

COAGULATION PROFILE IN VON WILLEBRAND'S DISEASE IN DOG

*Ingole K. H., Gaikwad R.V., Rohi R. R. and ¹Sawale G. K.

Animal Blood and Blood Component Bank and Referral Coagulopathy Laboratory, Department of Medicine, Mumbai Veterinary College, Mumbai-12, Maharashtra Animal and Fishery Sciences University, Nagpur

Introduction

Von Willebrand's disease (vWD) is one of the inherited bleeding disorder of dog characterized by prolonged bleeding time, marked reduction of both factor VIII procoagulant activity and factor VIII released antigen with an abnormal crossed immuno-electrophilic pattern. It is basic defect of multimeric plasma glycoprotein that supports the adhesion of platelet to vascular endothelium. In developed countries, it is routine practice to perform the coagulation profile. In India, these diagnostic tests are not done on routine basis. Recently, an animal and blood component bank has been established at Department of Medicine, Mumbai Veterinary College, Parel, Mumbai. A referral coagulopathy laboratory has also been started.

Material and Methods

In the present study, screening of dog for detection of von Willebrand's disease was carried out. The dogs were included from the Out Patient Department of Mumbai Veterinary College and Bhai Sakarbai Dinshaw Petit Hospital for Animals. The selection criteria for dogs were based on breed predilection, history of prolonged bleeding, bleeding episodes, swelling of joints and petechiae on the body surfaces.

Blood was collected in sodium citrate (3.2 %) in ratio of 1:9. Capillary blood clotting time was measured instantly during blood

collection. Samples were centrifuged at 2500 g for 10 minutes (Min.). Plasma was frozen in small aliquots until factor assays were performed. Buccal mucosa bleeding time (BMBT) was performed with the help of scalpel blade and incision of 1 mm deep by 5 mm long was taken and blood clotting time was recorded. Complete blood count with plate count performed as per the standard protocol (Benjamin, 1985).

Prothrombin time (PT) was determined by commercial Neopalm Plus Kit. Activated clotting time (ACT) was determined with the help of BD vacutainer glass tube and activated partly Thrombin time (TT) was determined by commercially STA Thrombin kit.

Result and discussion

All the dogs suspected for vWD were based on initial clinical and haematological investigation. Haematological findings in three dogs are presented in Table 1. These dogs were significantly anaemic as evidenced from lowered value of Hb, PCV and TEC (Table 1). In addition, dog showed bleeding disorder such as epistaxis, melena and haematuria. Similarly, Sophia *et al.* (1990), and Lobetti and Dippenar (2002) have reported haemorrhagic episodes such as epistaxis, melena and haematuria amongst hereditary coagulopathies that ultimately resulted in anaemia. The haematological findings of our study are in accordance with these findings.

Table 1: Haematological values and platelet count of the cases diagnosed for von Willebrand's disease

Sr. No.	Hb g%	PCV (%)	TEC	TLC	DLC					MCV	MCH	MCHC	Platelets
					N	L	M	E	B				
1	6.2	22	3.2	12	68	22	08	02	0	68.7	19.3	28.1	178000
2	7.0	24	3.6	8.0	72	22	02	04	0	66.6	19.4	29.4	276000

3	5.8	20	3.0	15	69	25	04	02	0	63.3	19.3	29.2	151000
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Table 2: Coagulation tests of the cases diagnosed for von Willebrand's disease

Sr. No.	Sex	Age (year)	BMBT (2.5-3.5 min.)	CBCT (3.5-5)	ACT (60-90 sec)	PT (10-14 Sec)	APTT (12-16 Sec.)	TT (10-12 Sec.)
1	F	8	6.5	14	70	11	16	12
2	M	6	7.0	6	80	13	16	11
3	F	1	5.0	5	75	11	15	12

Platelet count however was within the reference range for these three dogs (Table 1). An important differentiating feature is that platelet count in vWD remains unaltered since the basic defect is lack of functional von Willebrand factor (vWF) activity (Marjory, 2000). There appears to be no unequivocal criteria for screening dogs of vWD, because the evidence suggests that anaemia, elevated BMBT with or without thrombocytopenia should arouse suspicious of vWD (Arkel and Desposito, 1982). In our limited study, however thrombocytopenia was not evident (Table 1).

vWD is thought to be the most common inherited bleeding disorder in dogs. The disease has been recognized in 54 breeds as well as mixed breed of dogs including Doberman, German shepherd, Golden retriever and Shetland. Coagulation test results in these three dogs are presented in Table 2. vWD is characterized by decreased level of circulating vWF or low to normal level of an abnormal vWF. In dogs, it can be inherited as an autosomal dominant trait and autosomal recessive trait (Sophia *et al*, 1990). Lack of functional vWF causes abnormal primary hemostasis and prolongation of bleeding time. vWF, a multimeric plasma glycoprotein that play central role in hemostasis by supporting platelet adhesion at the site of vessel injury, endothelial cells are the major site of vWF synthesis and storage (Marjory, 2000). vWD dogs are known to have marked delayed haemostasis plug formation (Dodds, 1975).

Coagulation tests of three dogs indicated increased capillary blood clotting time (CBCT) apart from elevated BMBT. Prolongation of BMBT is considered specific for primary defects in hemostasis and indicates strong suspicious for vWD. The buccal mucosa bleeding time is inversely correlated with the degree of vWF deficiency or activity (Nelson and Coutol, 1992).

In the three cases that were suspected for vWD, other coagulation test such as ACT, PT, aPTT, TT and factor VIII were within the reference range. This finding is not surprising since all these factors are not related to vWD. PT is related to defect in extrinsic coagulation pathway where as ACT and aPTT are related to defect in intrinsic coagulation pathway. The available literature suggest that in majority dogs suspected for vWD, coagulation tests are normal (Nelson and Couto, 1992) with possible exception of mild prolongation of aPTT. The present results are in close agreement to these findings.

The initial point in coagulopathy is increased bleeding time. This defects could be ascribed factors such as inherited drugs induced platelet defects, vWD, bone marrow disorder thrombocytopenia, uremia, drug therapy (aspirin) or hypothermia (Jergens *et al*. 1987). In the present study, the dogs were diagnosed for vWD based on prolonged BMBT and excluding of other defects. For unequivocal diagnosis, however, Enzyme linked immunosorbent assay

(ELISA) and more accurately a polymerase chain reaction (PCR) based DNA test are recommended. It is recommended that further studies using tests like ELISA and PCR be carried to confirm the diagnosis of vWD.

Summary

Dogs were randomly screened for diagnosis of vWD, which include German shepherd, Pomerian and Doberman. Only, three cases were selected for further study based on haematological findings and BMBT result. Haematological findings revealed decreased Hb, PCV, TEC and normal level of platelet count. In coagulation test study, normal level of CBCT, ACT, PT aPTT, and TT, but increased BMBT were observed. Based on these result, these dogs were diagnosed for vWD.

Acknowledgement

Authors would like to thank Dean, Mumbai Veterinary College, Parel, Mumbai and Secretary, Bai Sakarbai Dinshaw Petit Hospital for Animals for providing necessary facility.

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