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RESEARCH ARTICLE

Hydrocephalus associated to cervical hydromyelia /syringomyelia in domestic carnivores secondary to brain inflammatory conditions: New insights on MR imaging comparing to humans and critical review of the literature

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ABSTRACT

Background: Communication or anatomic continuity of the fourth ventricle outlet (FVO) with the central cervical ependymal canal (CCEC) of the spinal cord in both humans and mammals is controversial.

Aim: We hypothesize that in chronic inflammatory brain conditions (CIBC) and in early stages of age this communication can be reopened. For this purpose we have conducted a study to check the potential continuity of FVO with the CCEC of the spinal cord in small domestic carnivores presenting with obstructive hydrocephalus (OH) secondary to CIBC.

Methods: Retrospective neuroradiological evaluation of a case series involving 23 domestic carnivores with CIBC presenting with both OH and cervical hydromyelia/syringomyelia. MR images checked specifically the continuity between the FVO and the CCEC.

Results: There were 18 adult and five young domestic carnivores. Anatomical continuity between the FVO and a dilated CCEC (hydromyelia) could be demonstrated on MR imaging in all young cases but in only 16 % of adult cases.

Conclusions: This study provides additional insights into understanding the relationship between the development of hydrocephalus and hydro/syringomyelia. MRI findings support that domestic carnivores have a virtual CCEC that is connected with the FVO at birth and might disappears over the years in normal, healthy animals, thus explaining hydromyelia in early stages of age rather than syringomyelia, in hydrocephalic conditions. When this anatomical continuity is present, the hydrodynamic theory have a pivotal role in the pathogenesis of hydromyelia. If not (most adult cases) other mechanisms may be activated and lead to spinal cord syringomyelia.

Key words: CNS, inflammatory diseases; CNS, animal diseases; Hydromyelia; Syringomyelia; MR imaging, hydromyelia; MR imaging, syringomyelia; MR imaging, obstructive hydrocephalus;

INTRODUCTION

Obstructive hydrocephalus (OH) describes the expansion of the ventricular system of the brain, and has traditionally been classified as being of obstructive and communicating types (non-obstructive). Communicating hydrocephalus refers to the expansion of the ventricular system (including the fourth ventricle) in which the foramina of the fourth ventricle remain open, whereas non-communicating hydrocephalus or OH refers to a form of ventricular expansion in which a blockage is present within the ventricular system[1,2]. Syringomyelia refers to an expanding CSF-filled cavity that is present within the substance of the spinal cord, arising primarily outside the central cervical ependymal canal (CCEC) and usually lined with glial cells rather than ependymal cells. In contrast, hydromyelia refers to a dilatation of the CCEC that is lined with ependymal cells and often communicates with the ventricular system[2,3].

In humans, chronic cervical hydro/syringomyelia typically occurs in Chiari type I malformation, malformations of the craniovertebral junction (CVJ), or secondary to brain tumors[4], whereas acute hydro/syringomyelia occurs infrequently in humans and most often secondary to brain infection or acute intracranial hemorrhage in children[5].

Also in humans, Chiari type I malformation refers to a condition characterized by decreased posterior fossa volume and caudal descent of the cerebellar tonsils, and often of the brainstem[6]. Chiari type I malformations who exhibit syringomyelia have, on average, greater tonsillar herniation than those without a syringomyelia and are most often associated to craniocervical bony anomalies[7]. It is debatable whether the term Chiari type I malformation should be applied to dogs, but analogous condition in dogs—characterized by decreased volume of the caudal fossa and caudal displacement of the caudal cerebellar vermis into or through the foramen magnum—is called *Chiari-like* malformation. However, the condition is inconsistent with the historical description, not in the least because dogs do not have cerebellar tonsils. Thus, anatomical descriptions may be more appropriate (i.e., occipital hypoplasia with hydro/syringomyelia or caudal occipital malformation syndrome)[8].

Magnetic resonance imaging (MRI) is the method of choice for the diagnosis of structural diseases involving the brain and spinal cord, enabling clinicians to diagnose not only hydro/syringomyelia, but often also its underlying cause.

In the veterinary literature there are only anecdotal reports concerning specific causes of hydro/syringomyelia secondary to OH in dogs and cats[8,9]. While previous studies have mainly focused on the development of hydro/syringomyelia in humans, anatomic and physiologic differences in these animals—such as the lack of cerebellar tonsils, absence of gravity-dependent valve mechanisms[10,11], existence of a rete caroticum that hampers cerebrospinal fluid (CSF) pulsations[12] and differences in pathology—render these theories incomplete when applied to the development of hydro/syringomyelia in animals.

In the present report we review our clinical experience with small domestic carnivores whose diagnoses of OH and hydro/syringomyelia were made MR imaging, highlighting the radiologic features of these conditions, and to discuss the various clinical pictures that can be associated with this radiological pattern, in the context of chronic inflammatory brain conditions (CIBC).

We will also propose the mechanisms underlying the MRI findings obtained and, finally, we will discuss the various theories that have been proposed to explain the mechanisms underlying the development of hydro/syringomyelia, emphasizing the differences between humans and small domestic carnivores.

METHODS

From our file record consisting of a total of 850 MRI studies of the brain and spine, performed in eight years, we collected 23 small carnivores whose brain and spinal MRIs showed signs of OH and hydro/syringomyelia secondary to CIBC. Patients with hydro/syringomyelia secondary to brain malformations, caudal fossa malformations (such as basilar impression, occipital or atlanto-occipital anomalies), tumors, or posttraumatic states were excluded.

Animal patients aged 2 years and older were considered adults, and all animals were clinically evaluated by one or two veterinary neurologists. Standard clinical veterinary and radiological assessments were performed. Laboratory studies included standard hematologic parameters (complete blood count; serum biochemistry profile), standard serological tests, and CSF tap. CSF samples obtained from the atlanto-occipital cistern of 18 patients were analyzed in the laboratory within 30 mn of collection, evaluating gross appearance, total protein level, total red blood cell count, and total/differential nucleated cell counts. At minimum, all animals underwent MRI of the brain and cervical spine.

Age-matched control group was obtained from our clinical record files. We selected 21 dogs and four cats with unremarkable cervical spine records. Inclusion criteria included complete cervical MRI study, lack of neurological disease, and lack of inflammatory CSF analysis (when available). Most animals included were referred because ENT pathologies, minor trauma, or rule out nonspecific diseases.

MRI scans were obtained using a commercial superconducting magnet operating at 0.5 T, with animals under general anesthesia. Anesthesia was induced with propofol (6 mg/kg of body weight) and maintained with isoflurane until the end of the procedure, as described elsewhere[13]. Our brain MRI standard protocol included T2-weighted images obtained using a fast spin-echo sequence (TR:4000 ms; TE:110 ms; echo train length, 16 ms) in dorsal, transverse and sagittal planes as well as T1-weighted images obtained using a spin-echo sequence (TR:500 ms; TE:14 ms), and transverse images obtained using a fluid-attenuated inversion recovery sequence (FLAIR), (TR:6000 ms; TI:150 ms; TE:, 80 ms). Slice thickness ranged from 3 mm to 5 mm, with an interslice gap of 1 mm. The FOV ranged from 18 cm to 22 cm.

The MRI protocol for the cervical spine included similar parameters, but FLAIR sequence, and different slice thickness (usually 4 mm, with 1-mm gaps) and FOV (14–16 cm). Intravenous (i.v.) gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA) was administered in all animals (0.1 mmol/kg). Post contrast T1-weighted sequences were always acquired in the transverse plane with or without fat saturation.

Neuroradiological assessment was performed by an experienced neuroradiologist (AM), who evaluated the following specific brain radiologic features: (i) ventricular dilatation, including that of the fourth ventricle, which was classified as normal (-), mild (+), fair (++), or remarkable (+++); (ii) presence or absence of periventricular edema, defined as an accumulation of interstitial water in the periventricular white matter; (iii) presence or absence of meningeal enhancement (mild to moderate) or intracranial parenchymal enhancing lesions (ring-rim enhancement and multiple enhancing parenchymal nodules).

For the purposes of the present study cervical hydromyelia consists on a dilation of the CCEC, that appeared on MRI as a central cord round region of hyperintensity on T2-weighted images and funnel-shaped pipe throughout the cervicomedullary junction on sagittal images connecting the fourth ventricle outlet with the cervical spinal cord, while dilation arising some distance from the foramen magnum or appearing below a syrinx-free segment of the spinal cord was regarded as syringomyelia[1,3].

Hydro/syringomyelia (syrinx) was defined as a fluid-containing cavity within the spinal cord parenchyma with a transverse diameter of greater than or equal to 2 mm. The size of the cervical syrinx was measured as the maximal width from transverse T2-weighted images[14], once excluded potential aliasing or central point artifact or anterior median fissure of the spinal cord[15].

The severity of hydro/syringomyelia was classified as remarkable (+++) if the widest point of the hyperintensity was >60% of the spinal cord diameter, mild (++) if it was between 30 to 60%, and fair (+) if it was up to 30%. The number of vertebral lengths affected with hydro/syringomyelia assessed as an accumulation of CSF within the spinal cord parenchyma was recorded but, when the thoracolumbar spine was not imaged, the full extent of hydro/syringomyelia was probably underestimated in some dogs.

Statistical Analysis

Data were analyzed using SPSS Statistics, version 20.0 (IBM, Armonk, New York). Neuroradiologic and clinical data were compared among patients using descriptive statistics, including *t*-tests for continuous variables and *chi*-square tests for categorical variables. Descriptive statistics are reported as median, standard deviation (SD), minimum, and maximum values. The Kruskal-Wallis test was used to examine associations among breed, age, sex, symptoms onset, and MRI findings. The level of statistical significance was set at $p<.001$.

RESULTS

Clinical Findings

In the present study we evaluated clinical and imaging data from a group of domestic carnivores with brain/spinal pathology secondary to CNS inflammatory processes. Details regarding patient characteristics, signalment, clinical status, and radiological findings are presented in Table 1. A total of 23 animals were evaluated, including 15 males (60%) and eight females (40%). The age of the animals ranged from 2 months to 11 years (median 59 months; SD 36.7), with 18 animals aged >2 years (adult) and five young animals. There was one cat (4 %) and 22 dogs (96%). Among dogs, there were seven Yorkshire Terriers (30%), four French Bulldogs (20%), two mixed breeds (10%), two Poodles, one Shih-Tzu (5%), one Boxer, one Pomeranian, one West Highland Terrier, one Irish Setter, one German Shepherds, and one English Bulldog .

TABLE 1: Summary of signalment, clinical neurologic findings, CSF significant abnormalities, and final diagnosis.

Patient ≠/age/sex/brand	CLINICAL STATUS	NEUROLOGIC EXPLORARTION	TIME OF SYMPTOMS	CSF/Others	DIAGNOSIS
1/1 y/F/ Mixed Breed	Seizures since birth with progression in the last 6 mo.	Obtundation, non-ambulatory tetraparesis with absent postural reactions on all limbs, left pleurothotonus, vertical nistagmus, bilaterally decreased menace response, aniscoria (left miosis), and ventral strabismus: Diffuse forebrain dysfunction.	6 mo.	Mild mononculear pleocytosis (35 cels/mm3): 60% monocytes, 25% lymphocytes, 5% neutrophils, 10% macrophages. Increased protein count (56 mg/dL).	Infectious meningoencephalitis (perinatal).
2/2 mo/M/Shihtzu	Progressive tetraparesis of 2 mo of duration with recent onset of seizures. Previous corticosteroids treatment.	Obtundation, ambulatory tetraparesis, decreased postural reactions in all limbs: Diffuse forebrain dysfunction.	4 D.	Mild mononculear pleocytosis (13 cels/mm3): 20% monocytes, 45% lymphocytes, 5% neutrophils, 30% macrophages. Increased protein count (72 mg/dL).	Infectious meningoencephalitis (distemper most likely).
3/1 y/M/Common Feline	Progressive abnormal walking since birth. Adopted puppy. Previous corticosteroids treatment.	Depressed mental status, severe ambulatory tetraparesis, decreased postural reactions in all limbs (worse on left side), decreased left menace response and facial sensation.	Since birth.	N-OB (Peripherical blood: pancitopenia)	Suspected infectious meningoencephalitis (feline panleukopenia, virus-infection suspected).

Patient ≠/age/sex/brand	CLINICAL STATUS	NEUROLOGIC EXPLORARTION	TIME OF SYMPTOMS	CSF/Others	DIAGNOSIS
4/3 mo/F/German Shepherd	Progressive neck pain since 3 w after minor trauma.	Vestibular ataxia, tetraparesis with decreased postural reactions worse on right limbs, right head tilt, vertical nystagmus, right ventrolateral strabismus, decreased left menace response and decreased flexor reflex on left front limb: Multifocal dysfunction including forebrain, central vestibular and C6-T2 spinal cord segments.	3 w.	N-OB	Suspected perinatal infectious meningoencephalitis.
5/11 mo/F/French Bulldog	Sudden blindness	Bilateral absence of menace response and pupillary light reflexes: Bilateral retinas, optic nerves or chiasm.	12 D.	Mild Mononculear pleocytosis (18 cels/mm3): 25%neutrophils, 75% macrophages. Increased protein count (47 mg/dL).	MUE
6/ 6 y/M/Yorkshire	2.5-y history of seizures with acute onset of blindness	Bilateral absence of menace response and pupillary light reflexes: Bilateral retinas, optic nerves or chiasm.	8 D.	Mild Mononculear pleocytosis (14 cels/mm3): 40% monocytes, 60% macrophages. Increased protein count (64 mg/dL).	MUE
7/8 y/M/Boxer	Cluster of seizures for 5 D.	Depressed mental status, circling to the right, decreased left menace response, and facial sensation: Left forebrain dysfunction.	5 D.	Mild Mononculear pleocytosis (65 cels/mm3): 35% monocytes, 10% macrophages, 45 neutrophils, 10% lymphocytes. Increased protein count (90 mg/dL).	Suspected infectious meningoencephalitis (rickettsia ricketsii, serum positive).

Patient ≠/age/sex/brand	CLINICAL STATUS	NEUROLOGIC EXPLORARTION	TIME OF SYMPTOMS	CSF/Others	DIAGNOSIS
8/2.5 y/M/Yorkshire	Progressive difficulty in swallowing/ dysphagia. Right middle ear otitis by fungi, treated with initial improvement but with further worsening.	Depressed mental status, left pleurototonus, non-ambulatory tetraparesis, absent postural reactions in all limbs, bilateral absence menace response and palpebral reflex, rotatory nystagmus (fast phase to the right), and ventrolateral positional strabismus of the left eye: multifocal dysfunction, including forebrain and medulla.	3 mo.	Mononculear pleocytosis (185 cels/mm3): 100% mononuclear cells 35% monocytes, 10% macrophages, 45 neutrophils, 10% lymphocytes. Increased protein count (58 mg/dL).	MUE
9/5 y/M/Yorkshire	Incoordination for 3 D.	Depressed mental status, right pleurothotonus, ambulatory tetraparesis, and decreased postural reactions in left limbs with decreased menace response in left eye: Right forebrain dysfunction.	3 D.	Mononculear pleocytosis (16 cels/mm3): 80% mononuclear cells, 20% neutrophils. Increased protein count (60 mg/dL).	MUE
10/6 y/M/Pomeranian	Chronic abnormal mental status (several mo)	Depressed mental status, hypermetric gait, ambulatory tetraparesis and decreased postural reactions in all limbs, and anisocoria (left pupil smaller than right): Multifocal dysfunction affecting brainstem and cerebellum.	Several mo.	Mononculear pleocytosis (16 cels/mm3): 80% mononuclear cells, 20% neutrophils Increased protein count (115 mg/dL).	MUE
11/4 y/M/French Bulldog	Two mo of progressive head tilt and ataxia.	Ambulatory tetraparesis, and decreased postural reactions in left limbs with decreased menace response and palpebral reflex in left eye. Left head tilt, horizontal nystagmus (fast phase to the right), and position strabismus: Right forebrain dysfunction.	2 mo.	Polimorphonuclear pleocytosis (89 cels/mm3): 20% mononuclear cells, 80% neutrophils. Increased protein count (25 mg/dL).	Infectious meningoencephalitis (otologic source).

Patient ≠/age/sex/brand	CLINICAL STATUS	NEUROLOGIC EXPLORARTION	TIME OF SYMPTOMS	CSF/Others	DIAGNOSIS
12/5 y/F/ Mixed Breed	Postraumatic epilepsy (since 1 y)	Forebrain dysfunction	1 y.	Mononculear pleocytosis (8 cels/mm3): 98% mononuclear cells, 2% neutrophils. Increased protein count (100 mg/dL).	MUE
13/5 y/M/Yorkshire	Abnormal mental status, since 1 mo.	Bilateral absence of menace response: Diffuse forebrain dysfunction.	1 mo.	Mononculear pleocytosis (28 cels/mm3): 87% mononuclear cells, 13% neutrophils. Increased protein count (120 mg/dL).	MUE
14/7 y/F/ West Highland Terrier	Recent onset of seizures (2 mo).	Decreased left menace response and facial sensation: Right forebrain dysfunction.	2 mo.	Mononculear pleocytosis (46 cels/mm3): 43% mononuclear cells, 57% neutrophils. Increased protein count (77 mg/dL).	MUE
15/4 y/F/ Irish Setter	Weakness since 6 w and bilateral facial palsy.	Tetraparesis more severe on left side, decreased postural reactions on left limbs, right head tilt and bilateral reduced palpebral reflex: Diffuse forebrain dysfunction.	6 w.	Mononculear pleocytosis (12 cels/mm3): 70% mononuclear cells, 30% neutrophils. Increased protein count (35 mg/dL).	MUE
16/6 y/F/French bulldog	Abnormal walking since 6 mo. Previous corticosteroids treatment for non-specific allergy.	Left side hemiparesis and bilateral decrease of menace reaction: Diffuse forebrain dysfunction worse on the right side.	6 mo.	N-OB	Suspected MUE

Patient ≠/age/sex/brand	CLINICAL STATUS	NEUROLOGIC EXPLORARTION	TIME OF SYMPTOMS	CSF/Others	DIAGNOSIS
17/4 y/M/Yorkshire	Ataxia for 1 w.	Depressed mental status with tetraparesis and decreased postural reactions in all limbs: Diffuse forebrain dysfunction.	1 w.	Mononculear pleocytosis (13 cels/mm3):100% mononuclear cells. Increased protein count (50 mg/dL).	MUE
18/10 y/ M/Yorkshire	Acute onset ataxia for 4 w.	Tetraparesis, vestibular ataxia with right head tilt, vertical nystagmus, and ventrolateral strabismus of right eye: Right medullar dysfunction.	4 w.	Mononculear pleocytosis (68 cels/mm3): 27% monocytes, 55% macrophagues, 12% lymphocytes, 6% neutrophils. Increased protein count (170 mg/dL).	MUE
19/ 4 y/F/French Bulldog	Acute onset blindness	Bilateral absence of menace response with absent pupillary light reflexes: Bilateral retinas, optic nerves or chiasm.	1 w.	Mononculear pleocytosis (90 cels/mm3):100% mononuclear cells. Increased protein count (57 mg/dL).	MUE
20/11 y/M/ Poodle	Abnormal mental status for two months. Weakness since 6 w.	Depressed mental status, tetraparesis worse on the left side, and decreased left menace response: Right forebrain dysfunction.	2 mo.	10 cells. Mononculear pleocytosis (10 cels/mm3): 60% macrophages, 40% lymphocytes. Increased protein count (60 mg/dL).	MUE
21/8 y/M/ Poodle	Chronic abnormal mental status (several w)	Depressed mental status, left pleurototonus, and non-ambulatory tetraparesis: Left forebrain dysfunction.	Several w.	N-OB	Suspected MUE

Patient ≠/age/sex/brand	CLINICAL STATUS	NEUROLOGIC EXPLORARTION	TIME OF SYMPTOMS	CSF/Others	DIAGNOSIS
22/5 y/M/ Yorkshire Terrier	Abnormal mental status for 1 w. Tetraparesis with severe ataxia. Tendency to scratch at its mid-cervical area	Ambulatory tetraparesis with severe ataxia. Postural reaction (paw replacement and hopping) deficits were noted in all four limbs, being more pronounced in the forelimbs: Diffuse forebrain dysfunction.	1 w.	Mononuclear pleocytosis (16 cels/mm3): 80% macrophages, 20% neutrophils. Increased protein count (140 mg/dL).	MUE
23/10 y/M/ English Bulldog	Abnormal mental status for 2 mo.	Depressed mental status, tetraparesis, cervical pain, hyperesthesia, neck stiffness, and left menace response: Right forebrain dysfunction.	6 w.	N-OB	Suspected MUE

CSF: cisternal cerebrospinal fluid analysis
D: days
F: female
M: male
Mo: months
MUE: meningoencephalitis of unknown etiology
NA: No abnormalities
N: No
N-OB: Not obtained
VPS: Ventriculo-Peritoneal Shunt
W: weeks
Y: Yes
y: years
-: negative

TABLE 2: MRI FINDINGS

Case ≠	VENTRICULOMEGALY	HYDROMYELIA/ SYRINGOMYELIA	LATERAL FORAMINA DILATATION (LUSCHKA)	BRAIN MR FINDINGS: Obstructive hydrocephalus/Meningeal enhancement /Others	OTHERS
1	+++	H+++	+++	Non-communicating obstructive hydrocephalus/No ME	
2	+++	H+++	+++	Non-communicating obstructive hydrocephalus/ME	
3	+++	H+++ (all over the spinal cord)	+++	Non-communicating obstructive hydrocephalus/ME	Cerebellar hipoplasia; Scoliosis, double
4	+++	H+++ cervical and dorsal	+++	Non-communicating obstructive hydrocephalus/No ME/Periventricular interstitial edema/Cerebellar hypoplasia	Scoliosis, double
5	++	H+++	++	Non-communicating asymmetric obstructive hydrocephalus/ME/Periventricular interstitial edema.	Multiple mild enchancing supra and infratentorial nodular lesions
6	+++	S+++	No valuable	Non-communicating obstructive hydrocephalus/ No ME/Periventricular interstitial edema.	T2-W signal abnormalities throughout the brainstem and cerebellum with swelling and lack of enhancement. (Rhombencephalitis)
7	+++	S++	+	Non-communicating asymmetric obstructive hydrocephalus/ No ME/Periventricular interstitial edema.	2 right hemisheric enhancing masses with ependymal and ventricular enhancement, and pyocephalus

Case ≠	VENTRICULOMEGALY	HYDROMYELIA/ SYRINGOMYELIA	LATERAL FORAMINA DILATATION (LUSCHKA)	BRAIN MR FINDINGS: Obstructive hydrocephalus/Meningeal enhancement /Others	OTHERS
8	+++	S+++	++	Non-communicating obstructive hydrocephalus/ ME	
9	++	S++	+	Non-communicating obstructive hydrocephalus/No ME	Multiple mild enchancing supra and infratentorial nodular lesions
10	++	S++	++	Non-communicating obstructive hydrocephalus/ No ME	Multiple mild enchancing supra and infratentorial nodular lesions
11	+++	S+++	++	Non-communicating asymmetric obstructive hydrocephalus/No ME	Hydromyelia extending towards lumbar region. Otobullitis (bilateral)
12	+++	S++	-	Non-communicating asymmetric obstructive hydrocephalus/ME	
13	+++	H+++	+	Asymmetric non-communicating obstructive hydrocephalus and focal encephalomalacia/No ME	Frontal lobe residual lesión
14	+++	S++	No valuable	Non-communicating obstructive hydrocephalus/ME and trigeminal enhancement	Disks extrusions L4-L5 y L6-L7
15	+++.	H+++	+++	Non-communicating obstructive hydrocephalus/ No ME	Disk extrusion C3-C4
16	++.	S+++ (all over the spinal cord)	+++	Non-communicating obstructive hydrocephalus/No ME	Disk extrusion C2-C3
17	+++	S+++ Cervical and dorsal	-	Non-communicating obstructive hydrocephalus/ No ME	Disk extrusion C6-C7.

Case ≠	VENTRICULOMEGALY	HYDROMYELIA/ SYRINGOMYELIA	LATERAL FORAMINA DILATATION (LUSCHKA)	BRAIN MR FINDINGS: Obstructive hydrocephalus/Meningeal enhancement /Others	OTHERS
18	+++	S+++ cervical and dorsal (non-continuous but skipped)	-	Non-communicating obstructive hydrocephalus/ No ME	
19	+++	S+++	+	Non-communicating obstructive hydrocephalus/ No ME	
20	+++	S++	++	Non-communicating obstructive hydrocephalus/basal ME	Disks bulging C3-C4 y C4-C5 and disk extrusion C5-C6
21	++	S+	++	Non-communicating obstructive hydrocephalus/ basal ME	
22	+	S+++ cervical and dorsal	++	Non-communicating obstructive hydrocephalus/ME	Multiple supra and infra tentorial mild enhancing nodular lesions
23	+++	S+++	-	Non-communicating obstructive hydrocephalus/N ME/Periventricular interstitial edema.	Multiple supratentorial mild enhancing nodular lesions

H: Hydromyelia
ME: Meningeal Enhancement
N: no
S: Syringomyelia
Y: yes

The clinical signs at disease onset, neurologic status at the time of MRI evaluation, and duration of clinical signs from onset to MRI evaluation were recorded. Fifteen patients (65.2%) presented with predominantly brain signs, three (13%) with ocular signs, two (8.4 %) with upper cervical cord signs, and three (13 %) with both upper cervical cord and brain signs. Three patients had previously undergone treatment with corticosteroids.

Inflammation of the central nervous system (CNS) was diagnosed based on the patient's clinical status, standard hematologic parameters, CSF sample findings, and MRI findings. Standard hematologic parameters were obtained in all animals. CSF samples were obtained in 18 of 23 animals, and hematologic parameters indicative of active meningoencephalitis were present in all the animals evaluated. Fourteen (60.8%) were diagnosed with meningoencephalitis of unknown etiology (MUE), two with perinatal infectious meningoencephalitis (8.6%) and most likely of viral etiology, one with meningoencephalitis associated with *Rickettsia rickettsii* infection (4.3%), and one with otogenic meningoencephalitis (4.3%). For the five patients without CSF samples, the diagnoses of perinatal meningoencephalitis (cases #3 and #4) and MUE (cases #16, 21, and 23) were established based on clinical history and MRI findings.

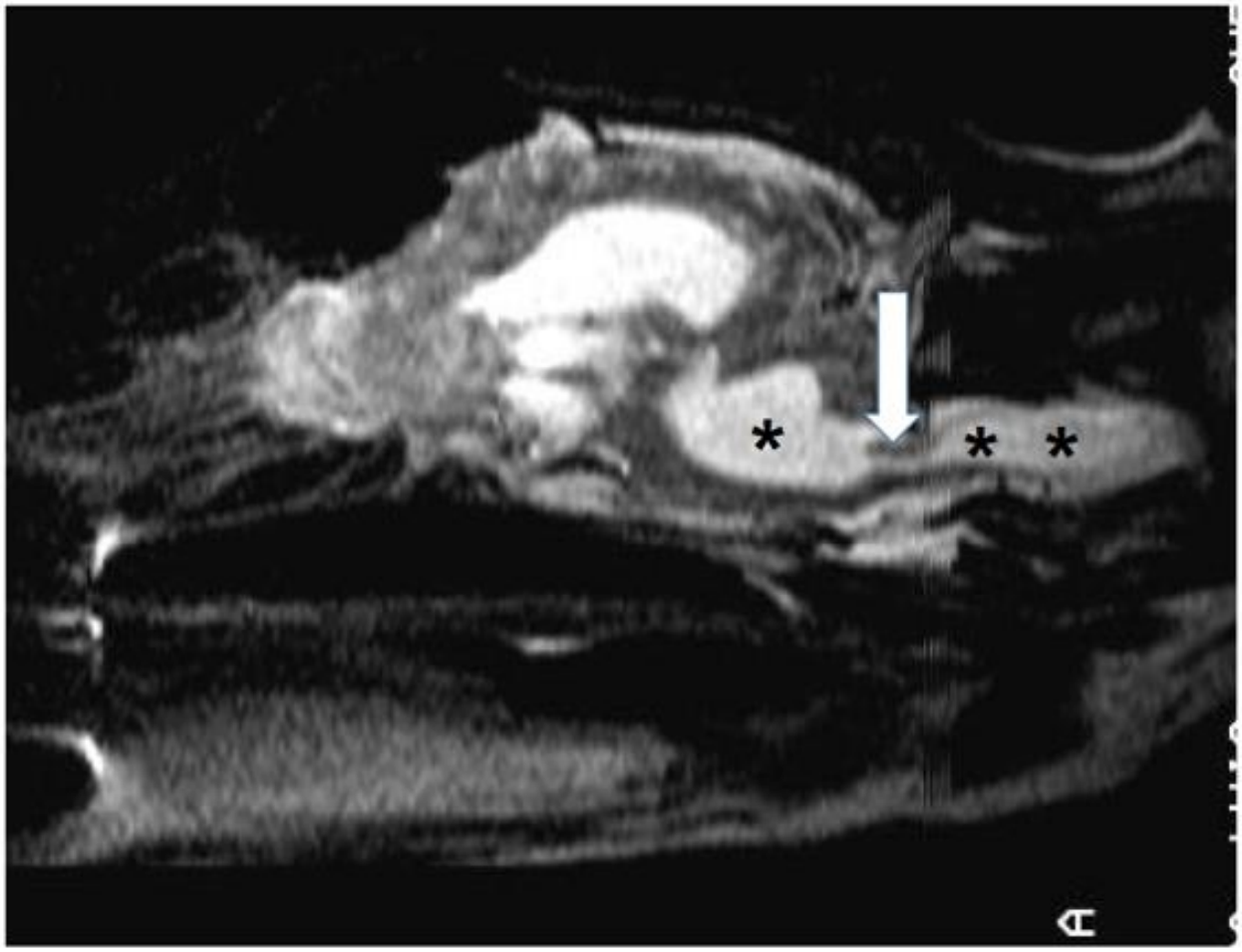
Breeds of control group of dogs included Pitbull (2), German Shepard (2), Doberman (2), Teckel (2), Yorkshire (2), French bulldog, greyhound, Beagle, Jack Russel Terrier, Schnauzer, Rottweiler, labrador retriever, bichon fries, cocker spaniel, West Highland Terrier, and mongered dog. Breeds of cats included common feline (2), British shorthair, and Siamese. The age at presentation ranged from 4 months to 11 years (median 61 months; SD 32.7). Fourteen dogs and the cat were male.

Magnetic Resonance Imaging Findings

Dilatation of all ventricular compartments—including the fourth ventricle—was present in all cases, consistent with the diagnosis of OH. OH was classified as remarkable in 15 cases, mild in seven, and minor in the remaining case. In five cases, OH was asymmetric, mostly due to an underlying hemispheric mass effect. In five cases, OH was associated with periventricular interstitial edema, all but one in young cases. The CCEC was dilated in continuity with the fourth ventricle outlet in eight cases (Figs. 1-3), whereas the continuity of the cavity could not be established in the remaining 15 cases (Fig. 4). In two puppies and one kitten we observed a small, flap-like, marginal-dorsal structure at the level of the obex (Figs. 1 and 2), which we assumed to be an embryological remnant. Among the 18 adult patients, three patients exhibited dilatation of the CCEC in continuity with the fourth ventricle, while the other 15 patients did not. All five young patients exhibited dilatation of the in continuity with the fourth ventricle. None of the cases exhibit eccentric cavity dilatation of CCEC within the spinal cord. Post-gadolinium meningeal enhancement was present in nine cases (Fig. 5).

Fig. 1 (A and B); (MRI features of case #1). Obstructive hydrocephalus and cervical hydromyelia in a puppy.

A: Midsagittal T2-weighted view at the level of the cervicomedullary junction level.
There is a continuity and connection between the 4th ventricle (*) and the central cervical ependymal canal (**) by a funnel-shape connection (**). Notice a small flap marginal-dorsal structure at the level of the obex (arrow) and markedly distended hyperintense third and lateral ventricles.



B: Transverse T2-weighted view at the C1-C2 level. Notice huge central hyperintense central cervical ependymal canal enlargement (*).

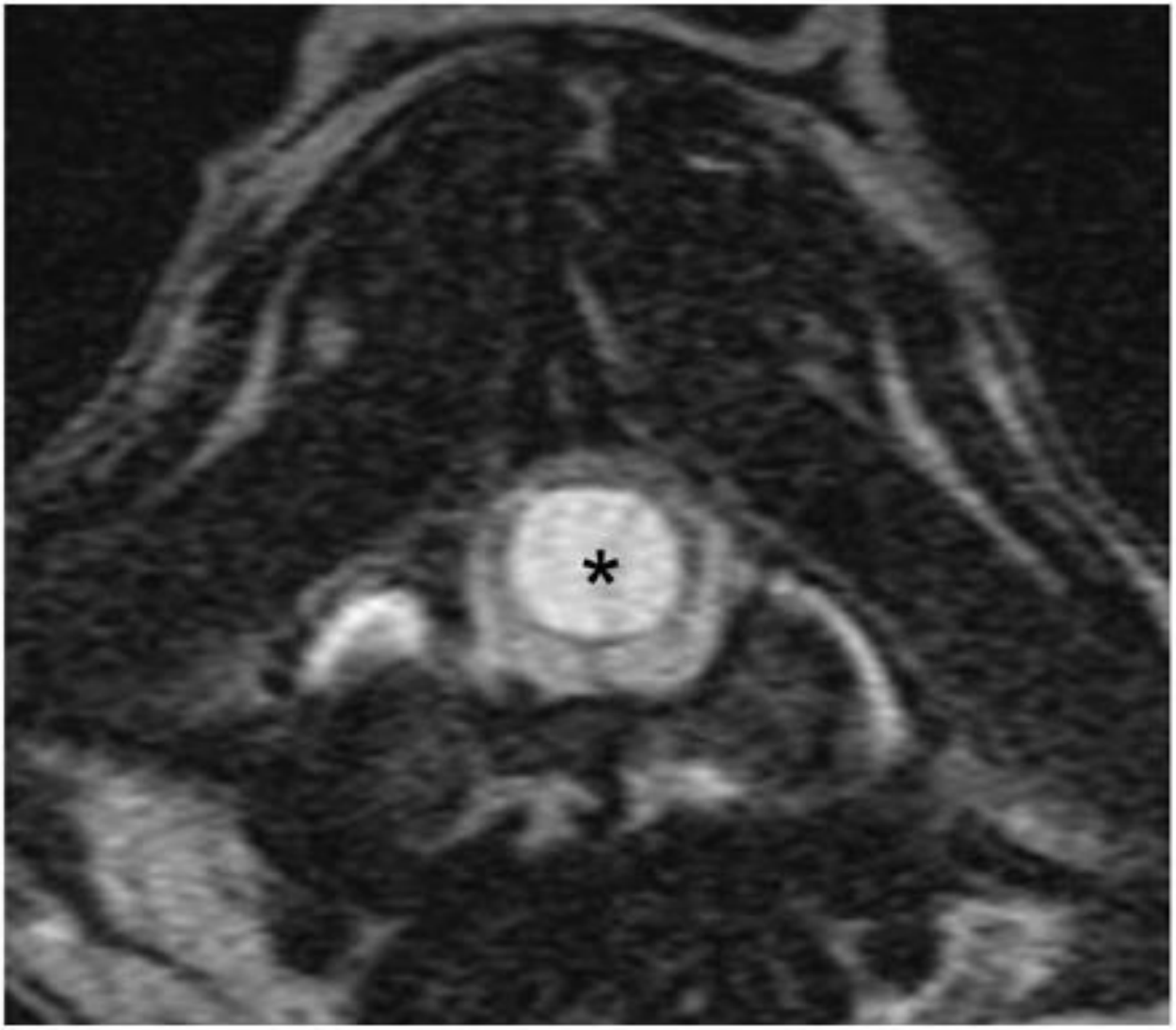
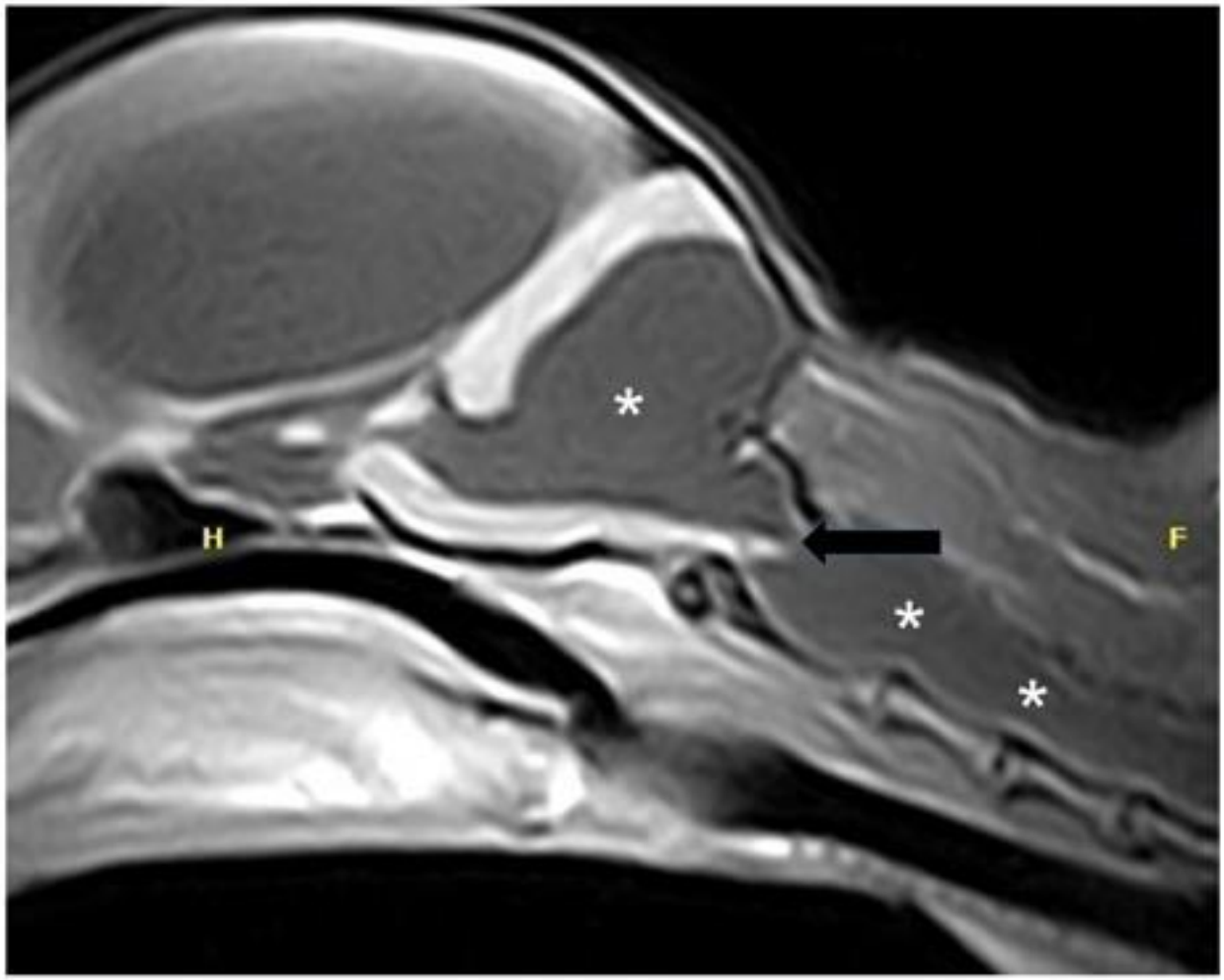


Fig. 2 (A and B); (MRI features of case #3). Obstructive hydrocephalus and cervical hydromyelia in a kitten.

A: Midsagittal T1-weighted view at level of the cervicomedullary junction.
There is a continuity and connection between the 4th ventricle (*) and the central ependymal cervical canal (**) by a funnel-shape connection. Notice a small flap marginal-dorsal structure at the level of the obex (arrow). Additional third, lateral ventricle, and cerebral aqueduct enlargement are seen.



B: Transverse T1-weighted view at the level of the caudal fossa. Notice huge 4th ventricle enlargement as well as both lateral foraminae (*) and temporal horns (T).

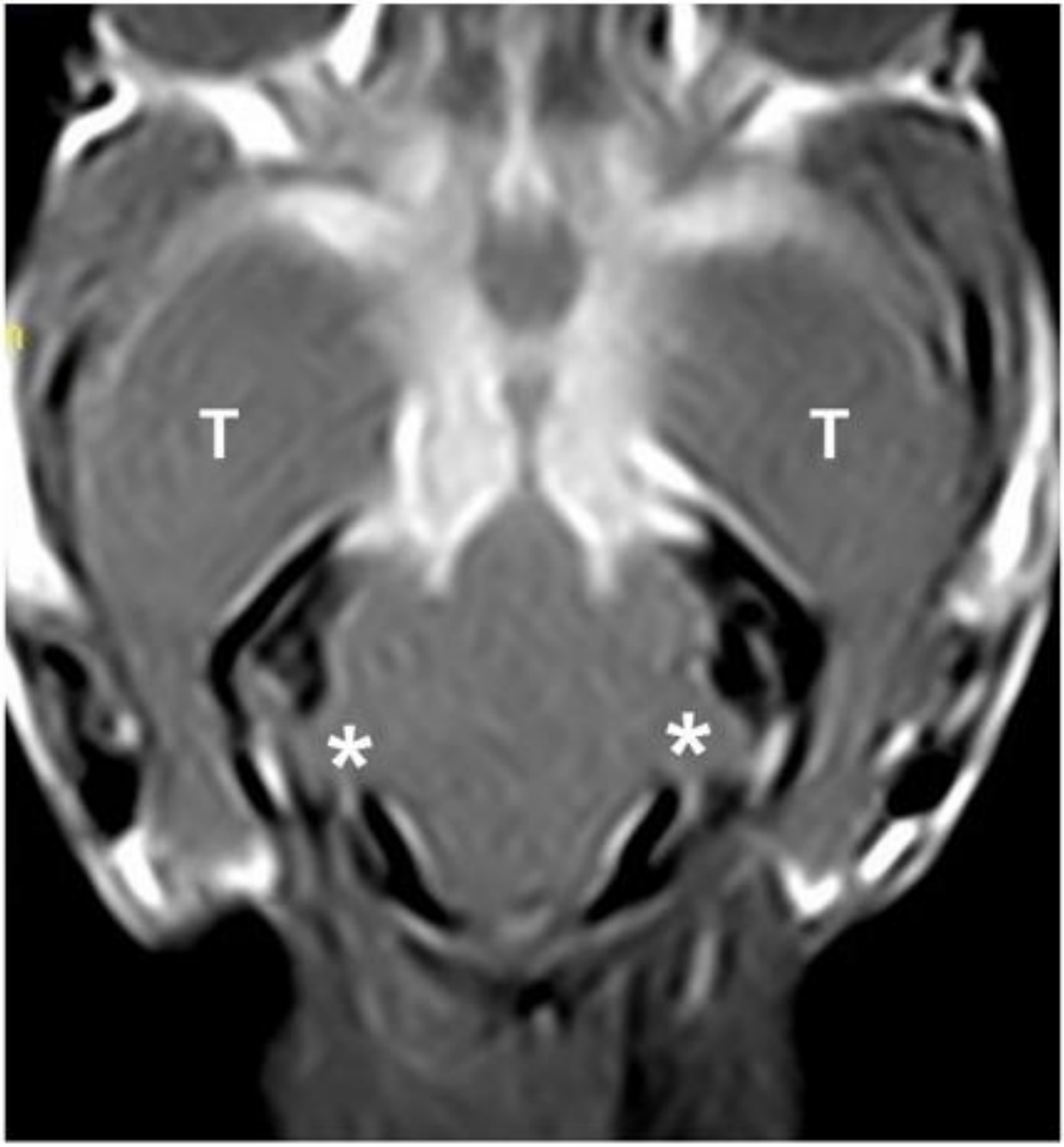
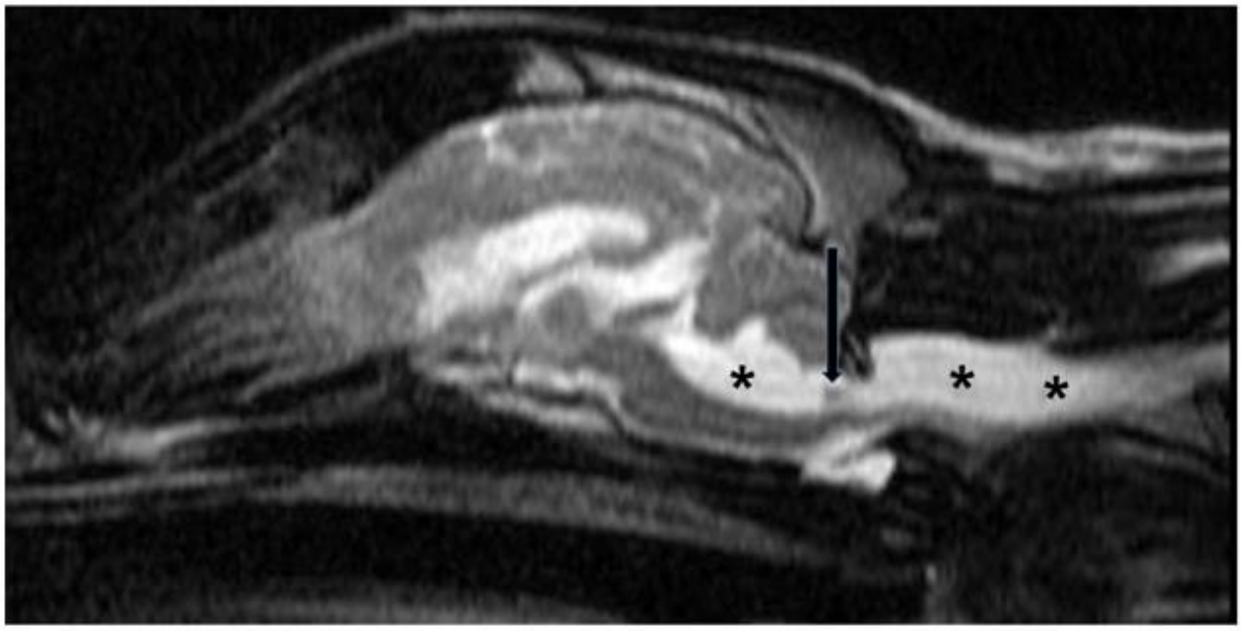


Fig. 3 (A and B); (MRI features of case #15). Obstructive hydrocephalus and cervical hydromyelia in an adult dog.

A: Midsagittal T2-weighted view at the level of the cervicomedullary junction. There is a continuity and connection between the 4th ventricle (*) and the central ependymal cervical canal (**) by a funnel-shape connection. Again, notice a small flap marginal-dorsal structure at the level of the obex (arrow).



B: Transverse T1-weighted view through the caudal fossa and cervical cord. There is a huge 4th ventricle dilatation as well as enlargement of the lateral foramina (*), (4th ventricle outlet dilatation).

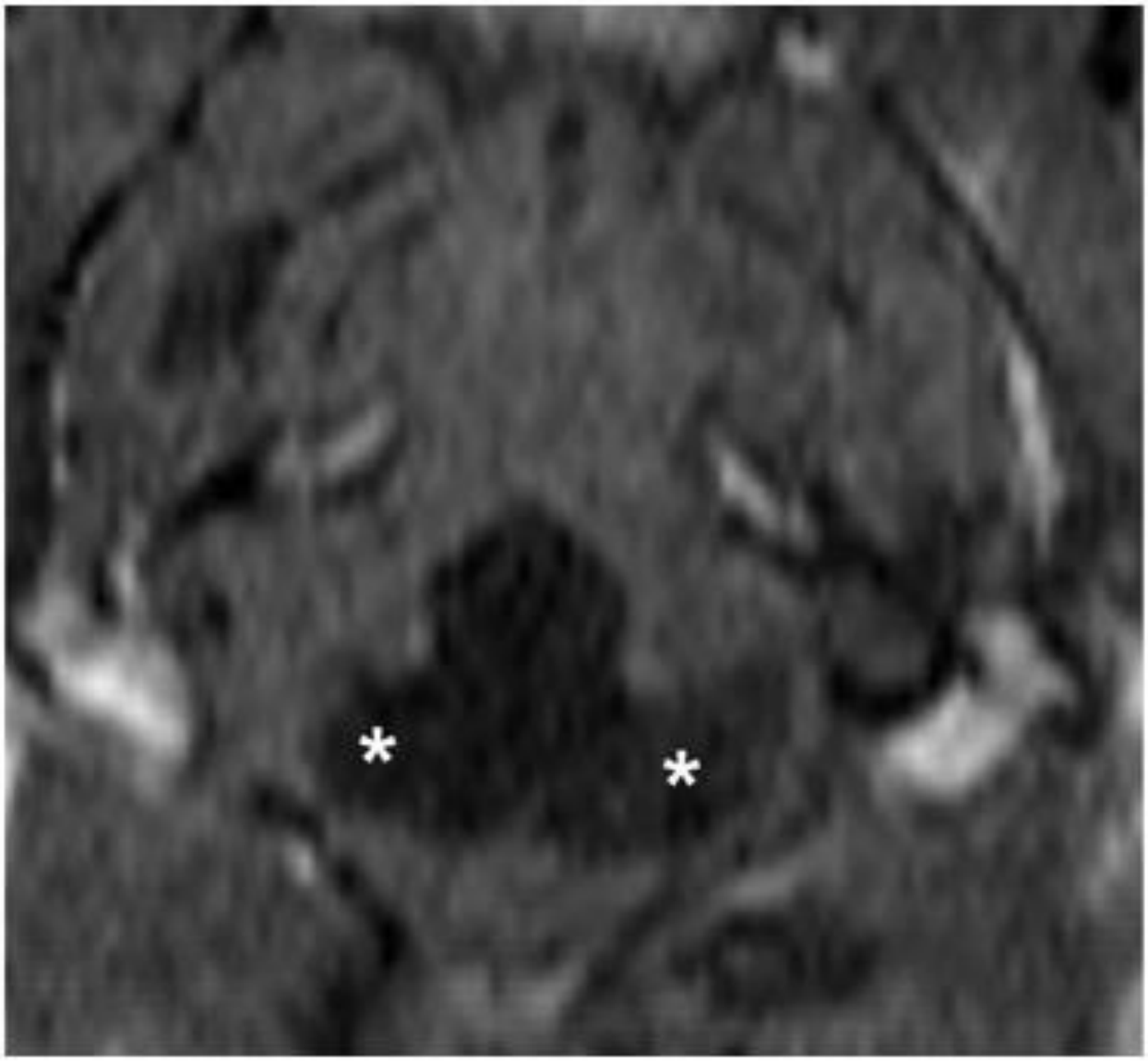
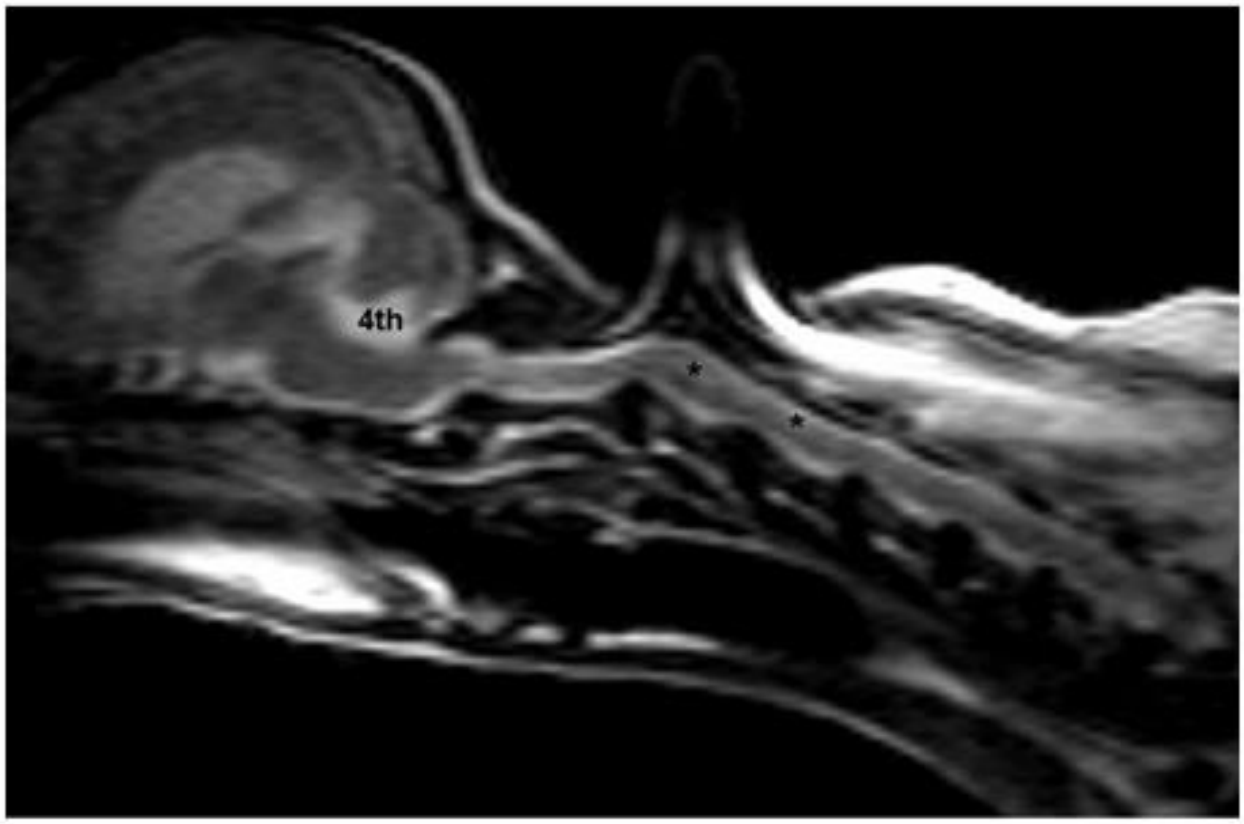


Fig. 4 (A and B); (MRI features of case #20). Obstructive hydrocephalus and cervical syringomyelia in an adult dog.

A: Midsagittal T2-weighted view at level of the cervicomedullary junction.
There is no continuity between the enlarged 4th ventricle and the central ependymal hyperintense filiform midline cervical cavity (**). Additional third, fourth (4th), lateral ventricle, and the brain aqueduct enlargement are seen. Hypointense C2-C3 chip artifact blurring the dorsal-paraspinal muscles is present.



B: Transverse T2-weighted view at C5-C6 level. Notice hyperintense central cervical ependymal canal enlargement (*).

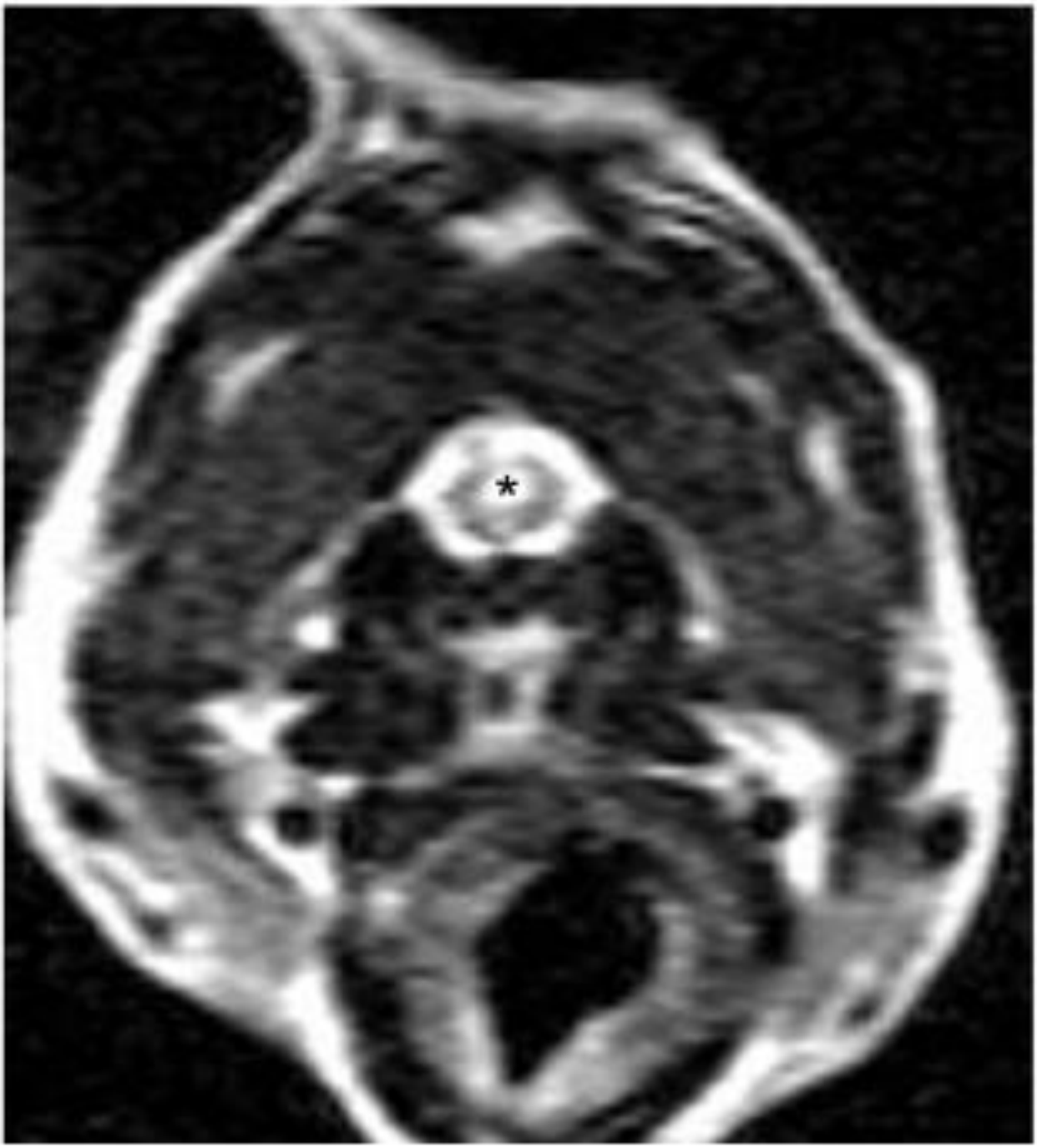
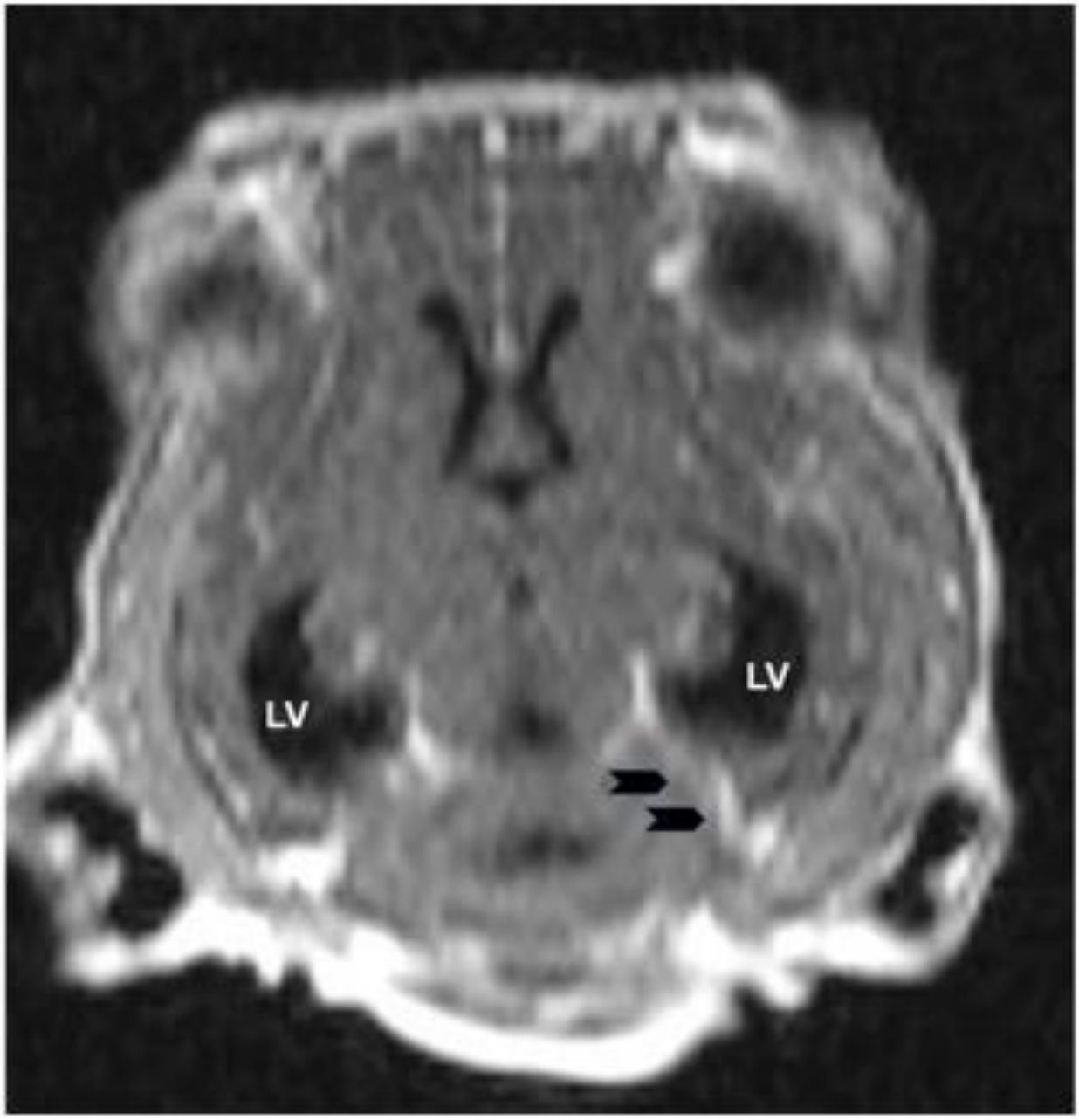


Fig. 5. MRI features of case # 8: meningeal enhancement.
Transverse post-Gadolinium T1-weighted views through the midbrain and caudal fossa. Notice diffuse meningeal enhancement, particularly at the region of the tentorium cerebelli (arrows). Also, enlarged hypointense lateral ventricles are identified (LV).



In all animals, cervical MRI revealed hyperintensity of the central spinal cord on T2-weighted images, with or without clear ependymal layer distinction (16 classified as remarkable, six as mild, and minor in one case). We also observed in all cases dilatation of the foramina of Luschka as well as CCEC dilatation that was either continuous or non-continuous with the fourth ventricle. All eight patients with continuous CCEC dilatation (hydromyelia) exhibited outlet dilatation (foramina dilatation) of the fourth ventricle. However, among the 15 patients with non-continuous CCEC dilatation, 10 exhibited outlet dilatation of the fourth ventricle, whereas four did not, and in the other remaining case this feature could not be ascertained. All five young patients exhibited CCEC dilatation in continuity with the fourth ventricle, as well as continuity of the fourth ventricle with the dilated foramina of Luschka. Dilatation of the CCEC extended into the thoracic segment in two cases and in four other cases this finding extended all over the spinal cord. Multiple enhancing supra and or infratentorial nodules were seen in four cases, probably consisting on granulomatous lesions. Pyocephalus was present in one case. Spinal associated lesions were present on MRI in seven cases. Lumbar disk extrusions were present in two cases, while both cervical disk extrusions and protrusions were present in three cases. Double scoliosis was present in two young patients. In one case, a residual, presumably posttraumatic, frontal brain lesion was discovered. Finally, one patient presented with signs consistent with bilateral otomastoiditis.

No statistically significant associations were observed between adult age and any of the following radiological signs: dilatation of the foramina of Luschka, syringomyelia, sex, symptoms onset, or breed. However, significant associations were observed between young age and dilatation of the foramina of Luschka or hydromyelia ($p<.001$).

In the control group no significant CCEC dilatation was observed in any animal (transverse diameter of greater than or equal to 2 mm), once excluded potential aliasing or central point artifact or anterior median fissure of the spinal cord.

DISCUSSION

We reported a case series in which OH and hydro/syringomyelia was discovered during the neuroradiological work-up of animals whose owners had sought neurological veterinary care for a variety of neurological signs and symptoms, all of which were discovered to have occurred secondary to CIBC.

In this series, we specifically excluded animals with hydro/syringomyelia secondary to brain or CVJ anomalies, tumors, or posttraumatic states, to avoid the influence of confounding factors related to primary CSF or dynamic craniospinal abnormalities. Moreover, all animals presented with a particular form of OH that promoted cervical hydro/syringomyelia, with some patients' conditions extending into the thoracic or lumbar spinal cord.

Syringomyelia refers to an expanding CSF-filled cavity that is present within the

substance of the spinal cord, arising primarily outside the CCEC and usually lined with glial cells rather than ependymal cells. In contrast, hydromyelia refers to a dilatation of the CCEC that is lined with ependymal cells and often communicates with the ventricular system[1,3]. Severe hydro/syringomyelia produces a CCEC dilatation with a haustra-like appearance on MRI, possibly due to differences in resistance at the somite level, which may act on the dentate ligaments or septa within. Previous studies have revealed that communicating syringomyelia may occur secondary to hydromyelia[1,11]. In contrast, non-communicating syringomyelia may occur secondary to intramedullary tumors, myelitis, meningitis, trauma, hemorrhage, or hernias rather than upstream (i.e., brain and coverings) condition[4,6,12]. When intramedullary cavities are large, it may be difficult to differentiate syringomyelia from hydromyelia using imaging techniques. However, when the spinal cavity communicates with the ventricular system, the diagnosis of hydromyelia is always correct[4,6], a finding supported by the results of the present study.

In the past, many any authors have used the indistinct term "syringohydromyelia," since, in many cases, it was not possible to determine the origin of the cavity or distinguish between the two types. However, due to advancements in technology and MR imaging refinements, it is now possible to make this distinction "in vivo". In this study we have chosen to distinguish the terms syringomyelia and hydromyelia because our MRI features allowed for differentiation between the two conditions: the absence or the presence of a funnel-shaped connection between the fourth ventricle outlet and the CCEC, which can be observed throughout the cervicomedullary junction, particularly on sagittal images.

The pathophysiology of hydro/syringomyelia has been extensively debated, and conflicting results and theories regarding its underlying mechanisms have been reported, in both humans and animals. From classical to contemporary times, numerous theories have been proposed based whether on CSF pressure gradients, fluid dynamics (the Venturi effect), or computerized models. All theories agree that alterations in the flow of CSF are required for hydro/syringomyelia formation[16]. Theories for explaining hydro/syringomyelia in humans were published as early as 1950[17]. These authors proposed the water-hammer or hydrodynamic theory, suggesting that obstruction of systolic CSF flow through the foramen magnum and outflow from the fourth ventricle forces the CSF into the CCEC with each arterial pulse, thereby forcing the CCEC to expand at the level of the obex. This dilates the CCEC, eventually resulting in hydro/syringomyelia. Failure of the foramina of Magendie and Luschka to perforate during fetal life forces ventricular CSF into the CCEC, promoting cervical hydromyelia.

Later, the concept of "sloshing" was introduced by Williams, who proposed the craniospinal dissociation or "suck effect" theory[18] to explain syringomyelia secondary to Chiari type I malformation, suggesting that the cerebellar tonsils act as a one-way valve that obstructs downward CSF flow. This

theory states that the valve mechanism of the tonsils prevents increases in intracranial pressure following Valsalva maneuvers from reaching the spinal CSF compartment, resulting in craniospinal pressure dissociation such that the intracranial pressure becomes higher than the spinal pressure, causing fluid to be sucked from the ventricles into the CCEC. The relatively low pressure in the spinal compartment then causes syringomyelia. This theory was supported by Oldfield[19] who proposed the tonsillar-piston theory. This theory relays on that by means of a venous or arterial mechanism CSF produces pressure waves in the spinal subarachnoid space, resulting in abrupt external compression of the spinal cord and rapidly propelling cavity fluid in a longitudinal direction. This results in not only enlargement of the cavity but also further dissection of the spinal cord parenchyma. However, two main drawbacks against the piston effect being the sole mechanism underlying syrinx formation are argued. First, this mechanism also relies on CSF being forced into the spinal cord from the subarachnoid space. Second, if increased pressure in the subarachnoid space is the driving force for CSF propulsion through the cord into the syrinx, this does not explain how the cavity is filled when pressure is increased at its external surface. Such pressure would rather compress and empty the cavity, and if the relatively soft spinal cord were exposed to such an external force, it would most likely collapse rather than expand or develop a syrinx[20,21].

Contrary to the aforementioned theories, which hypothesized that CSF is responsible for filling of the syrinx, other theories postulate that both filling and distension of the syrinx occur with and not against pressure gradients, in accordance with the second law of thermodynamics[22-24]. The main principles of contemporary theories are (i) that hydro/syringomyelia is caused by repeated mechanical distension of the spinal cord, and (ii) that the ensuing cavitation arises from extracellular fluid that originates from the high-pressure system in the microcirculation of the spinal cord (or microglia), not from the CSF that originates from the low-pressure system in the subarachnoid space. Thus, filling occurs down the pressure gradient from the spinal-cord microcirculation to the syrinx, and distension occurs down the pressure gradient from the syrinx to the subarachnoid space. Consequently, development of hydro/syringomyelia is independent of the presence of a pathway between the subarachnoid space and the syrinx. This implies that cavity formation occurs due to increased pulse pressure within the cord tissue itself, and that the source of the fluid in the cavity is extracellular fluid rather than CSF[17]. This hypothesis also provides an explanation for the potentially reversible edema that develops in the spinal cord of some patients prior to syrinx development or "pre-syrinx state" [23,24]. Hydromyelia and syringomyelia may also develop without preceding cord edema by the distension of preformed microscopic fluid-filled cavities, like the central canal or small rifts in the medulla[21].

Studies on intracranial dynamics using flow-sensitive MRI and radionuclide cisternography[4,25] supported the notion that the CSF is absorbed by the capillaries of the CNS rather than the arachnoid villi, as previously thought. Furthermore, as brain tissue exhibits similar mechanical properties and is characterized by high plasticity, increased pulse pressure in the cord may produce cord distension, thereby resulting in hydro/syringomyelia due to the accumulation of extracellular fluid in the distended cord. The transmedullary pressure gradients that produce cord distension may occur just above and below a fixed obstruction in the subarachnoid space, and anywhere in the spinal cord in patients with Chiari type I malformations[26], although the maximum pulsatile pressure waves are known to occur in the upper cervical canal and dissipate with increasing distances down the canal[25]. Cyst´ progression would occur as a result of the CSF pulse pressure originating from the expansion of the intracranial extracerebral arteries or from Valsalva-like maneuvers[16]. The intramedullary pulse pressure theory is also in accordance with the Venturi effect, which refers to a flow-related suction effect that produces a regional decrease in CSF pressure. Indeed, the Venturi effect explains syrinx formation in various pathologies that involve narrowing or obstruction of the CVJ, such as Chiari type I malformation, posttraumatic states with subarachnoid scarring or adhesions, or cervical compression (i.e.: herniated disk). Interestingly, such effects may be due to the synergistic effect of systolic pressure and hydrostatic pressure. However, it is the gravity-dependent valve mechanism that better would explain that human patients´ symptoms worsen in upright position or in Valsalva maneuver as a result of craniospinal pressure dissociation[26,27]. Raveling more the riddle in animals, in one hand the upright position is not the regular position in small carnivores, therefore the gravity-dependent valve mechanism does not apply in dogs and cats and, on the other hand, Chiari type I malformation does not fully exist in these animals. Moreover, dogs and cats have a rete caroticum that hampers CSF pulsations[12], therefore other mechanisms may also take place in pathophysiology of hydro/ syringomyelia in small carnivores.

In later human studies, the focus has shifted from the outside of the spinal cord to the inside. The intramedullary pulse pressure theory proposed by Greitz[22,28] is the first general theory that provides an explanation of the pathophysiology of hydro/syringomyelia regardless of etiology in humans (i.e., from Chiari type I malformation to tumors in the posterior fossa or arachnoiditis). Back then, this theory marked a paradigmatic shift regarding CSF absorption in the brain.

A recent study in human patients with degenerative cervical myelopathy using Phase-Contrast MR imaging data and based on the fact that cervical spinal cord is subject to physiologic craniocaudal motion supposedly due to cardiac pulse wave dynamics[29], analyzes spinal cord motion in patients with a cervical spinal stenosis also remote from the stenotic segment, focusing on the motion pattern throughout the cardiac

cycle and the impact of the distance to the next stenotic segment and the number of cervical stenotic segments, revealing a propagation of increased motion of the spinal cord tissue up to 3 adjacent cervical segments, apart from the next cervical stenosis, and continuous ("restless") spinal cord movement throughout the whole cardiac cycle, reflecting an emerging pathophysiologic pattern, and showing the focal level of stenosis. These findings would provide a potential surrogate of spinal cord tissue distress, contributing to intramedullary damage even before it becomes clinically evident.

Nevertheless, at present, no consensus regarding these theories has been reached, and the exact mechanisms underlying syrinx development and progression remain elusive.

Magnetic Resonance Imaging Findings and New Insights in the Pathophysiology of Hydro/Syringomyelia in Small Carnivores

In our study eight of 23 patients exhibited continuous communication between the ventricular system (fourth ventricle outlet) and the dilated CCEC, although this was particularly true in young animals (all five cases) rather than in adults (three out of 18 cases, 16%). Such findings are in accordance with those obtained in experimental studies of kaolin-induced hydrocephalus/syringomyelia in cats and dogs[10,11,16,30,31] as well as those in embryologic studies in dogs and cats[32,33], and it is in accordance with those or in experimental occlusion of the CCEC in rats[10], and with those observed in humans due to idiopathic stenosis of the foramina of Magendie and Luschka[34]. In each of these previous studies, progressive dilatation of the ventricles and CCEC was observed. In one such study, the attenuation of the increase in intracranial pressure due to OH occurred in conjunction with dilatation of the CCEC[30]. Taken together, these observations suggest that dilatation of the CCEC acts as a natural by-pass between the ventricles and the spinal subarachnoid space, and that hydromyelia functions as a "sink" or fifth ventricle to relieve the OH, as Gardner firstly proposed[35], but it does not work in humans because of the differences in embryology. Our MRI findings support that, at birth, small carnivores not only have an anatomic continuity between the fourth ventricle outlet and CCEC but also the CCEC has a functional role under pathologic conditions, such as OH secondary to brain inflammations. Furthermore, this embryologic connection likely disappears functionally over the years in normal, healthy animals, although it may be re-opened under pathologic conditions (i.e., chronic brain inflammations). Therefore, in young animals, OH easily promotes hydromyelia as a sink mechanism for draining overpressured CSF, and less likely in animal cases. This mechanism stands in contrast to the development of hydro/syringomyelia in human adults, where it may develop by the accumulation of extracellular fluid in the distended cord[16,22], because the embryologic and anatomic differences in the components of the posterior/caudal fossa between humans and dogs or cats.

Our MRI findings, besides the notion that obstruction of normal CSF flow pathways results in OH, further support that, in dogs and cats with remnant embryological communication between the fourth ventricle outlet and CCEC, a continuous dilatation of the CCEC from the fourth ventricle outlet is the most plausible explanation for hydromyelia in cases with OH. These facts also stands in conjunction with the classical Williams theory[18], which relies on transmission of the CSF to and from the fourth ventricle via a patent CCEC to the syrinx. Although the classical theories are easy to understand, they are not applicable in adult humans, who usually do not possess a patent CCEC. However, as observed in the present study, this is not the case at least in young dogs and cats. Therefore, it appears that *lex parsimoniae* or Occam's razor principle is fulfilled in this issue when it comes to dogs and cats.

From a human clinical perspective, it is interesting to note that atresia or cystic dilation of the foramina of Magendie and Luschka is unlikely to cause inhibition of normal cerebrospinal egress from the fourth ventricle in children, resulting in OH with or without hydro/syringomyelia[34-36], resembling the radiological picture observed in our young and some adult animals with OH (enlargement of the lateral foramina, and hydromyelia), albeit secondary to CIBC. When the anatomic continuity is not present or when reopening of embryologic remnants is not possible, as we observed in 15 out of 18 adult animals, hydro/syringomyelia may be explained by other mechanisms that imply the lack of anatomic continuity of the fourth ventricle outlet and the CCEC, such as the distension of preformed microscopic fluid-filled cavities, or small rifts in the medulla[37] but not necessarily those proposed so far in humans such as alterations in CSF flow, gradient pressure differences between the posterior/caudal fossa and subarachnoid spinal space, venous ischemia, intramedullary pulse pressure theory, and the Venturi effect[1,4,6,16-19,22,23,28,38-40], again because of the anatomic and physiologic differences between humans and dogs and cats, such as lack of cerebellar tonsils, absence of gravity-dependent valve mechanisms, existence of a rete caroticum that hampers CSF pulsations, potential persistence of the CCEC over the lifespan, and differences in patholog[11,12]. In addition, variations in the patency of the CCEC of the spinal cord may promote the development of different types of syringomyelia[10] and, most likely, play a role in determining the location of a syrinx remote from a focus of CSF obstruction. Furthermore, in some cases the hyperintensity of the central spinal cord seen on transverse T2-weighted images was not accompanied by a clear ependymal layer and would be explained either by lack of MRI spatial resolution or by the so called "presyrinx" state[24].

In our case series no adult case showing hydromyelia/central cord hyperintensity exhibit eccentric cavity dilatation within the spinal cord, which would support the embryological studies demonstrating the anatomic persistence of the CCEC in dogs and cats over the lifespan[32,33,41], and then such syringomyelia is

a hydromyelic cord dilatation of the CCEC after a cephalic hydromyelic-free segment.

It was previously theorized that the main mechanism underlying hydromyelia is the establishment of a pressure gradient between the intracranial-intraventricular compartment and the intra-spinal CSF compartment[17]. Whether this difference results in central spinal cord edema or true dilatation of the CCEC remains uncertain or it could even be a question of time. Moreover, our findings reinforce the hypothesis that CCEC dilatation is only possible when an ependymal canal had previously existed, which is likely in dogs and cats. Still, this cavity may collapse or disappear functionally with age in any individual, thus explaining why only three of 15 adult animals in our series exhibited continuity between the fourth ventricle outlet and the CCEC, while all five young animals exhibited such continuity. Also, dilatation of the foramina of Luschka and continuous/non-continuous ependymal dilatation were observed in all 23 cases of the present series. All animals, but one, with continuous dilatation of the fourth ventricle exhibited remarkable dilatation of the foramina of Luschka (+++), although mild dilatation (+) was observed in one adult case. Such findings support the notion that continuous CCEC dilatation, when present, occurs because the outlets at the foramina of the fourth ventricle are closed, probably related to inflammatory scarring. Our findings, in young patients, also support the one of the seminal Gardner´s observation in this field: "Failure of the foramina of the fourth ventricle to open with continuing communication between the fourth ventricle and the cystic space within the spinal cord via the obex may allow increased pressure within the ventricles to be transmitted to the central canal" [35], and also with some reports referring atresia of the fourth ventricle foramina, both in humans and animals, which promotes congenital OH[34,36,42-44]. Spinal central ependymal cavitation in the other adult animals with syringomyelia, whose cervical cord probably lacked functional CCEC, could be explained by blockage of CFS circulation around the foramen magnum secondary to arachnoiditis, which causes cranio-spinal pressure dissociation and resulted in CSF accumulation in the central canal or, in other clinical framework, secondary to tumor-promoting occlusion of the subarachnoid space at the foramen magnum, as it has been reported in posterior/caudal fossa tumors in humans[4,34,36,45-49], cats[9], and dogs[50] .

The clinical groundwork and radiologic framework in the present case series differ from those seen in patients with primary brain malformations, CVJ region anomalies, posttraumatic states, or disk herniation, in which cervical syrinx formation can be explained by fluid-state theories or intramedullary pulse pressure theory. Importantly, such effects should only be considered in conditions characterized by partial obstruction of the CSF flow. In such cases, the pathophysiological development of syringomyelia is likely manifold, and it is unlikely that there is a sole satisfactory explanation for this process. However, in our cases, we speculate that OH and their causes (i.e., inflammatory conditions), rather than

anatomic factors associated with the primary outside of the cervical cord and cervical spine, are involved in cervical hydro/syringomyelia formation, particularly considering the different mechanisms by which OH can occur in cases with varied etiology[51].

Our case series included a single young cat (case #3). In this case, we think that a prenatal infection resulted in the development of marked OH, accompanied by continuous dilatation of the CCEC that extended to the lumbosacral region. This kitten exhibited the same anatomic pattern of disturbances/etiology that we observed in young dogs of similar age. Previous studies have reported an association between OH and hydro/syringomyelia in both cats and dogs[9,52]. In addition, one group reported partial occlusion of the third and fourth ventricles due to pyogranulomatous reactions in a cat with feline infectious peritonitis, thereby resulting in OH and hydromyelia[53].

In animals like ours with CIBC, OH and hydro/syringomyelia are thought to be caused by disturbances in CSF flow, which occur secondary to progressive arachnoiditis/ventriculitis due to meningeal adhesions and ependymal inflammation. Such injuries are likely associated with previous aggressive infection of the CNS. Nevertheless, in some animals whose CSF was negative for inflammation the onset of clinical symptoms ranged from several weeks to 1 year. In addition, some animals had been treated empirically with antibiotics and steroids. These factors, among others, may explain the relatively low sensitivity of radiological studies for demonstrating definitive signs of meningeal inflammation, as occurred in our case series where meningeal enhancement was only observed in nine of 21 valuable cases. Regular symmetrical meningeal enhancement is nonspecific neuroradiological sign, as it can be observed after various events such as CSF puncture, trauma, or radiation. This finding represents a well-recognized sign of meningeal inflammation, although the detection of such meningeal enhancement depends on several factors, including the strength of the magnetic field, image acquisition parameters, dose of paramagnetic contrast agent, time delay to scan, and time from onset of clinical symptoms to imaging[54-56].Therefore, in our case series, we regarded meningeal enhancement as a nonspecific sign, with relative radiological value for understanding the causes or mechanisms associated with OH and hydro/syringomyelia.

In the present case series, only five of our patients exhibited periventricular interstitial edema. Symptoms in these five patients had begun relatively shortly before MRI evaluation, highly suggestive of active OH. Indeed, long-term active OH that is left untreated leads to brain herniation and death, and is thus unlikely to be encountered in common clinical veterinary practice. Whether patients with MRI findings consistent with severe OH and hydro/syringomyelia will develop such findings within a few days or months of presentation remains unknown

MRI is the ideal non-invasive imaging technique for investigating suspected animals of hydro/syringomyelia, allowing for concomitant assessment of pathology and

potential etiology. Our critical radiologic hallmark to label cervical cord hydromyelia on MR images in our cases is the presence of a funnel-shaped connection between the fourth ventricle outlet and the CCEC, which can be observed throughout the cervicomedullary junction, particularly on sagittal images. Of interest, in some young animals included in the present study (two puppies and one kitten), we also observed a small, flap-like, marginal-dorsal structure at the level of the obex, better seen on sagittal images (Figs. 1, 2, and 3) within the funnel-shape connection. Although this structure has not been previously described in imaging studies, we speculate that it may be a vestige of embryological remnant or area membranacea inferior of Weed, "a plug of acellular material lying within the central ependymal canal", that funnels the pulsations of the ventricular fluid into the CCEC in human and pig at least in embryonic state[57], although further studies are required to obtain pathological evidence.

It was previously stated that, with the advent of MRI, "it was evident that most syrinx cavities do not communicate with the fourth ventricle and, in humans, approximately 90% arise at some distance from the foramen magnum, and many are found below a syrinx-free segment of the spinal cord that is frequently distorted or compressed"[58]. Advances in MRI technology and refinements in sequence parameters have made possible to detect and distinguish hydromyelic and syringomyelic cavities with far greater precision, and to determine the relationship among such cavities and other structures. Among the MRI techniques available, refined T2-weighted imaging of the bulbo-medullary junction in the sagittal plane is essential for anatomic demonstration of continuity between the fourth ventricle and the CCEC, as this method is associated with high anatomic submillimetre resolution and high tissue contrast. The sequencing requirements can be met using balanced steady-state free-precession techniques, such as fast imaging employing steady-state acquisition (FIESTA), constructive interference in steady state (CISS), fast imaging with steady-state free precession, and balanced fast field echo sequences. Such sequences provide strong T2 contrast and high spatial resolution, emphasizing CSF signals. In addition, these sequences have a high signal-to-noise ratio and inherent flow compensation and are suitable for direct three-dimensional imaging[59-61]. Therefore, images acquired using such sequences can depict small structures surrounded by CSF and can thus be used to evaluate posterior/caudal fossa lesions. Although FIESTA or CISS sequences are usually used for heavily T2-weighted images, they also enable T1 contrast. Unfortunately, our scanner did not have these software capabilities at the time of our recorded studies. These technical refinements would have increased the imaging resolution of sagittal images, allowing for improved discrimination between continuous and non-continuous fourth ventricle outlet and CCEC, potentially resulting in higher detection of anatomical continuity between the fourth ventricle outlet and the CCEC and, therefore, we might have observed more hydromyelic cases in adult animals.

Clinical Context

Clinically, it is important to recognize the underlying structural cause of hydro/syringomyelia, and to differentiate the sole cause of the process, in order to ensure that the patient's condition is accurately diagnosed, and that cervical spine involvement is properly identified. Pain can be regarded as the most important clinical sign of hydro/syringomyelia[16] and most commonly localized to the cervical region but may be intermittent and difficult to localize. Owners may report that their dog appears to be feeling worse pain at night, when first getting up, during hot or cold temperature extremes, when excited, or when changing posture. In addition, affected dogs often scratch at one area of the shoulder, ear, neck, or sternum, and may have other neurological deficits such as limb weakness, and pelvic limb ataxia[16]. Neurological signs such as ataxia, paresis, spinal pain, and scoliosis reflect spinal cord dysfunction[62-64]. Also, a lesion in the brainstem or in the cervical portion of the spinal cord can cause both ataxia and proprioceptive deficits.

The animals in our series encompassed a variety of clinical signs and symptoms. In most cases, clinical signs and symptoms revealed forebrain dysfunction in 65.2% of the animals, although primary ocular signs were observed in 13%, both upper cervical and forebrain signs were observed in another 13% of cases, and upper cervical signs were observed in 8.4%. Although the signs of intracranial and spinal diseases can appear indistinct from one another. MRI findings can be used to definitively identify the extent of CNS inflammation[52].

Disease Etiology in Our Case Series

In the present study, the diagnoses of inflammatory processes affecting the CNS were made based on clinical status, standard hematologic parameters, CSF sample findings, and MRI findings. MUE was diagnosed in 17 animals. The term MUE is currently preferable when referring to common inflammatory conditions of the canine CNS, such as granulomatous meningoencephalomyelitis, necrotizing meningoencephalitis, and necrotizing leukoencephalitis. MUE is used to describe those cases in which MRI and CSF alterations indicate inflammatory non-infectious CNS disease but definitive histopathological analysis is lacking[63-65]. The antemortem diagnosis is often complicated by an overlap in the neurodiagnostic profiles of several conditions[63-66], as was also observed in most of our cases. MRI-based study offers a broader assessment of the burden of parenchymal lesions and might make prognosis more reliable; this may, in turn, guide therapy[67].

This work may also help to elucidate some pathogenic clues in specific neurological human diseases, particularly in the development of cervical hydromyelia in hydrocephalic preterm infants and newborns secondary to acute intracranial hemorrhage[5], as it occurred in our young domestic carnivore population, although further studies are warranted to support this hypothesis.

The present study has several limitations of note. First, this study was retrospective, observational, and included a

limited number of clinical cases. In addition, the strength of the scanner field (0.5 T) did not enable us to attain images with the finest anatomic resolution. Limitations in the spatial resolution of our scanner may have caused us to underestimate or overlook some forms of early filiform hydromyelia and its potential connection with the fourth ventricle. Using higher magnetic fields (i.e., 1.5 or 3 T) and additional technical refinements might have increased the resolution of sagittal images[60,61], allowing to improve discrimination between continuous and non-continuous fourth ventricle outlet and CCEC connection, potentially resulting in higher detection of anatomical continuity (hydromyelia) in our adult animals population. Second, methodologically, ventricular dilatation and lateral foramina dilatation were grade according to qualitative evaluation rather than quantitative assessment, because breed and age differences among animals rends morphometric criteria comparison unreliable. Nevertheless, the MRI critical radiologic hallmark of the study is the demonstrations of the anatomic continuity of the fourth ventricular outlet and the CCEC, rather than the assessments of the ventricular size. Third, we were also unable to confirm CSF inflammation parameters in some few animals, excluding cases that were felt to pose too high a risk for CSF tap, as reported in other studies[67]. In such few cases, the clinical history and MRI findings strongly suggested an inflammatory etiology. Finally, a large longitudinal control population MRI study of normal young small domestic carnivores are needed for better understanding the development and closure of the fourth ventricular outlet and its connection with the CCEC. Despite these limitations, our MRI findings support the notion that the anatomic continuity of the fourth ventricular outlet and the CCEC is the putative factor for the development of cervical hydromyelia secondary to OH, rending the hydrodynamic mechanisms and theories the most suitable for its explanation.

CONCLUSION

We have evaluated a case series in which concomitant OH and cervical hydro/syringomyelia were discovered during the neuroradiological work-up of domestic carnivores brought in for neurological veterinary care for a variety of neurological symptoms secondary to CIBC. The CCEC can either be observed in continuity with the fourth ventricle (hydromyelia) or below a syrinx-free segment of the spinal cord (syringomyelia). The critical MRI hallmark for differentiating both conditions is the appearance of a continuous funnel-shaped connection between the fourth ventricle and the CCEC, which can be observed throughout the cervicomedullary junction on sagittal images, revealing anatomic continuity between both structures, and was observed in all young animals evaluated, but only in 16 % of adult animals. These finding is accompanied by dilatation of the CCEC which is observed as a central cord round region of hyperintensity on transverse T2-weighted images and might be used as a biomarker for detecting cases at risk of developing cervical hydromyelia.

Our study explores a natural inflammatory model of hydrocephalus and hydro/syringomyelia in small carnivores. The results taken from the young population allows to witness a regular communication between the fourth ventricular outlet and the CECC before the complete embryological development takes place and its eventual closure. When anatomic continuity is present, the hydrodynamic effect may play a fundamental role in the pathogenesis of hydromyelia. Such continuity is variable and likely related to both age and individual anatomic ventriculo-ependymal characteristics. Based on these findings, it appears that most dogs and cats have a virtual CCEC that is connected with the fourth ventricle outlet at birth yet disappears over the years in normal, healthy animals, thus explaining why hydromyelia rather than syringomyelia is present in early stages of the development, in hydrocephalic status. However, when functional anatomic continuity is not present, as it has happened in most adult animals, other mechanisms, not fully explained by current theories applied to humans, may be activated and lead to spinal cord syringomyelia. MR imaging facilitates both accurate diagnosis of the etiology of symptoms, as well as identification of the anatomic basis.

Abbreviations

CCEC: central cervical ependymal canal
CIBC: chronic inflammatory brain conditions
CNS: central nervous system
CSF: cerebrospinal fluid
CVJ: craniovertebral junction
FVO: fourth ventricle outlet
MRI: Magnetic Resonance Imaging/images
MUE): meningoencephalitis of unknown etiology
OH: obstructive hydrocephalus

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Authors' contributions

AM initiated and designed the study. AM, P Martín, and P Martínez were involved in the interpretation of results and drawing conclusions. AM wrote the first draft of the manuscript. All authors have read and approved the final manuscript.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Declarations

Ethics approval and consent to participate

This study did not require official or institutional ethical approval. The animals were handled according to high ethical standards and national legislation

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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