

## **Magnetic resonance as a part of a broad approach to seizures in dog - two cases of hydrocephalus in dogs with cluster seizures**

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### **ABSTRACT**

This paper describes two cases of hydrocephalus in dog. Both dogs were presented at the Clinic for Internal Diseases, Faculty of Veterinary Medicine, Zagreb, after having experienced cluster seizures and status epilepticus, respectively. In each dog physical and neurological examination was performed, revealing no abnormalities. Complete laboratory workup and urinalysis were included for each dog and all results were within reference range. Both dogs underwent magnetic resonance (MR) imaging and through this procedure a diagnosis of hydrocephalus was established. Anticonvulsive therapy and therapy against increased intracranial pressure was introduced in both dogs. Treatment resulted in marked clinical improvement.

**Key words:** dog, hydrocephalus, seizures, cluster seizures, magnetic resonance (MR)

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### **Introduction**

Seizures are the most common neurologic disorder in small animal medicine (PODELL et al., 1995). Any involuntary event that is brief and episodic should be considered a possible seizure (SHELL, 1993c). Estimates of seizure incidence during a lifetime vary from 0.5% to 5.7% in all dogs, and from 0.5% to 1.0% in all cats (WHEELER, 1995).

Seizures are transient, paroxysmal disturbances of the electrical activity of cerebral neurons that result in a period of clinical abnormality (CHRISMAN, 1995). Therefore,

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seizures are always a clinical sign of cerebral dysfunction. Epilepsy is defined as appearance of recurrent seizures, regardless of etiology. Primary epileptic seizures (PES) are the result of a biochemical defect in the brain cells or their environment since there is no detectable structural histopathologic damage. Secondary epileptic seizures (SES) are known as acquired or symptomatic, because they are consequence of brain structural changes, e. g. encephalitis, trauma and hydrocephalus (SHELL, 1993b). Reactive epileptic seizures (RES) are a reaction of a normal brain to transient systemic insult or physiological stress, e. g. portosystemic shunts, lead intoxication or insulinoma (PLATT and HAAG, 2002).

Status epilepticus and cluster seizures are life-threatening manifestations of recurrent epileptic seizure activity (BATEMAN and PARENT, 1999). Status epilepticus is a continuous series of two or more seizures lasting at least 5 minutes, between which there is incomplete recovery of consciousness (PLATT and MCDONNELL, 2000). Cluster seizures are two or more seizures occurring over a relatively brief period from minutes to 24 hours within which time the patient regains consciousness (BRAUND, 1994).

In the broad use of the term, hydrocephalus is an increase in the volume of cerebrospinal fluid (CSF) (DELAHUNTA, 1983). In this condition the cerebral ventricular system is enlarged due to an increased amount of CSF. Secondary compression or atrophy of the surrounding neurologic tissue occurs (NELSON and COUTO, 1998). WÜNSCHMANN and OGLESBEE (2001) reported loss of ependymal lining and presence of astroglial scars along the lesion margins and unilateral or bilateral periventricular diverticula and cleft formation in fifty percent of dogs with hydrocephalus. Breeds at higher risk for developing a congenital form of hydrocephalus are Maltese, Yorkshire Terrier, English Bulldog, Chihuahua, Lhasa Apso, Pomeranian, Toy Poodle, Cairn Terrier, Boston Terrier, Pug, Chow Chow and Pekingese (NELSON and COUTO, 1998).

Magnetic resonance imaging (MRI), is a non-invasive technique that provides accurate, detailed anatomic images, and has had a major impact in diagnosis in human medicine. This technique is based upon the inherent magnetic properties of certain nuclei. Induction of the nuclei into a low energy state is achieved by placing them in a static magnetic field. The nuclei may then be excited into a high energy state by application of a radio frequency pulse. When the second field is stopped, the nuclei return to ground state and emit the absorbed energy in the form of a radio signal. This signal is received by a coil that generally surrounds the specimen and is converted to an anatomic image through a process of computer-assisted reconstruction. Contrast is altered by applying the second pulse in different sequences and using enhancing agents such as gadolinium (THOMSON et al., 1993). Tissues of CNS are ideal for MRI due to their water and lipid structure. Because of high resolution and soft tissue contrast achieved with MRI it has been especially useful to identify many normal and abnormal anatomic features of the

CNS. Unlike CT scanning, beam-hardening artifact originating from thick compact bone does not occur with MRI (THOMSON et al., 1993).

The aim of this paper is to present the role of MRI as a part of broad approach to seizures and in diagnosing cases of spontaneous hydrocephalus in two dogs in Croatia.

### **Materials and methods**

A 15-month-old female English Bulldog was presented at the Clinic for Internal Diseases, Faculty of Veterinary Medicine, University of Zagreb. The dog was presented due to cluster seizures every three weeks that started a few months previously. The dog was fully clinically and neurologically examined and laboratory work-up was also included. Additionally, a 13-month-old German Boxer was admitted to the Clinic for Internal Diseases, Faculty of Veterinary Medicine, University of Zagreb. The dog was presented after status epilepticus that lasted 48 hours and following one seizure three weeks previously. This dog was also fully clinically and neurologically examined; laboratory work up was also included.

Blood samples were taken for haematologic and biochemical analysis. Haematologic analysis was performed using haematologic counter Baker System Serrono 9120 CP (Serrono-Baker Diagnostic, INC., Allentown, U.S.A.). Biochemical analysis was performed after centrifugation at 1200 g for ten minutes. Creatinine, blood urea nitrogen (BUN), glucose, total serum proteins, albumin, calcium, sodium, potassium and activity of aspartate aminotransferase (AST), alanine aminotransferase (ALT),  $\gamma$ -glutamyl transferase (GGT) and serum creatine kinase (CK) were measured using biochemical autoanalyser Technicon RA 1000 (Technicon Instrument Corporation, New York, U. S. A.). Reagents were supplied by Randox (Randox Laboratories Ltd., United Kingdom).

Urinalysis consisted of physical and dipstick examination and sediment evaluation.

Magnetic resonance imaging of the brain was performed using a 0.2 Tesla permanent magnet (Siemens AG, Erlangen, Germany). T1-weighted images and T2-weighted images in the transverse, sagittal and dorsal planes were acquired.

Food was withheld for 12 hours prior to MRI. After administration of atropine (0.02 mg/kg, IV, Atropin, Belupo, Koprivnica, Croatia) and diazepam (0.25 mg/kg IV; Apaurin, Krka, Slovenia), both dogs were anesthetized by administration of 2.5% thiopental sodium (Thiopental, Nycomed, Roskilde, Denmark) intravenously. Six mg/kg was given rapidly as a bolus and additional increments of the remainder was given to effect (light endotracheal intubation). An endotracheal tube was inserted and secured in place. Under general anaesthesia dogs were placed in sternal recumbency. Prolonged anaesthesia was achieved by additional bolus injections of 1-3 mg/kg of thiopental sodium. There were no complications during or immediately after anaesthesia.

For the first dog the T1-weighted scan sequences used a repetition time (TR) of 800 ms and echo time (TE) of 30 ms, and the T2-weighted scans a TR and TE of 3900 ms and 96 ms, respectively. The field of view used was 160×160 mm, and slice thickness was 4 mm. The imaging matrices were 170×256 for the T1-weighted scans and 180×256 for the T2-weighted scans.

For the second dog the T1-weighted scan sequences used TR of 600 ms and TE of 15 ms, and the T2-weighted scans a TR and TE of 5000 ms and 96 ms, respectively. The field of view used was 200×200 mm, and slice thickness was 5 mm. The imaging matrices were 180×256 for the T1-weighted scans and 252×256 for the T2-weighted scans. For dog two, following intravenous bolus injection of 0.1 mmol/kg body weight gadolinium DTPA-dimeglumine (Magnevist®, Shering AG, Berlin, Germany) contrast medium T1-weighted images were acquired in dorsal and sagittal planes.

After diagnosis in both dogs the following therapy was introduced: prednisone 0.5 mg/kg orally twice daily. This was gradually reduced at weekly intervals and with phenobarbitone 2.5 mg/kg orally twice daily. There was marked clinical improvement in both dogs.

## Results

There were no abnormalities detected on physical examination in both dogs, nor during neurological examination. Haematology (Table 1) and biochemistry values (Table 2); the results of urinalysis were also in the reference range.

Table 1. Results of haematologic findings in both dogs with hydrocephalus

Hematologic findings	Dog 1	Dog 2	Standard values Kraft and Dürr (1997)
Red blood cells (x 10 <sup>12</sup> /L)	6.47	7.18	5.5-8.5
Haemoglobin (g/L)	154	159	150-190
PCV (%)	44.7	51.4	44-52
MCV (fL)	65.5	71.6	60-77
WBC (x 10 <sup>9</sup> /L)	13.1	8.7	6-15
Neutrophils (%)	74	68	55-75
Bands (%)	0	0	0-4
Lymphocytes (%)	25	26	13-30
Monocytes (%)	0	2	0-4
Basophils	0	0	0-1
Eosinophils (%)	1	4	0-6

Table 2. Serum biochemistry values in both dogs with hydrocephalus

Biochemical findings	Dog 1	Dog 2	Standard values Kraft and Dürr (1997)
Blood urea nitrogen	7.1	4.9	3.3-8.3 mmol/L
Creatinine	42	81	35-106 $\mu$ mol/L
Aspartate aminotransferase (AST)	18	23	do 25 U/L
Alanine aminotransferase (ALT)	40	28	do 55 U/L
Alkaline phosphatase (AP)	57	64	do 108 U/L
Gamma-glutamyltransferase (GGT)	1	3	do 5 U/L
Glucose	3.5	4.2	3.1-6.7 mmol/L
Total serum proteins	63	57	54-75 g/L
Albumins	28	30	25-44 g/L
Sodium	148	142	140-155 mmol/L
Potassium	4.4	3.9	3.5-5.1 mmol/L
Calcium	2.5	2.6	2.3-3.0 mmol/L

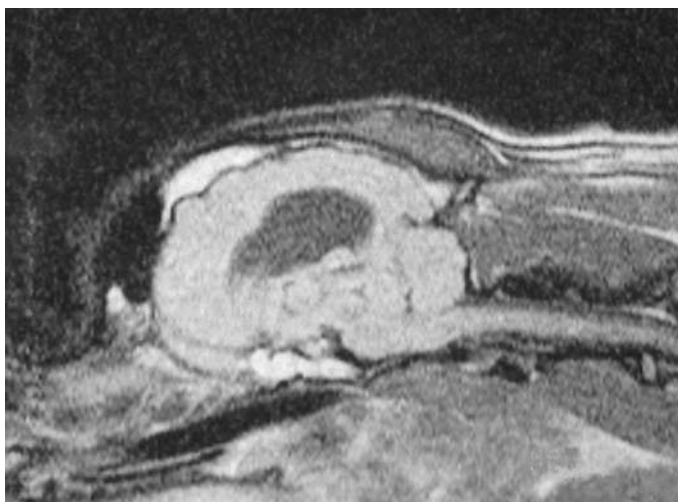


Fig. 1. Midsagittal T1 weighted image of the first dog in which the ventriculomegaly and the presence of tissue over the communication between first and second ventricle can be clearly seen.

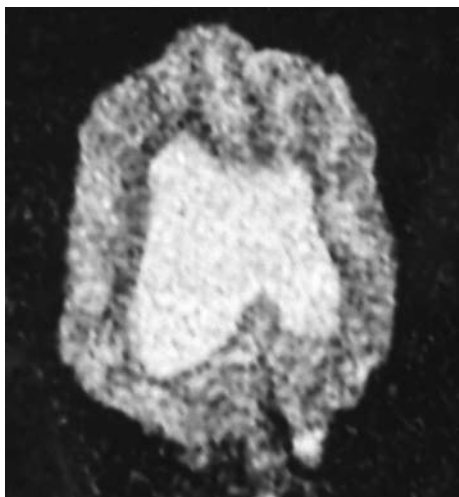


Fig. 2. Dorsal T2 weighted image of the first dog at height over the third ventricle, in which the communication between two lateral ventricles and ventriculomegaly is apparent.

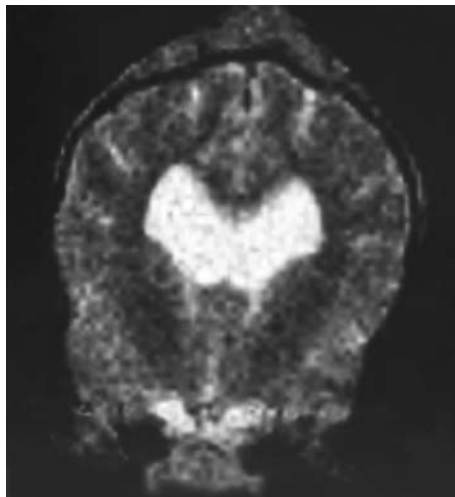


Fig. 3. Transversal T2 weighted image of the second dog in which moderately dilated and communicating lateral ventricles are clearly visible.



Fig. 4. Transversal T1 weighted image of the first dog in which ventriculomegaly, communication between lateral ventricles and loss of normal brain tissue architecture is visible.



Fig. 5. Midsagittal T1 weighted image of the second dog in which lateral ventricles are communicating and there is a moderately dilated third ventricle.

For both dogs there was ventriculomegaly affecting both lateral ventricles clearly seen on sagittal, dorsal and transversal planes, seen on the MR images. Also, in both dogs there was communication between lateral ventricles, with loss of brain parenchyma. In the same images no cause for obstruction of CSF flow could be identified. In the second dog, after application of contrast medium there was no contrast enhancement (Figs 1 to 5).

## Discussion

A broad approach to seizures is necessary because dogs and cats with a seizure disorder frequently have similar histories and physical signs, despite a wide variety of underlying causes of cerebral dysfunction (WHEELER, 1990). The decision to pursue diagnostic testing should not be based on the number or severity of prior seizures, rather, the decision should be based upon signalment, history, and initial neurologic examination (PODELL, 1996). Thus, it is crucial to include both clinical and neurological examinations in the evaluation of each patient with seizures. For both our patients this signified that the list of differential diagnoses should include: congenital, hereditary, metabolic, inflammatory and toxic disorders. In their study PLATT and HAAG (2002) reported that dogs with status epilepticus have a significantly higher likelihood to suffer seizures as a result of pathologic changes in brain tissue than dogs with simple seizures. This also proved to be the case for our two patients. This should not be interpreted in the sense that dogs with non status epilepticus do not need a thorough work-up, but rather it emphasizes the importance of a rapid and thorough diagnostic plan for dogs with status epilepticus. Hydrocephalus was the most common diagnosis (35%) in dogs with secondary epileptic seizures in the study of PODELL et al. (1995). Interestingly, in the same paper the authors reported that the onset of seizures was observed at an older age than that expected (after 1 year of age) for that associated with a developmental anomaly, suggesting that hydrocephalus was a progressive disease, with a variable onset of clinical signs (PODELL et al., 1995). Findings in our patients are in accordance with this report, rather than with what has been typically reported (BECKER and SELBY, 1980).

Knowing the breeds of dogs that have high incidence of primary epilepsy for which an inherited basis is known warrants the clinician to include this diagnosis in the list of differential diagnosis (SHELL, 1993a). Nevertheless, the diagnosis of primary epilepsy is established by exclusion of all possible causes for seizures, i.e. the underlying cause cannot be identified (PODELL et al., 1995).

Magnetic resonance imaging is widely used in diagnostics of multifocal and intracranial neurologic diseases (KRAFT and DÜRR., 1997; GAROSI et al., 2001). Therefore, this advanced technique was applied in establishing a diagnosis in our two patients. For both dogs in our study the two most important differential diagnoses through MRI imaging were ventriculomegaly and Chiari I-type malformation.

Ventriculomegaly describes ventricular dilatation that can be moderate or severe, and asymmetry between the ventricles is observed in many instances. Dogs with ventriculomegaly have no clinical signs of neurological dysfunction, therefore ventriculomegaly is usually diagnosed only by a neuroradiologic examination performed for other pathologies or at autopsy. This phenomenon is observed in beagles, but can be present in other breeds too (VULLO et al., 1997). The fact that both our patients have had seizures and the existence of communication between ventricles excludes this differential diagnosis for our two dogs.

Chiari I-type malformation in humans is diagnosed when there is cerebellar dysplasia and elongation of the cerebellar tonsils visible in MRI. Hydrocephalus in these cases is usually mild. In man, Chiari I-type malformation, as well as other congenital brain malformations, are usually diagnosed incidentally due to the increased use of computed tomography and MRI (LEE et al., 1985). In humans, Chiari I-type malformation is presented with variety of symptoms such as ataxia, sensory deficits, cerebellar signs and lower cranial nerve palsies (PAUL et al., 1983). As our dogs were presented with cluster seizures and status epilepticus we did not include Chiari I-type malformation in our list of differential diagnoses. Moreover, in our patients there was no caudally displaced velum of the fourth ventricle, nor caudally displaced ventral lobe of the cerebellar vermis, which should be present in MRI (KIRBERGER et al., 1997) of dogs considered to have Chiari I-type malformation.

In magnetic resonance images of our two patients no cause for hydrocephalus could be identified. There are reports in which the cause of hydrocephalus was discovered through magnetic resonance imaging (TERUO et al., 1996; TARGETT et al., 1998), which was not the case with our patients since there were no abnormalities or causes for CSF flow obstruction that could be identified. The second dog received the contrast medium, but no enhancement could be detected on his images. Therefore, a diagnosis of congenital hydrocephalus was established.

The cause of congenital hydrocephalus is not always apparent (HARRINGTON et al., 1996). According to the literature the maldevelopment of mesencephalic aqueduct could be a cause for development of congenital hydrocephalus. The maldevelopment of mesencephalic aqueduct results in third ventricle enlargement. This occurs in brachycephalic breeds, such as bulldogs (SIMPSON, 1989). This could not be the cause of hydrocephalus in our patients since the third ventricle was not enlarged. Another potential cause of hydrocephalus in toy breed dogs is maldevelopment of absorptive sites (SIMPSON, 1989). In this case the proportional enlargement of conducting system is expected, which was not found in our patients. The cause of development of the closed hydrocephalus in these two dogs remains to be discovered through further analysis.



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**MATIJATKO, V., I. KIŠ, D. VNUK, M. BRKLJAČIĆ, D. STANIN: Magnetska rezonancija kao dio šireg pristupa dijagnostici epileptičnog napadaja u pasa - dva slučaja hidrocefalusa u pasa s višestrukim epileptičnim napadajima. *Vet. arhiv* 77, 377-386, 2007.**

**SAŽETAK**

U radu su prikazana dva slučaja hidrocefalusa u pasa. Psi su dovedeni na Kliniku za unutarnje bolesti Veterinarskog fakulteta Sveučilišta u Zagrebu nakon epileptičnih napadaja koji su se javljali u nizu, tj. kao status epilepticus. Oba su psa bila podvrgnuta općoj kliničkoj pretrazi te neurološkom pregledu prilikom kojih nisu otkrivena odstupanja od normale. Sve hematološke i biokemijske vrijednosti te nalazi analize mokraće nalazili su se unutar referentnih vrijednosti. U oba je psa provedena magnetska rezonancija kojom je postavljena dijagnoza hidrocefalusa. Pacijenti su podvrgnuti antikonvulzivnoj terapiji te terapiji za smanjenje intrakranijalnog tlaka, nakon čega je uslijedilo znatno kliničko poboljšanje.

**Cljučne riječi:** pas, hidrocefalus, epileptični napadaji, magnetska rezonancija

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