# Intracranial haemorrhage in a dobermann puppy with von Willebrand's disease

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**Neurological examination of a lethargic, ataxic 12-week-old dobermann revealed decreased conscious proprioception in all its limbs. Haematological examination revealed a low platelet count. Cytological examination of a sample of cerebrospinal fluid revealed evidence of haemorrhage and chronic inflammation. The levels of von Willebrand's factor antigen were extremely low. Skull radiographs were consistent with mild hydrocephalus. Treatment resulted in little clinical improvement and the animal was euthanased. Post mortem examination of the brain revealed an internal hydrocephalus with haemorrhage into the ventricles. It was considered that the animal had suffered severe intracranial haemorrhage as a result of its low level of von Willebrand's factor antigen and that the bleeding may have been potentiated by the low platelet count.**

SPONTANEOUS bleeding in a thrombocytopenic dog with low levels of von Willebrand's factor antigen has been reported by Littlewood and others (1987), but the bleeding had occurred in response to trauma before the development of the thrombocytopenia. This report describes a case of intracranial bleeding associated with neurological signs in a dog with von Willebrand's disease and thrombocytopenia.

**TABLE 1: Haematological and biochemical results observed in a 12-week-old dobermann puppy with von Willebrand's disease**

| Measurement | Value in puppy | Normal range |
|---|---|---|
| Total red blood cells (x $10^{12}$/litre) | 5·92 | 5·5-8·5 |
| PCV (litre/litre) | 0·39 | 0·37-0·55 |
| Haemoglobin (g/dl) | 13·8 | 12-18 |
| Plasma protein (g/litre) | 66 | 60-77 |
| Platelets (x $10^9$/litre) | 78 | 175-500 |
| Total white blood cells (x $10^9$/litre) | 8·5 | 6-17 |
| Neutrophils (x $10^9$/litre) | 4·8 | 3-11·5 |
| Lymphocytes (x $10^9$/litre) | 2·65 | 1-4·8 |
| Monocytes (x $10^9$/litre) | 0·34 | 0·2-1·5 |
| Eosinophils (x $10^9$/litre) | 0·68 | 0·1-1·3 |
| Fibrinogen (g/litre) | 2 | 2-4 |
| Urea (mmol/litre) | 5·7 | 3·3-6·7 |
| Creatinine (μmol/litre) | 72 | 70-170 |
| Sodium (mmol/litre) | 149 | 135-155 |
| Potassium (mmol/litre) | 4·7 | 3·7-5·8 |
| Chloride (mmol/litre) | 108 | 105-120 |
| Calcium (mmol/litre) | 2·83 | 2·2-2·7 |
| Phosphate (mmol/litre) | 2·31 | 0·6-1·3 |
| Alkaline phosphatase (iu/litre) | 448 | 3-142 |
| ALT (iu/litre) | 16 | 21-59 |
| AST (iu/litre) | 22 | 20-32 |
| CPK (iu/litre) | 386 | 76-228 |

ALT Alanine aminotransferase, AST Aspartate aminotransferase
CPK Creatine phosphokinase

## Case report

A 12-week-old male dobermann pinscher had become anorexic, lethargic and progressively incoordinated and ataxic within 48 hours of being vaccinated with live canine distemper, hepatitis, parainfluenza, parvovirus and killed leptospirosis vaccines. Twenty-four hours before it was examined by the authors it received an injection of flunixin meglumine (Finadyne; Schering Plough Animal Health) to relieve pain associated with a suspected cervical lesion. On initial examination, the puppy was depressed and had a base-wide stance. Its neck was extended and it carried its head low, with a right-sided tilt. Its gait was mildly ataxic and the puppy had a tendency to circle to the left. The prescapular lymph nodes were enlarged and the animal resented dorsiflexion of the neck.

A full neurological examination revealed decreased conscious proprioception in all its limbs and poor wheelbarrowing reflexes. Muscle tone was normal although the dog was poorly muscled. The presence of congenital vestibular disease was ruled out by eliciting normal post-rotational and positional nystagmus responses and measurements of brainstem auditory evoked response (Wilkes and Palmer 1992).

### *Pathology*

The haematological and biochemical results are shown in Table 1. The most significant finding was a low platelet count (78 x $10^9$/litre). Plasma phosphate (2·31 mmol/litre) and calcium (2·83 mmol/litre) concentrations and the activity of alkaline phosphatase (448 iu/litre) were slightly high but these changes were compatible with the young age of the dog. A serum toxoplasma antibody titre of less than 2 iu/ml showed no serological evidence of exposure to *Toxoplasma gondii*. The whole blood clotting time was normal.

Radiographs of the lateral cervical spine, skull, thorax and abdomen showed no significant abnormalities. A dorsoventral view of the skull revealed that the calvarium extended to the lateral limits of the mandibles, suggesting possible enlargement of the cranium. However, there was no obvious thinning of the cortical bone and the fontanelles were closed.

A sample of cerebrospinal fluid (CSF), taken under general anaesthesia by cisternal puncture, appeared xanthochromic. Cytological examination revealed moderate numbers of red cells with only occasional platelets. Erythrophagocytosis was evident and increased numbers of nucleated cells were present (approximately 40 per cent reactive macrophages/monocytes and 40 per cent lymphocytes). These findings are consistent with a chronic inflammatory response to previous haemorrhage into the subarachnoid space or ventricular system. The lack of platelets in the sample and the presence of phagocytosed red cells indicated that the haemorrhage was not caused by the collection procedure. A sample of CSF was examined for distemper antibodies but no titre was detected. The lack of a detectable titre does not rule out a diagnosis of distemper infection, but high antibody titres are often found in the CSF of dogs infected with distemper virus which are showing signs of involvement of the central nervous system.

The dog was treated with antibiotics (ampicillin 250 mg three times a day) and anti-inflammatory doses of corticosteroids (0·5 mg dexamethasone once a day). There was some improvement in the clinical signs within 48 hours and the puppy became noticeably brighter. A guarded prognosis was given and over the following days its condition deteriorated rapidly and it had to be euthanased. In view of the dog's breed and the history of haemorrhage, von Willebrand's factor antigen was measured in a sample of plasma. The result, received after the death of the dog, revealed a low level of the antigen (<0·05 u/ml, equivalent to less than 5 per cent of the activity of pooled normal plasma).

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*Post mortem examination*

Only the brain was available for a pathological examination. Grossly, there was collapse of the cerebral hemispheres with marked dilation of the lateral ventricles and the fourth ventricle. The cerebral cortex was reduced in thickness to a depth of 5 to 10 mm. Histological examination demonstrated the patency of the aqueduct of Sylvius, which was dilated to a diameter of 1 to 2 mm. In addition, there was blood-stained CSF in both lateral ventricles, indicating more recent haemorrhage. Some of the blood vessels in the cerebrum showed prominent extravasation of blood and the presence of a cellular reaction indicated that this intracerebral haemorrhage had occurred before death and was not a post mortem artefact. There was no evidence of meningitis or of a space-occupying lesion. The above findings are consistent with internal hydrocephalus due to non-patency of the lateral apertures of the fourth ventricle. The specific source of haemorrhage into the ventricles could not be found and it was presumed to have originated from blood vessels subjacent to the walls of the ventricles.

## Discussion

The thrombocytopenia is an interesting feature of this case, and it is possible that the dog had a concurrent immune-mediated thrombocytopenia. An anti-platelet test was not performed. However, transient thrombocytopenia has previously been reported after live virus vaccination, particularly in association with the live paramyxovirus vaccines (Dodds 1980). The thrombocytopenia usually peaks between two and seven days after vaccination and may persist for up to three weeks (Pineau and others 1980). Studies in experimental animals have shown that the reduction in the numbers of platelets is usually mild (30 to 50 per cent of pre-vaccination levels) with the count rarely falling below the normal range (Jones 1984), although more significant degrees of thrombocytopenia have been reported (McAnulty and Rudd 1985). Thus, in the majority of otherwise healthy animals the degree of thrombocytopenia recorded would not have been severe enough to cause spontaneous haemorrhage. However, spontaneous bleeding could occur in a dog with low levels of von Willebrand's factor antigen, as has been reported in a dog with immune-mediated thrombocytopenia (Littlewood and others 1987).

No specific platelet function tests were performed although, with such a severe deficiency of von Willebrand's factor antigen, platelet adhesion would certainly have been abnormal. Flunixin meglumine is a potent cyclo-oxygenase and thromboxane $B_2$ inhibitor and would be expected to prolong bleeding times by the inhibition of platelet function (McKellar and others 1991). The duration and severity of this effect is not known but the inhibition of platelet cyclo-oxygenase by flunixin, in contrast with some other non-steroidal anti-inflammatory drugs, is reversible and transient, peaking after about three hours and returning to near normal levels within 24 hours (McKellar and others 1989). Thus, although the injection of flunixin may have potentiated the initial bleeding episode it is unlikely to have contributed to the subsequent, more severe, haemorrhage just before the dog was euthanased.

A moderate degree of hydrocephalus may be present in young animals with no apparent clinical signs. Although haemorrhage into the ventricles, and the resultant thrombus formation, could have obstructed the flow of CSF, resulting in acquired hydrocephalus, the age of the dog and the pathological findings suggest that this was a congenital hydrocephalus. It is likely, therefore, that the rapid progression of neurological signs was initiated by a further, critical increase in CSF pressure brought about by spontaneous haemorrhage into the ventricles.

In dogs with von Willebrand's disease, bleeding usually occurs from mucosal surfaces in the oral or nasal cavities, although it has been reported to be more common from the mucosa of the urogenital tract in dobermanns (Brooks and others 1992). In cases of severe von Willebrand's factor deficiency the bleeding may be spontaneous but is more typically induced by surgery or trauma (Littlewood 1989). The study by Brooks and others (1992) reported that 40 per cent of dobermanns with von Willebrand's disease suffered spontaneous haemorrhage, and in 60 per cent the haemorrhage was induced. It would appear that intracranial haemorrhage is unusual. The severity of the deficiency of von Willebrand's factor in this case was probably the most significant cause of the bleeding. The thrombocytopenia and/or a possible additional defect in the function of the platelets may have contributed to the severity of the bleeding. In cases of von Willebrand's disease with very low levels of von Willebrand's factor, factor VIII levels may also be low, and if this had been the case it might have contributed to the severity of the bleeding in this unusual site.

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# Abstracts

## Immunisation against equine streptococcal metritis

FIVE normal mares were immunised by the intramuscular and intrauterine administration of an antigen with adjuvant, and they and five unimmunised mares were later challenged by the intrauterine instillation of pathogenic *Streptococcus zooepidemicus*. Significantly fewer *S zooepidemicus* were present in cervical swabs taken from the immunised mares ($P<0{\cdot}01$) and the degree of inflammation in the genital tract of the immunised mares was also significantly less than in the unimmunised mares ($P<0{\cdot}001$). This protective effect of the immunisation was associated with a specific IgG response in the serum, and an IgG and IgA response in the uterine secretions.

WIDDERS, P. R., WARNER, S. & HUNTINGTON, P. J. (1995) *Research in Veterinary Science* **58,** 75

## Melanocytic neoplasia in the cat

THE clinical and histopathological findings in 13 cats with melanocytic neoplasia are described. Five of the cats had an intraocular melanoma, two had a limbal melanoma, five had a dermal melanoma and one had a metastatic melanoma the primary site of which could not be identified. In the intraocular tumours there was an apparent correlation between the degree of cellular pleomorphism, the mitotic rate and the extent of local infiltration, but there was no such correlation for the melanomas arising from the limbus or the skin.

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