (8 m)	Brainstem (central vestibular)	Encephalitis, brain tumour	Suspected viral encephalitis (CT, CSF)	Acral lick granuloma	Medical	Unknown
16	8	Gekas	F	Cognition dysfunction, facial and trigeminal nerve paralysis	Acute (3 d)	Diffuse (cerebrum, brainstem)	Encephalitis, brain tumour	Encephalitis (histopathology)	None	None	Euthanasia
17	9	Mongrel	F	Asymmetric ataxia, incoordination, hypermetria	Chronic (1 m)	Diffuse (brainstem, cerebellum)	Encephalitis, brain tumour	Encephalitis (MRI)	Mammary mass	Medical	Improvement with subsequent waxing-waning course
18	8	Mongrel	F	Ataxia, tetraparesis	Acute (3 d)	Brainstem	Encephalitis, brain tumour	Encephalitis (CSF)	None	Medical	Euthanasia
19	4	Griffon terrier	M	Ataxia, falling	Acute (1 d)	Cerebellum	Brain tumour, ischaemic encephalopathy	Cerebellar tumour (MRI)	Bilateral patellar subluxation	None	Improvement, stable after 4 m
20	14	Samoyed	M	Cognition dysfunction, posterior weakness	Chronic (10 m)	Diffuse (cerebrum, brainstem)	Encephalitis, brain tumour	Liver tumour with secondary brain metastasis (histopathology)	None	None	Euthanasia
21	12	American Staffordshire terrier	F	Dysphonia, depression, facial asymmetry	Subacute (15 d)	Caudal brainstem	Encephalitis, brain tumour	Nasal cavity tumour (histopathology)	Distortion of facial bones, keratoconjuctivitis sicca	Intensive care	Death at hospital
22	5	Boxer	F	Depression, abnormal posture	Subacute (10 d)	Caudal brainstem	Encephalitis, brain tumour	Brain tumour (histopathology)	None	None	Euthanasia
23	11	Golden retriever	M	Cognition dysfunction, right sided circling	Chronic (2 m)	Cerebrum	Encephalitis, brain tumour	Brain tumour (MRI)	None	None	Euthanasia
24	8	German shepherd cross	F	Circling, cognition dysfunction	Subacute (15 d)	Cerebrum	Encephalitis, brain tumour	Brain tumour (histopathology)	None	Medical	Euthanasia
25	12	Collie cross	M	Disorientation, cognition dysfunction, depression, right head tilt, positional strabismus tetraplegia	Subacute (10 d)	Brainstem	Encephalitis, brain tumour	Brain tumour (MRI)	Perianal gland adenoma	Medical	Waxing-waning for 2 y, acute deterioration, euthanasia
26	12	Mongrel	M	Asymmetric ataxia, strabismus, right head tilt	Chronic (3 m)	Brainstem	Encephalitis, brain tumour	Brain tumour (CT)	Benign prostatic hyperplasia	Medical	Temporary improvement, euthanasia

27	2	Boxer	M	Ataxia, hypermetria, left head tilt, nystagmus, intention tremor	Acute (3 d)	Brainstem	Encephalitis, brain tumour	Brain tumour (MRI)	None	Medical	Euthanasia
28	13	Mongrel	F	Ataxia, falling, rolling	Subacute (10 d)	Brainstem	Encephalitis, brain tumour	Brain tumour (MRI)	Mitral valve disease	Medical	Death as the result of acute heart failure
29	13	Siberian husky cross	F	Seizures	Chronic (1 m)	Cerebrum	Brain tumour, ischaemic encephalopathy	Multifocal ischaemic cerebrocortical necrosis	None	Medical	Euthanasia
30	7	Yorkshire terrier	M	Ataxia, torticollis	Chronic (1 m)	Diffuse (cerebrum, central vestibular)	Breed specific / other encephalitis, brain tumour	NE	Bilateral patellar subluxation	Medical	Stable after 10 m
31	14	Poodle	M	Ataxia, falling	Subacute (10 d)	Diffuse (cerebrum, central vestibular)	Encephalitis, brain tumour	NE	Testicular enlargement, chronic skin disease	None	Death after 4 m
32	13	West Highland white	M	Seizures, tetraplegia	Subacute (15 d)	Cerebrum (focal seizures), caudal brainstem	Encephalitis, brain tumour	NE	Rhinitis, conjunctivitis	Intensive care	Death at hospital
33	12	Samoyed	M	Head tilt, falling, ataxia	Chronic (10 m)	Diffuse (cerebrum, central vestibular)	Encephalitis, brain tumour	NE	None	None	Euthanasia
34	13	Pit bull cross	F	Cognition dysfunction, ataxia	Chronic (2 m)	Diffuse (cerebrum, cerebellum)	Encephalitis, brain tumour	NE	Mitral valve disease, sebaceous gland adenomas	None	Euthanasia
35	5	Mongrel	M	Seizures, cognition dysfunction	Chronic (2 m)	Cerebrum	Encephalitis, brain tumour	NE	None	Medical	Alive, on treatment course with phenobarbital
36	0.3	Mongrel	F	Depression, tetraparesis, myoclonus	Chronic (1.5 m)	Diffuse (cerebrum, spinal cord)	Distemper	NE	Rhinitis, enteritis, conjunctivitis	Medical	Death
37	13	Mongrel	F	Seizures positional strabismus	Acute (1 d)	Diffuse (cerebrum, brainstem)	Brain tumour, ischaemic encephalopathy	NE	Multiple mammary tumours	Intensive care	Death at hospital
38	14	Cocker spaniel	F	Compulsive walking, circling, disorientation, cognition dysfunction, aggression	Chronic (4 m)	Cerebrum (left)	Encephalitis, brain tumour	NE	Mammary tumour, uveitis, mitral valve disease	Medical	Euthanasia
39	12	Doberman pinscher	F	Ataxia, circling, dementia, disorientation	Acute (1 d)	Cerebrum	Brain tumour, ischaemic encephalopathy	NE	Cardiomyopathy	Medical	Stable for 1 week, then lost to follow up

40	11	Mongrel	F	Ataxia, depression, head tilt, positional strabismus	Chronic (1 m)	Brainstem (central vestibular)	Encephalitis, brain tumour	NE	None	None	Unknown
41	10	Spitz	F	Seizures	Subacute (15 d)	Cerebrum	Encephalitis, brain tumour	NE	None	Intensive care	Death at hospital
42	10	Poodle cross	M	Asymmetric ataxia, hypermetria, intention tremor, left sided plagiotonus	Acute (2 d)	Brainstem	Brain tumour, ischaemic encephalopathy	NE	Mitral valve disease	Medical	Unknown
43	15	Collie cross	F	Cognition dysfunction, ataxia, compulsive walking, anisocoria	Chronic (2 m)	Cerebrum	Encephalitis, brain tumour	NE	Mammary mass	None	Euthanasia
44	13	Mongrel	F	Loss of vision, cognition dysfunction, seizures	Acute (3 d)	Cerebrum	Encephalitis, brain tumour	NE	Right ear canal ablation (excision of mass)	Medical	Unknown
45	5.5	Poodle cross	F	Asymmetric ataxia, cognition dysfunction, anisocoria, cervical hyperesthesia	Subacute (15 d)	Brainstem	Encephalitis, brain tumour	NE	Fever of unknown aetiology	Medical	Unknown
46	19	Poodle	M	Asymmetric ataxia, circling, tetraparesis, cognition dysfunction	Subacute (10 d)	Brainstem	Encephalitis, brain tumour	NE	Chronic dermatitis	None	Euthanasia
47	10	Mongrel	M	Lethargy, tetraplegia	Chronic (1 m)	Diffuse (cerebrum, brainstem)	Encephalitis, brain tumour	NE	Unilateral otitis	Intensive care	Death at hospital
48	8	American Staffordshire terrier	M	Ataxia, intention tremor, hypermetria	Chronic (12 m)	Cerebellum	Cerebellar abiotrophy, cerebellar tumour	NE	Callous pyoderma	None	Euthanasia

1. Age expressed in years
2. S: sex, M: male, F: female
3. m: month(s), d: day(s)
4. MRI: magnetic resonance imaging, gross pathology: gross pathological examination, US: ultrasound examination, histopathology: histopathological examination, CSF: examination of cerebrospinal fluid, CT: computed tomography, NE: not established.
5. y: years, d: day, m: months

DISCUSSION

Primary encephalopathies can be classified according to their specific aetiology and clinical features into congenital, inherited (or degenerative), inflammatory, neoplastic, vascular and toxic/traumatic disorders, which were not included in this case study (Dewey, 2008; Thomas, 2010a).

Congenital and inherited diseases were diagnosed in six dogs. Hydrocephalus is a common congenital disorder of the central nervous system and affects toy and brachycephalic breeds. In the latter animals, the usually reported anatomic cause is stenosis of the mesencephalic aqueduct, although there are also cases with no apparent deformity present (Vite, 2006; Thomas, 2010b). Three of the affected dogs belonged to high risk breeds (Shih Tzu, Miniature pinscher, Chihuahua) and presented typical signs associated with the progressive increase in intracranial pressure and cortical pressure induced atrophy. In particular, they had a dome shaped calvarium with open fontanelles, divergent strabismus, mild to severe cognitive dysfunction, compulsive circling and seizures (Table 1) (Vite, 2006; Thomas, 2010b). Diagnosis was established objectively by magnetic resonance imag-

ing, ultrasonography through the open fontanelles and pathological examination, each of these used in one case. Although prognosis is generally guarded to poor, especially when severe neurological dysfunction is present, one hydrocephalic dog is still alive after two years, period during which only symptomatic treatment is performed.

One Rottweiler was diagnosed with a rare inherited disorder, characteristic for this dog breed, neuronal vacuolation and spinocerebellar degeneration. Clinical presentation was typical of this disease and included progressively deteriorating spastic tetraparesis and laryngeal paresis. The dog also presented ocular anomalies, which have been reported to accompany this rare condition (Eger et al., 1998). We have in the past reported two cases of the disorder in Rottweiler puppies, offspring of the same sire in the Thessaloniki area (Polizopoulou et al., 2009), but there was no clear association of the dog in this study with the previous ones. Young Rottweiler dogs present various neurological disorders of genetic aetiology, with focal (e.g., neuroaxonal dystrophy, leukoencephalomalacia, laryngeal paralysis-polyneuropathy complex) or multifocal (e.g., neuronal vacuolation and spinocerebellar degeneration) lesions (Davies and Irwin, 2003). Selective in-breeding stimulated by periodic public interest in various dog breeds has been identified as the cause of emergence of rare inherited disorders. A thorough review of the dog's history may help to trace affected animals back to specific dams or sires or exclude other inherited conditions based on the dog's age and evolution of signs.

The diagnosis of another presumed inherited condition, progressive cerebellar cortical degeneration was based on history, development of signs and diagnostic imaging findings (case 5, Table 1). In contrary to the previous case, this uncommon disorder is slowly progressive and affects adult middle-age or even elderly American Staffordshire terriers, thus an extensive diagnostic work up is essential to rule out other diagnostic differentials, such as neoplasia and encephalitis (Olby et al., 2004, Sisó et al., 2006). There was no evidence of a space occupying lesion or inflammation in the magnetic resonance examination of this dog, however the small size of the cerebellum and the ongoing very slow exacerbation of cerebellar dysfunction support a diagnosis of progressive cerebellar cortical degeneration (Olby et al., 2004).

Canine distemper virus encephalitis (CDVE) was the most common cause of encephalitis, diagnosed in four of nine dogs with signs of inflammatory brain disease (Table 1). Three of these dogs were puppies younger than 6 months, in an erroneous vaccination schedule had been followed, which another dog was 12 year-old, but not up-to-date with vaccination for the previous five years. All animals had neurological signs of diffuse or multifocal encephalopathy, including focal or generalized myoclonus, a rather typical manifestation of this viral infection (Koutinas et al., 2002; Vite, 2005; Dewey, 2008). Extraneural signs such as upper respiratory and/or gastrointestinal tract disease, nasal and/or digital hyperkeratosis, impetigo, were observed in three cases (Table 1). These non-neurological manifestations, although inconsistent, frequently precede or accompany neurological dysfunction and may help to reach an initial diagnosis (Koutinas et al., 2002; Vite, 2005). Meningoencephalitis of presumed viral aetiology was diagnosed in three dogs based on magnetic resonance findings and results of analysis of cerebrospinal fluid. The same diagnosis was reached in another two dogs post-mortem, based on histopathological examination. Advanced imaging (magnetic resonance) usually does not reveal cerebral lesions in cases of viral encephalitis, but contributes to the diagnosis by ruling out other potential disorders (e.g., neoplasia, granulomatous encephalitis). Results of analysis of cerebrospinal fluid are indicative of viral infection and, as recorded in two dogs, include a predominantly lymphocytic pleocytosis and a moderate increase in protein content (Vite, 2005; Dewey, 2008).

Extensive ischaemic necrosis of the cerebral cortex was evident histologically in one dog (case 29) with acute neurological signs, which was admitted late in the course of the disease. In dogs and cats, cerebrovascular disease is currently a well-recognized clinical syndrome classified into ischaemic and haemorrhagic strokes (Garosi, 2010). Underlying aetiological factors that have been associated with ischemic strokes, include septic or cardiac thromboembolism, parasitic migration or emboli, fibrocartilaginous embolism, metabolic disorders (hyperlipoproteinemia) and metastatic tumour embolism (Garosi et al., 2005). This dog was also diagnosed with mammary adenocarcinoma, which could have been the initiating factor for this episode (Joseph et al., 1988). Previous studies, however, have shown that a concurrent medical condition was detected in just over 50% of dogs with evidence of ischaemia. In humans, similar cases, where

no apparent predisposing factor could be identified, are referred to as 'cryptogenic infarction (Garosi et al., 2006; Garosi, 2010).

Brain tumours were among the most common disorders recorded in this study, an observation which is in agreement with epidemiological data, reporting an incidence risk of 14.5 in 100,000 animals for the disorder (Polizopoulou et al., 2004). Typically affected animals are middle-aged to elderly dogs (aged >5 years); however, exceptions can occur in breeds predisposed to cerebral cancer and certain tumour types (primitive neuroectodermal tumours) that affect younger animals. Although the majority of dogs with brain neoplasms in this report were elderly (8-14 years), three animals were younger than 5 years of age (Table 1). Of these, two animals were Boxers, a breed predisposed to gliomas, which was the tumour type (oligodendroglioma) histologically identified in one of them. Notably, in over half of the cases (6/10), onset of signs was acute or subacute, an evolution pattern not uncommon in brain neoplasia caused by the sudden exhaustion of compensatory protective mechanisms, obstructive hydrocephalus or haemorrhage (Polizopoulou et al., 2004; Long, 2006). When interpreting evolution patterns in brain tumours, the histological *versus* the biological malignancy has to be considered. Tumours located in some anatomic sites (i.e., frontal cerebral lobes) may be clinically silent or tolerated for long periods than others neoplastic lesions located in highly vascular areas or the ventricular system (Polizopoulou et al., 2004; Long, 2006).

Diagnosis of primary neoplasias in all eight animals was carried out by diagnostic imaging methods, which are the only way to reach aetiologic diagnosis *ante-mortem* in these cases. Clinical and diagnostic imaging lesion localization corresponded well, as shown previously in other clinical studies, confirming the need for a systematic neurological evaluation of patients (Polizopoulou et al., 2004). Interestingly, in five cases the lesion localization was determined to be the cerebellopontine angle, with all the affected animals showing signs of central vestibular disease. Unfortunately, owner compliance allowed detailed histopathological examination of tumour types in only two dogs with primary tumours. Primary brain tumours outnumbered those that invaded the cranium after local (nasal cavity) or distal (abdomen) metastasis. In relation to those, clinical signs caused by the primary neoplasm had been recorded in one dog that showed facial deformity due to bony destruction by the nasal tumour (Dewey, 2008).

Cognitive dysfunction syndrome (CDS) has been diagnosed in three old (>12 years) dogs. Duration of signs was prolonged and ranged from 8 to 12 months. All dogs presented typical cognitive dysfunction syndrome signs, e.g., demented behaviour, disturbance of sleep/wake cycle, loss of house training, aimless wandering and loss of owner recognition (Landsberg, 2011). Diagnosis of cognitive dysfunction syndrome is performed by exclusion of other medical or neurological conditions that may present similar clinical signs. Among such problems in geriatric dogs are endocrine (e.g., hyper-/hypo-adrenocorticism, hyper-/hypo-thyroidism, diabetes, insulinoma), metabolic (e.g., hepatic or kidney failure), neurological (e.g., brain tumours, encephalitis), orthopaedic (e.g., osteoarthritis), dermatological (e.g., chronic pruritic diseases) and senile visual and/or auditory dysfunctions (Lansberg, 2011). For this reason, an extensive clinical, clinicopathological and diagnostic imaging investigation is required before a tentative diagnosis of cognitive dysfunction syndrome is reached, as done in all three dogs of the present study with no evidence of other medical or neurological problems.

For the remaining 19 cases (Table 1) a diagnosis was attempted by interpreting data from history, clinical presentation and initial clinicopathological evaluation. Case 30, a Yorkshire terrier (Table 1) was presumed to suffer from breed-specific encephalitis based on clinical findings, chronic (~12 month-long) waxing and waning disease course and response to periodic administration of corticosteroids (Schatzberg, 2010). Canine distemper virus encephalitis was the most probable diagnosis in a young puppy (case 36) that presented multifocal signs, myoclonus and extraneural symptoms compatible with the condition (Vite, 2005). Case 37 that had been admitted as an emergency for acute status epilepticus, had multiple mammary tumours, therefore, brain metastasis or ischaemia from metastatic emboli could have been the inciting cause. Similarly, mammary neoplasia was detected in case 9 that was presented with a more protracted clinical course (Dewey, 2008). Two dogs (cases 39 and 42) with acute neurological dysfunction had concurrent cardiac disease (dilated cardiomyopathy and degenerative mitral valve disease, respectively) that may have precipitated a cerebral infarct (Garosi, 2010). In another animal (case 44) admitted with acute cerebral syndrome,

a neoplastic mass had been surgically removed from the external ear canal a few weeks earlier, thus direct metastasis or metastatic embolism might have been the cause of neurological signs (Dewey, 2010). Finally, an American Staffordshire terrie (case 48) presented signs similar to the dog of the previous group diagnosed with cerebellar abiotrophy, which might have been the cause of cerebellar disease taking into account the long (12 months) duration of signs and the lack of any other abnormalities (Olby et al., 2004).

CONCLUDING REMARKS

The multifactorial and complex aetiology of canine primary encephalopathies emphasizes the need for a systematic diagnostic approach, taking into consideration history and evolution of neurological signs, clinical and clinicopathological findings to exclude other systemic disorders with neurological manifestations. Analysis of cerebrospinal fluid and diagnostic imaging techniques are certainly the appropriate means to reach an aetiologic *ante-mortem* diagnosis. However, when financial constraints limit their application, the aforementioned clinical work up may limit the list of differential diagnoses considerably, facilitate prognostic evaluation and choice of treatment regime.

CONFLICT OF INTEREST STATEMENT

None of the authors of this paper has a financial or personal relationship with other people or organizations that could inappropriately influence or bias the content of the paper.

REFERENCES

Braund KG (2003) Degenerative disorders of the central nervous system. In: (ed.: Vite CH) Braund's Clinical Neurology in Small Animals - Localization, Diagnosis and Treatment. International Veterinary Information Service, Ithaca A3220.0303

Chrisman CL (1991) The neurologic history. In: (ed.: Chrisman CL) Problems in Small Animal Neurology, 2nd edn. Lea and Febiger, Philadelphia, pp. 25-40.

Davies DR, Irwin PJ (2003) Degenerative neurological and neuromuscular disease in young Rottweilers. J Small Anim Pract 44:388-394.

Dewey CW (2008) Encephalopathies: disorders of the brain. In: (ed.: Dewey CW) A Practical Guide to Canine and Feline Neurology, 2nd edn. Wiley and Blackwell, Ames, pp. 115-220.

Dewey CW, Bailey KS (2008) Signalment, history and the differential diagnosis: The first consideration. In: (ed.: Dewey CW) A Practical Guide to Canine and Feline Neurology, 2nd edn. Wiley and Blackwell, Ames, pp. 3-15.

Drum MG (2010) Physical rehabilitation of the canine neurologic patient. Vet Clin N Am Small Anim Pract 40:181-193.

Eger CE, Huxtable CR, Chester ZC, Summers BA (1998) Progressive tetraparesis and laryngeal paralysis in a young rottweiler with neuronal vacuolation and axonal degeneration: an Australian case. Aust Vet J 76:733-737.

Garosi LS (2010) Cerebrovascular disease in dogs and cats. Vet Clin N Am Small Anim Pract 40: 65-79.

Garosi LS, McConnell JF, Platt SR, Barone G, Baron JC, DeLahunta A, Schatzberg SJ (2006) Clinical characteristics and topographical magnetic resonance of suspected brain infarction. J Vet Intern Med 20:311-321.

Joseph RJ, Greenlee PG, Garillo JM (1988) Canine cerebrovascular disease: clinical and pathological findings in 17 cases. J Am Anim Hosp Assoc 24:569-576.

Koutinas AF, Polizopoulou ZS, Baumgaertner W, Lekkas S, Kontos V (2002) Relation of clinical signs to pathological changes in 19 cases of canine distemper encephalomyelitis. J Comp Path 126:47-56.

Landsberg GM, DePorter T (2011) Clinical signs and management of anxiety, sleeplessness and cognitive dysfunction in the senior pet. Vet Clin N Am Small Anim Pract 41:565-590.

Long S (2006) Neoplasia of the nervous system. In: (ed.: Vite CH) Braund's Clinical Neurology in Small Animals - Localization, Diagnosis and Treatment. International Veterinary Information Service, Ithaca A3227.1106.

Olby N, Blot S, Thibaud J, Phillips J, O'Brien DP, Burr J, Berg J, Brown T, Breen M (2004) Cerebellar cortical degeneration in adult American Staffordshire terriers. J Vet Intern Med 18:201-208.

Polizopoulou ZS, Koutinas AF, Souftas VD, Kaldrymidou E, Kazakos G, Papadopoulos G (2004) Diagnostic correlation of CT-MRI and histopathology in 10 dogs with brain neoplasms. J Vet Med A 51:226-231.

Polizopoulou ZS, Soubasis N, Tsingotjidou A, Giannakopoulou A, Papadopoulos GC, Oevermann A, Koutinas AF (2009) Neuronal vacuolation and spinocerebellar degeneration in two Rottweiler siblings. J Vet Intern Med 19:410.

Schatzberg SJ (2010) Idiopathic granulomatous and necrotizing inflammatory disorders of the canine central nervous system. Vet Clin N Am Small Anim Pract 40:101-120.

Sisó S, Hanzlicek D, Fluehmann G, Kathmann I, Tomek A, Papa V, Vandevelde M (2009) Neurodegenerative diseases in domestic animals: a comparative review. Vet J 171:20-38.

Thomas WB (2010a) Evaluation of veterinary patients with brain disease. Vet Clin N Am Small Anim Pract 40:1-19.

Thomas WB (2010b) Hydrocephalus in dogs and cats. Vet Clin N Am Small Anim Pract m 40:143-159.

Vite CH (2005) Inflammatory diseases of the central nervous system. In: (ed.: Vite CH) Braund's Clinical Neurology in Small Animals - Localization, Diagnosis and Treatment. International Veterinary Information Service, Ithaca A3228.0205

Vite CH (2006) Developmental disorders. In: (ed.: Vite CH) Braund's Clinical Neurology in Small Animals - Localization, Diagnosis and Treatment. International Veterinary Information Service, Ithaca A3217.0706