Veterinary Emergency and Critical Care Chapter
Surfers Paradise Room 1, July 6, 2019

The effect of elapid snake envenomation on coagulation factor activities in dogs in the inner west of Melbourne

Dr Louis Mark Eramanis[1], Dr Natalie Courtman[1], Dr Andrew Padula[2], Dr Ken Winkel[1], Dr Dez Hughes[1], Dr Manu Boller[1]

[1]*U-Vet Werribee Animal Hospital, The University of Melbourne, Werribee, Australia*
[2]*Bairnsdale Animal Hospital, Bairnsdale, Australia*

Snake venom-induced consumption coagulopathy (VICC) is a common consequence of elapid snake envenomation in dogs which can clinically manifest as haemorrhage at mucous membranes, the gastrointestinal tract, extradural space and pulmonary alveoli.[1–3] In elapids, this consumptive coagulopathy is the result of prothrombin activators in the snake venom, leading to thrombin and ultimately fibrin formation; as a by-product, depletion of coagulation factors occurs in a venom-dose dependent fashion.[4–7] Thus VICC can be identified by prolongation of *in-vitro* coagulation times (e.g., PT, aPTT, ACT), hypocoagulant viscoelastic test (e.g., thromboelastography) results and reduced clotting factor activities. In people with VICC, rapid consumption of coagulation factors (F) I (i.e., fibrinogen), FV and FVIII occurs within 1 – 2 hours of snake bite with return to normal activity of FV and FVIII by 15 hours, and fibrinogen by 24 hours post-envenomation.[8] Whether a similar time course occurs in dogs remains unexamined.

Our study aimed to characterise the coagulation factor changes over time in naturally occurring snake envenomed dogs that presented to our emergency service in Werribee, Melbourne. At that hospital, around 75% of snake envenomations in dogs occurs due to tiger snake bite and the remainder due brown snake bite. Coagulation activities (FI, II, V, VII, VIII, X) at presentation and over the first 24 hours after antivenom administration were compared to a control group of clinically healthy dogs (n=20). We enrolled 19 snake envenomed dogs into the study. Diagnosis was based on appropriate history, clinical signs (lower motor neuron paresis/paralysis, mydriasis, reduced gag),

and at least one of the following: positive snake venom detection kit, CK > 1000 u/L, off scale aPTT or seen bitten by a snake. Citrated whole blood samples were collected at presentation and 3, 12 and 24 hours after anti-venom administration, cool centrifuged and plasma samples stored at -80°C until analysis. Individual coagulation factor analysis (STA Compact Max®, Stago) was performed by the use of factor depleted plasma and a standard curve generated with previously collected pooled control sample of normal dogs.[9] Fibrinogen activity was determined by the Clauss[10] method (STA Compact Max®, Stago). Preliminary results after the analysis of 10 of the cases, showed near absent fibrinogen activity at presentation with progression to normal activity by 24 hours. Similarly, a tendency towards reduced activity of FV and to a lesser extent FVIII during early snake envenomation occurs; while FII, VII and X appear not affected. Availability of the entire data set will allow further insight into the significance of these findings.

This study provides new data on coagulation factor changes in naturally occurring elapid snake envenomation in dogs. Although data analysis requires to be completed at the time of writing, the results suggest that VICC in dogs has a similar effect to people, although to a lesser extent, with fibrinogen most affected followed by FV and FVII. The latter two however, were uncommonly dropped below an activity of 50% and thus constituted only mild reductions. Whether there is a differing effect of tiger versus brown snake envenomation will need to be further elucidated.

References

1. Indrawirawan Y, Sheridan G, McAlees T. Clinical features of Mainland tiger and Eastern brown snake envenomation in dogs and cats in Melbourne. *Aust Vet Pract* 2014;44:704–712.
2. Ong RKC, Lenard ZM, Swindells KL et al. Extradural haematoma secondary to brown snake (Pseudonaja species) envenomation. *Aust Vet J* 2009;87:152–156.
3. Padula AM, Leister E. Eastern brown snake (Pseudonaja textilis) envenomation in dogs and cats: Clinical signs, coagulation changes, brown snake venom antigen levels and treatment with a novel caprylic acid fractionated bivalent whole IgG equine antivenom. *Toxicon* Elsevier Ltd, 2017;138:89–97.
4. Lewis PF. Some toxicity thresholds for the clinical effects of common tiger snake (Notechis scutatus) envenomation in the dog. *Aust Vet J* 1994;71:133–5.
5. Rosing J, Tans G. Structural and functional properties of snake venom prothrombin activators. *Toxicon* 1992;30:1515–1527.

6. Isbister GK. Snakebite doesn't cause disseminated intravascular coagulation: Coagulopathy and thrombotic microangiopathy in snake envenoming. *Seminars in Thrombosis and Hemostasis* 2010;36:444–451.
7. Gulati A, Isbister GK, Duffull SB. Effect of Australian elapid venoms on blood coagulation: Australian Snakebite Project (ASP-17). *Toxicon* Elsevier Ltd, 2013;61:94–104.
8. Isbister GK, Scorgie FE, O'leary MA et al. Factor deficiencies in venom-induced consumption coagulopathy resulting from Australian elapid envenomation: Australian Snakebite Project (ASP-10). *J Thrombosis Haemostasis* 2010;8:2504–2513.
9. Smith SA, McMichael MA, Gilor S et al. Correlation of hematocrit, platelet concentration, and plasma coagulation factors with results of thromboelastometry in canine whole blood samples. *Am J Vet Res* 2012;73:789–798.
10. Clauss A. [Rapid physiological coagulation method in determination of fibrinogen]. *Acta haematologica* 1957;17:237–46.