https://doi.org/10.17221/58/2018-VETMED

Dandy-Walker malformation in Polish hunting dogs: long term prognosis and quality of life

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Citation: Kwiatkowska M, Rose JH, Pomianowski A (2019): Dandy-Walker malformation in Polish hunting dogs: long term prognosis and quality of life. Veterinarni Medicina 64, 37–43.

Abstract: In the last few years, it has become easier to diagnose congenital brain malformations in dog's *antemortem*. This is probably due to the wider availability of advanced diagnostic imaging, in particular computed tomography or magnetic resonance imaging (MRI). Despite this, there is still not much literature available about potential treatments, outcome and overall prognosis with respect to the patient's quality of life. We present three cases of Dandy-Walker malformation in Polish hunting dogs with up to five years follow up including assessment of their quality of life. A nine-week-old Polish hunting dog was presented with progressive signs of ataxia that had developed over the preceding few weeks. MRI revealed a Dandy-Walker malformation. The dog underwent MRI at the ages of 12 and 36 months, and his neurological condition was followed for five years. No other subsequent abnormities were found on further diagnostic tests. The dog showed transient behavioural problems which improved after castration and training. The ataxia seen at first visit improved with time and intensive physiotherapy, and the dog was considered to have a good quality of life in the owner's eyes. A further two cases shared a similar disease course. Dandy-Walker malformation was confirmed with MRI, but diagnostic imaging could not be reported here because the owner did not consent to publication. The Dandy-Walker malformations described in these three Polish hunting dogs had a stable disease course and revealed that dogs suffering from this condition may have a good quality of life, providing no other abnormalities are detected and rehabilitation is performed.

Keywords: age; MRI; anatomic anomaly; ataxia; prognosis

In human medicine, the Dandy-Walker malformation is described as a congenital disease of the central nervous system which is characterised by partial or complete agenesis of the cerebellar vermis, cystic dilatation of the fourth ventricle and an enlargement of the posterior fossa combined with superior displacement of the cerebellar hemisphere. This malformation is an extremely variable condition, particularly regarding the patency of the outlet foramina of the fourth ventricle, hydrocephalus degree, hypoplasia of the vermis and size of the posterior fossa cyst (Bindal et al. 1990; Limperopoulos et al. 2006; Bolduc et al. 2009). Therefore, the human literature describes three types of this congenital disease: (1) Dandy-Walker malformation, which is characterised by an absent or small cerebellar vermis, cystic malformation of the fourth ventricle and enlargement of the posterior fossa; (2) Dandy-Walker variant which describes fourth ventricle enlargement without posterior fossa enlargement; (3) enlargement of the cistern magna with formation of cysts compressing the cerebellum leading to its atrophy.

In human medicine, the incidence of Dandy-Walker malformation (DWM) is rare and estimated as 1 : 25 000–1 : 30 000 births with slight female predominance (Ecker et al. 2000; Bolduc et al. 2009). In veterinary medicine, there are no data concerning disease prevalence. This may in part be because puppies that are non-ambulatory and show neurological symptoms such as ataxia and intention

https://doi.org/10.17221/58/2018-VETMED

tremors are more likely to be euthanised without further diagnostics.

In the veterinary literature, cases of Dandy-Walker-like syndrome have been documented in several breeds, including the Beagle, Briard, Bull terrier, Chow Chow, Labrador retriever, Silky terrier, Tervueren, Weimaraner and Dachshund (Kornegay 1986; Schmidt et al. 1992; Summers et al. 1995; Choi et al. 2007; Lim et al. 2008; Schmidt et al. 2008). Recently, a Dandy-Walker-like malformation due to autosomal recessive inheritance was reported in a Eurasier dog (Bernardinio et al. 2015).

Here, we report three cases of Polish hunting dogs diagnosed with Dandy-Walker malformation and describe the disease course, long-term observations and owners' perceptions of the patients' quality of life. Magnetic resonance imaging (MRI) images at the ages of 12 and 36 months are reported only for one dog (case 1); therefore, we decided to focus on this case and present the other two cases (2 and 3) for comparison. The owners of dogs 2 and 3 did not consent to the publication of their dogs' MRI images, but did give their permission for us to describe the disease course and their observations regarding life quality.

Case description

Clinical examination. A nine-week-old Polish hunting dog was referred to the Small Animal Teaching Hospital, Veterinary Medicine Faculty of Warmia and Mazury University, Olsztyn, Poland, because of a progressive uncoordinated gait. No abnormalities were detected on physical exam. On neurological exam, the dog displayed four-limb ataxia with hypermetria of the forelimbs and intention tremors. Proprioceptive testing (paw placement and hopping) were delayed in all four limbs, with the left side observed to be slightly worse than the right. Muscle tone was slightly increased in all four legs. Menace was absent bilaterally, and this was suspected to be due to the dog's age at this time (Videos S1 and S2 in electronic supplementary material (ESM); see the electronic version).

Based on neurological exam, a lesion involving the cerebellum was suspected. Differential diagnoses were anatomic anomalies, infectious diseases (parvovirus, distemper, toxoplasmosis and neosporosis) and non-infectious inflammatory conditions. A repeat assessment was performed at the age of 12 months (Video S3 in ESM). At this time, the dog was sporadically aggressive, especially towards other dogs, and sometimes he was agitated and moody. The dog continued to display ataxia in all four limbs with associated hypermetria and intention tremors. He also exhibited a wide base stance with a truncal sway and a tendency to lean and fall towards the left. The dog had difficulty turning to the right and exhibited intermittent positional nystagmus. A marked improvement was noted in the dog's proprioceptive test compared to the previous exam with only paw placement being reduced in the left fore- and hindlimb. Menace response was absent bilaterally and was attributed to the suspected cerebellar localisation on this occasion, as vision and papillary light reflexes were normal and no other forebrain signs were apparent.

At five years of age, neurological examination revealed the same deficits (ataxia, truncal sway and intention tremors); however, these were less severe and the dog's gait had improved markedly. The dog still lacked menace response at this time.

Diagnostics. At first presentation, haematology and biochemistry profile were performed. These were normal. Titres for toxoplasmosis, neosporosis and parvovirus were negative.

The first MRI exam was performed at 12 months of age and the second at 36 months of age (Figure 1). The first was performed with an Esaote Vet Grandę 0.2 T magnet and the second with a 3 Tesla Siemens magnet. The MRI exam revealed a cerebellar malformation with a vermis agenesis, symmetrical right and left hemisphere hypoplasia, barely discernible folia and sulcia and poor grey-white matter differentiation. In the retro-cerebellar space, accumulation of a large amount of fluid was visible in sagittal and dorsal views; it compressed the cerebellum hemispheres, displacing them laterally and rostrally. The ventricular system – including the lateral ventricles and fourth ventricle – was enlarged, and the ventricles seemed to be continuous with a large retrocerebellar space. Based on the MRI scan findings and human terminology guidelines, Dandy-Walker malformation was suspected. No changes in MRI images were documented over time.

Treatment. Intensive physiotherapy was started at the dog's first presentation with the aim of reducing the generalised spasticity. This focused around balance exercises on a ball and soft ground, target-reaching exercises and regular water treadmill exercises. Additionally, the dog was treated with

https://doi.org/10.17221/58/2018-VETMED

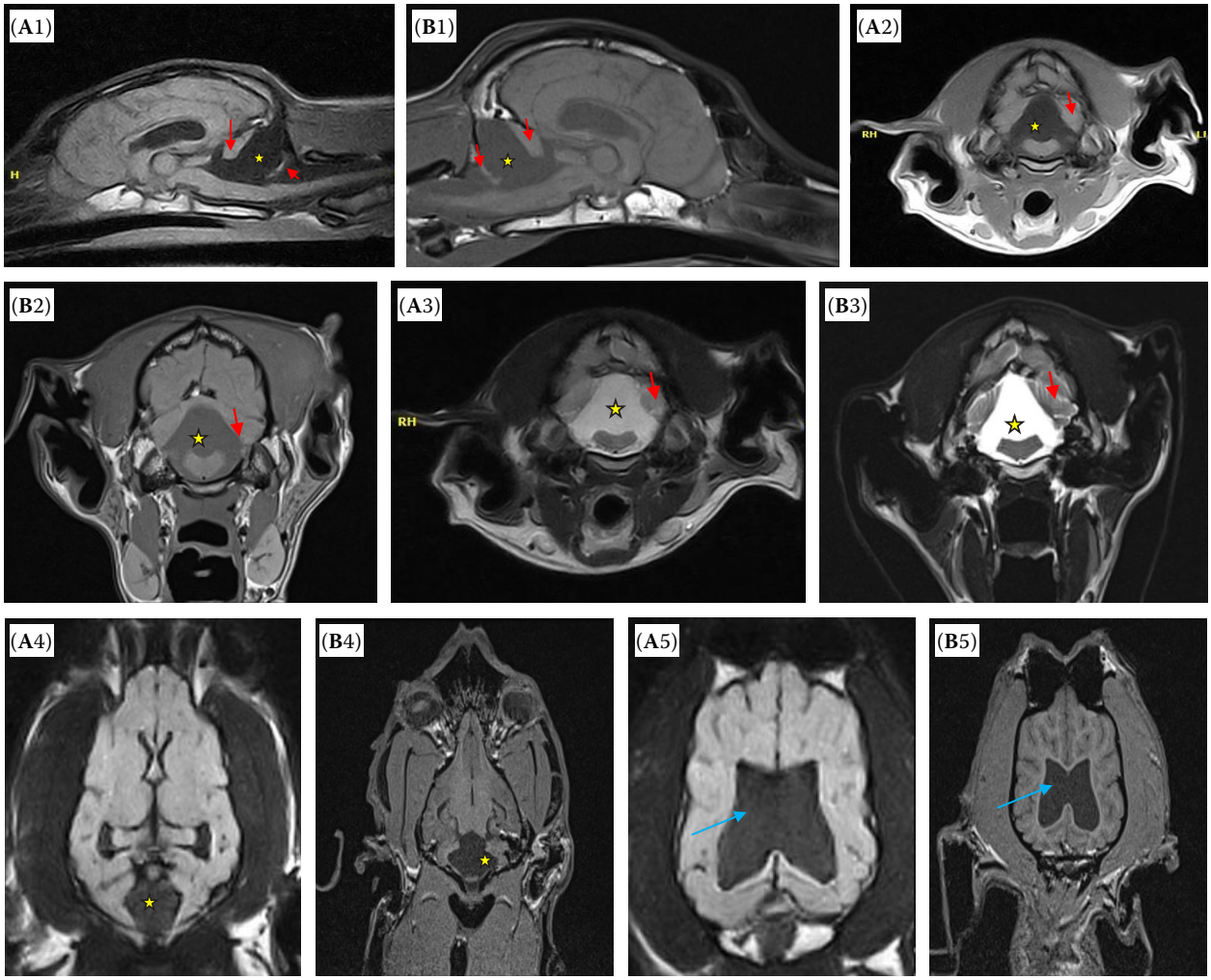

Figure 1. Magnetic resonance imaging examinations at the age of 12 and 30 months. Images labelled with (**A**) were taken at the age of 12 months with a 0.2 Tesla magnet; for comparison, we show images taken at the age of 36 months with a 3 Tesla magnet (**B**), (**A**1 and **B**1) are midsagittal T1 view, (**A**2 and **B**2) are transverse T1 images, (**A**3 and **B**3) are transverse T2 images at the level of the cerebellum, (**A**4, **B**4 and **A**5, **B**5) are coronal views in FLAIR and MPR sequence, respectively. The yellow star shows fluid accumulation in the region where the cerebellum vermis has not developed. Red arrows indicate incompletely developed cerebellum hemispheres. Blue arrows show enlarged lateral ventricles

omeprazole and acetazolamide to try and reduce cerebrospinal fluid production.

DISCUSSION AND CONCLUSIONS

In this paper, we described the clinical presentation and long-term observation of three Polish hunting dogs diagnosed with Dandy-Walker malformation. Further, MRI findings are described in one case.

All three dogs had an early onset of cerebellar ataxia with variable degree of severity, from not being able to walk without assistance (dog 1), to ataxia with front limb hypermetria (dog 3) and finally mild ataxia and truncal sway (dog 2). All patients improved by one year of age and could thus walk unassisted. Dog 1 (the most severely affected), showed the biggest improvement in comparison to initial examination; however, signs of ataxia and left-sided vestibular deficits persisted. In dogs 2 and 3, residual ataxia persisted (Table 1). Interestingly, in a group of 14 Eurasier dogs (Bernardinio et al. 2015), only some cases showed neurological improvement, while the other dogs failed to exhibit any improvement and the severe ataxia persisted as life-long condition. The patients described here

Table 1. Comparison of neurological deficits in three dogs diagnosed with Dandy-Walker malformation between nine weeks and three years of age

	Dog 1 (Video S1–S3 in ESM)			Dog 2		Dog 3	
	9 weeks	1 year	3 years	12 weeks	1 year	9 weeks	1 year
Behaviour	considered normal for the age and condition	aggression towards other dogs over food and toys; possessive behaviour over toys and owner	less pronounced signs as at the age of one, which might have been due to obedience training and castration	considered normal for the age and condition	normal, according to the owner; quiet and very calm but could become agitated with toys	considered normal for the age and condition; however, according to the owner slept more than the other puppies	normal
Gait	abnormal; unable to stand up on his own; falling and rolling to the sides; ambulatory with assistance – front limb hypermetria and cerebellar ataxia	abnormal; cerebellar signs (intension tremors and four-limb hypermetria); leaning towards the left – left-sided vestibular ataxia	intension tremors improved (less frequent); cerebellar ataxia, hypermetria; less pronounced leaning/falling to the left	abnormal; moderate cerebellar ataxia; truncal sway; dog was ambulatory on his own	abnormal; minimal cerebellar ataxia; however worsened when walking down the stairs	abnormal; cerebellar ataxia with pronounced front-limb hypermetria and intension tremors	abnormal; cerebellar ataxia and, albeit less pronounced, minimal front-limb hypermetria and intension tremors
Postural reactions	abnormal on all four limbs; slightly worse on the left	abnormal on all four limbs; worse on the left	abnormal on all four limbs, but much better than at the age of one; mildly worse on the left	abnormal on all four limbs; front limb hypermetria	minimally delayed on all four limbs	abnormal	abnormal, but with much improvement in comparison to nine weeks old
Spinal reflexes	normal	normal; increased tone on the left	normal; normal tone bilaterally	normal; increased tone in front limbs	normal; normal tone	normal; increased tone on all four limbs	normal; minimally increased tone in front limbs
Cranial nerves	normal for a puppy at this age	no menace response; intermittent positional nystagmus predominantly with a fast phase to the right	no menace response bilaterally; no nystagmus	normal for a puppy at this age	no menace response	normal for a puppy at this age	no menace response

Veterinarni Medicina, 64, 2019 (01): 37–43

https://doi.org/10.17221/58/2018-VETMED

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all underwent intensive rehabilitation (1–3 times weekly), and this could have contributed to their improvement. However, further studies would be needed to confirm this theory.

In humans, apart from the abnormal gait, posture and hypotonia, other signs such as intellectual retardation, speech problems, neurobehavioral problems and seizures may be present; however, these signs have been suggested to be dependent on the presence of other CNS anomalies, such as corpus callosum agenesis and cerebral gyri anomalies (Golden et al. 1987; Boddaert et al. 2003; Patek et al. 2012). Patek et al. (2012) suggested that if DWM is unaccompanied by any visceral and central nervous system anomalies, then prognosis is favourable, and surviving children manifest normal intellectual and neurological development. In contrast, in the human literature, seizures, cranial nerve deficits, hearing and visual problems accompanied by visceral anomalies are related to poor outcome and mental retardation (Bindal et al. 1990; Klein et al. 2001; Limperopoulos et al. 2006; Patek et al. 2012). Based on our observations (three Polish hunting dogs) and those made in Eurasier dogs (Bernardinio et al. 2015), it seems that a similar relationship may define the condition in canines. No other brain and visceral abnormalities were detected in these dogs; they learned clean behaviour and obedience and were able to learn fetching games as quickly as other dogs. At one year of age, one of our patients developed aggressive behaviour towards other dogs with regard to food and toy behaviours. This may have been due to fact that this patient was in the adolescent period, as the behaviour markedly improved after castration and obedience training. In veterinary medicine, there are case reports and studies regarding the neurobehavioral signs associated with other congenital brain abnormalities; however, the most severe ones are usually associated with prosencephalic congenital anomalies, e.g., hydrocephalus (Estey 2016), which may lead to aggression, agitation, difficulty with training, circling and pacing. Similar signs were reported to be associated with meningocele, meningomyelocele (MacKillop 2011), porencephaly and holoprosencephaly (Lazzerini et al. 2017). Both we and the dog's owners (who were breeders) judged the patient's mental development to be normal when compared to the other dogs in the litter. Similar conclusions were made in the case of Eurasier dogs where no signs of mental retardation or neurobehavioral abnormalities were reported. None of our patients developed seizures; however, one of the 14 Eurasier dogs was euthanised due to seizures that were refractory to normal seizure therapy (Bernardinio et al. 2015).

No correlation between the size of the residual cerebellum and intellectual deficits has been proven in human medicine, but it was proven that there is a correlation between the degree of vermis lobulation and intellectual outcome: the more lobulated the vermis, with the presence of two main fissures (primary and secondary), the better the intellectual prognosis is for humans (IQ > 85) (Sawaya et al. 1981; Hirsch et al. 1984). If more cases emerge in veterinary medicine, it would be worth considering investigating this potential correlation with learning ability.

Dandy-Walker malformation in human medicine is described as a multifactorial disease and may be caused by many conditions affecting brain development during the prenatal period such as exposure to rubella, cytomegalovirus, toxoplasmosis, toxins and alcohol and maternal diabetes. In dogs, generalised hypoplasia of the cerebellum can occur as a result of viral infection (parvovirus), potentially protozoa infection (toxoplasmosis, neosporosis), trauma, ischaemia, hypoxia or toxicity (Hart et al. 1972; Hirsch et al. 1984; Murray et al. 1985). In our cases, both the bitches and the patients had negative toxoplasmosis and neosporosis titres, and PCR was negative for parvovirus. There was no history of any infection, trauma or any drug administration during gestation which might have influenced the development of the foetus, and therefore we suspect a genetic mutation to be the underlying cause in our dogs. Further genetic testing would be needed to confirm this theory. In human medicine, Dandy-Walker malformation may be caused by a Mendelian condition such as a chromosomal aberration. It has been estimated that the risk of reoccurrence of the disease in subsequent human pregnancies may be as high as 10%. The most common chromosomal defects in people are trisomy 18, triploidy and trisomy 13. In veterinary medicine, a VLDLR receptor mutation has been found in Eurasier dogs (Bernardinio et al. 2015).

In summary, this paper reports Dandy-Walker malformation in Polish hunting dogs for the first time, and we additionally describe multiple MRI investigations in one of the dogs. With time and intensive physiotherapy, improvement was seen in ataxia, hypermetria and truncal sway, although no

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Table 2. Questionnaire regarding owner perspective on the quality of life of dogs with Dandy-Walker malformation

Question	Grading		
	case 1	case 2	case 3
In the last month, how often did you feel that caring for your dog caused conflict with your work?	1	2	2
In the last month, how often did you feel that caring for your dog caused conflict with your daily activities?	1	2	1
In the last month, how often did you feel that caring for your dog caused conflict with your social life?	1	1	1
How worried were you in the last month about your dog with DWM in comparison to the other dogs you have?	2	3	2
How often were you bothered by the regular administration of medication?	1	1	1
How often were you bothered by the necessity of performing rehabilitation exercises once weekly?	2	3	3

Grading system: 1 = never, 2 = rarely, 3 = sometimes, 4 = often, 5 = very often

changes were observed over time at repeat MRI scans. The dogs in our study had a good quality of life and so euthanasia need not be considered for every case with similar pathology (Table 2).

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Received: March 29, 2018
Accepted after corrections: August 2, 2018