Case report

Severe acute pulmonary haemorrhage and haemoptysis in ten dogs following eastern brown snake (Pseudonaja textilis) envenomation: Clinical signs, treatment and outcomes

Oriana S. Leonga, Andrew M. Padulab,∗, Ellie Leistera

a Pet Intensive Care Unit (Pet ICU), Underwood, Queensland 4119, Australia
b Australian Venom Research Unit, Department of Pharmacology and Therapeutics, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne, 3010, Australia

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ABSTRACT

This report describes a series of ten cases of fulminant pulmonary haemorrhage in dogs following envenomation by the eastern brown snake (Pseudonaja textilis) in south eastern Queensland, Australia. All cases were presented for veterinary treatment during 2011–2018 at a specialist veterinary emergency centre. Each case received prompt antivenom treatment and supportive care. Pulmonary haemorrhage was diagnosed based on clinical examination; overt haemoptysis; thoracic radiographic demonstration of a diffuse alveolar pattern; and, the presence of venom induced consumptive coagulopathy. The median elapsed time from hospital admission to onset of haemoptysis was 2 h (range 0–18 h). In 80% (8/10) of cases endotracheal intubation was required, whilst 20% (2/10) were successfully treated with mask oxygen supplementation alone, and 40% (4/10) received mechanical ventilation; but only 25% (1/4) of these survived to hospital discharge. Fresh frozen canine plasma was administered to 70% (7/10) of cases and 43% (3/7) of these survived. Of the total number of cases presented for treatment, 30% (3/10) survived to hospital discharge, 60% (6/10) were euthanised due to poor prognosis and 10% (1/10) died from cardiac arrest. Initial serum brown snake venom antigen levels were retrospectively measured from frozen serum samples by venom specific sandwich ELISA in two dogs at 154 ng/mL (survived) and 3607 ng/mL (euthanised); no free venom was detected post-antivenom. Dogs that survived were discharged from hospital without apparent complications. Pulmonary haemorrhage is an uncommon event following envenomation by P. textilis in dogs and has not been described in similarly envenomed humans. This case series highlights the potential for fulminant and fatal pulmonary haemorrhage in dogs following eastern brown snake envenomation.

1. Introduction

The Australian eastern brown snake (Pseudonaja textilis) is a frequent cause of potentially fatal snakebite in dogs and cats in eastern Australia (Padula and Leister, 2017). Envenomed dogs commonly present with clinical signs relating to neurotoxicity such as lower motor neuron dysfunction and potentially fatal respiratory paralysis. Other physiological disturbances such as prolonged blood clotting time, and infrequently intravascular haemolysis and haemoglobinuria also occur. Neurotoxicity is arguably the most significant clinical sign in dogs following P. textilis envenomation, requiring antivenom, supportive care and mechanical ventilation for survival (Padula et al., 2016). However, some envenomed cases present with minimal lower motor neuron signs and subsequently experience haemoptysis, progressing to fulminant, catastrophic, and fatal pulmonary haemorrhage. The syndrome of pulmonary haemorrhage is poorly described in P. textilis envenomed dogs and has not been reported in similarly envenomed humans despite much knowledge of the toxicity of the venom and its components (Padula and Leister, 2017).

Despite coagulation parameters being prolonged pulmonary haemorrhage was not reported in a case series of 149 definite brown snake envenomed humans (Allen et al., 2012). Major haemorrhage was documented in five cases though, with three gastrointestinal bleeds and two intracranial bleeds associated with hypertension (Allen et al., 2012). Intracranial haemorrhage (ICH) in humans was reported from retrospective analysis of hospital records with 2% (5/248) brown snake cases resulting in ICH (Berling et al., 2015). There are only limited reports available in dogs of clinically significant haemorrhage following
brown snake envenomation. An extradural haematoma was diagnosed and successfully treated by decompressive spinal surgery in a dog following brown snake (Pseudonaja sp.) envenomation in Western Australia (Ong et al., 2009). The physiological response of dogs to P. textilis venom shares both similarities and differences with human envenomation. Dogs frequently develop neurotoxicity (Padula and Leister, 2017), whilst this is rare in humans; however, both dogs and humans develop venom induced consumptive coagulopathy (VICC) (Padula and Leister, 2017). VICC is characterized by a coagulopathy in a patient after envenomation where there are low or undetectable fibrinogen levels which results from the activation of clotting pathway by procoagulant toxins in venom (Ibsister et al., 2010). Other coagulation abnormalities manifest as a prolongation of prothrombin time (PT) and/or activated partial thromboplastin time (aPTT) as well as activated clotting time (ACT) (Padula and Leister, 2017). In these patients, VICC is a result of the activation of the coagulation pathway by the prothrombin activator and P. textilis contain group C prothrombin activators (Ibsister et al., 2010).

The following report retrospectively describes the clinical signs, treatment and outcomes of ten cases (see Table 1) of severe acute pulmonary haemorrhage in dogs in south eastern Queensland following brown snake envenomation. This is the first report of a series of pulmonary haemorrhage cases in dogs following P. textilis envenomation and confirms the potential for VICC to result in fatal complications in dogs.

2. Case reports

2.1. Case 1

A two-year-old 34 kg desexed female Maremma Sheepdog presented to the veterinary hospital after the owner found the dog playing with a brown snake in its yard 6 h earlier. At initial examination, the dog had subcutaneous haemorrhage from a presumed bite site on its left ear, was tetraparetic, exhibited haemoptysis and was hypoxaemic, saturating at 93% (normal 96–100) despite oxygen flow by. A blood sample was collected from a peripheral vein and an activated clotting time test performed (ACT) no clot formed. The packed cell volume (PCV) and total serum protein (TP) levels were 42% and 60 g/L respectively. Two vials of antivenom C were administered by slow intravenous infusion. Three hours post-admission the PCV, TP and ACT were 32%, 56 g/L and no clot respectively. Two units of canine fresh frozen plasma (FFP) was administered due to the concern for an ongoing pulmonary haemorrhage. An anxiolytic, which improved its clinical status. A further one unit of FFP was infused to improve circulating clotting factor levels and control bleeding. The dog's respiratory distress further deteriorated. Its PCV and TP were 24% and 58 g/L respectively. Three hours post-admission the PCV, TP and ACT were 32%, 56 g/L and no clot respectively. Two units of canine fresh frozen plasma (FFP) was administered due to the concern for an ongoing pulmonary haemorrhage as demonstrated in the dog's drop in PCV and TP. After the transfusion the prothrombin time (PT) and activated partial thromboplastin time (aPTT) (Coag Dx™ Analyser, IDEXX Laboratories, Rydalmere, Australia) were measured at 16 s (normal 11–17 s) and 133 s (normal 72–102 s) respectively. At 22 h post-admission, the dog's respirations further deteriorated. Its PCV and TP were 24% and 58 g/L respectively. Thoracic radiographs were taken which revealed a marked alveolar pattern in the cranial and caudal lung fields. It was then placed on mask oxygen supplementation as well as butorphanol at 0.2 mg/kg/hr (Butorgesic, Ilium Veterinary Products, Australia) intravenously as an anxiolytic, which improved its clinical status. A further one unit of canine FFP was infused to improve circulating clotting factor levels and control bleeding. The dog's thoracic radiographs were repeated 60 h post-admission and showed a marked resolution of alveolar infiltrates. It was subsequently successfully weaned off mask oxygen support at 65 h post-admission and the dog started ambulating and eating the same night. The dog was discharged from the hospital 80 h after admission and appeared fully recovered (see Fig. 1).

2.2. Case 2

A five-year-old 51 kg desexed female Great Dane dog presented to the veterinary hospital in the evening shortly after the owner found a
dead brown snake and the dog bleeding from small wounds on the leg and tail. On presentation the dog was haemorrhaging subcutaneously from the suspected bite sites, was weak on ambulation and other vital parameters were within normal limits. A blood sample was collected from a peripheral vein and an ACT performed but no clot formed. At this time, the PCV and TP were 43% and 66 g/L respectively, the serum was mildly haemolysed. Retrospective measurement of the initial PT on frozen citrated plasma samples demonstrated it was extremely prolonged (> 300s). Two vials of antivenom A were administered by rapid intravenous infusion without complications. At the completion of antivenom infusion, a venous blood gas was performed together with a repeat PCV and TP. The results of the blood gas were unremarkable, but the PCV and TP had decreased to 28% and 64 g/L which indicated acute blood loss and the crystalloid fluid therapy may have further exacerbated haemodilution. At 3.5 h post-admission the dog developed a soft cough which progressed to haemoptysis and the dog became hypoxaemic (blood oxygen saturation 90% on room air). At 4 h post-admission two units of FFP was administered, and the dog was started on mask oxygen therapy. At 8 h post-admission the respiratory status of the dog had stabilised on supplemental oxygen. Radiographs (Fig. 3) of the thorax showed diffuse foamy alveolar pattern present in right-sided pulmonary parenchyma, most marked in the right cranial lung lobe. An interstitial pulmonary pattern was present in the left lung. Approximately 12 h post-admission the dog’s PCV was 32% and the ACT 160 s. The dog was discharged from the veterinary hospital at 40 h post-admission and appeared to have fully recovered. Thoracic radiographs were repeated a week later and were unremarkable at this time. Retrospective analysis of initial serum brown snake venom antigen (154 ng/mL) and subsequent brown snake venom and antivenom levels are presented in Fig. 2. No free venom was detected after the initial antivenom administration (10 h post-envenomation) indicating that the antivenom level was adequate to neutralise any circulating free venom.

2.3. Case 3

A three-year-old 30 kg desexed female German Short Haired Pointer dog was found by the owner in a collapsed state with a dead brown snake in the yard. The snake was later positively identified as an eastern brown snake by scale count (Cogger, 1978). The dog was presented for veterinary treatment 3 h after the event. On initial physical examination the dog was bradycardic, had weak femoral pulses and had a mild respiratory effort and a soft cough noted on admission. Neurologically the dog was ambulatory with hind leg weakness and bilaterally dilated pupils. There was continuous haemorrhage from the skin on her ear, which was suspected to be the bite site. A blood sample was collected from a peripheral vein and an ACT test performed but no clot formed. The dog was administered two vials of antivenom A as a rapid infusion. The dog had a transient improvement, however, 2 h post-admission, it developed severe haemoptysis and respiratory distress. Anaesthesia was immediately induced with 2 mg/kg of alfaxalone (Alfaxan, Jurox Pty Ltd, Australia) intravenously. Endotracheal intubation performed, and manual ventilation initiated. A further vial of antivenom A was administered, followed by three units of FFP. A significant volume of blood was drained via the endotracheal tube whilst manually ventilated, prior to commencing mechanical ventilation. The dog was unable

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Fig. 1. Fulminant and fatal pulmonary haemorrhage from case No. 6.

Fig. 2. Serum brown snake venom antigen (BSV) and brown snake antivenom (BSAV) levels by hours post-admission in case No. 2.

Fig. 3. Thoracic radiograph of case No. 2 demonstrating a diffuse alveolar pattern present in right-sided pulmonary parenchyma. The pattern appears most marked in the cranial lung lobe.
to maintain oxygenation despite positive pressure ventilation and due to likely poor prognosis, it was euthanised at 4 h post-admission. The dog's brown snake venom serum concentration was retrospectively measured from frozen serum at 3607 ng/mL.

2.4. Case 4

A two-year-old 20 kg desexed male Staffordshire Bull Terrier dog was found by the owner in its yard with a brown snake. The dog presented to the veterinary hospital shortly thereafter and was clinically unremarkable on physical examination aside from a bleeding skin laceration ventral to his right eye. A blood sample was collected from a peripheral vein for an ACT test and no clot formed. A single vial of antivenom B was administered by slow intravenous infusion without complications. Three hours after admission the dog developed a soft cough which progressed to severe haemoptysis by 4.5 h post-admission. Shortly after the dog suffered a cardiac arrest and cardiopulmonary resuscitation was performed but return of spontaneous circulation was not achieved and the dog declared dead.

2.5. Case 5

A seven-year-old 20 kg desexed female Border Collie dog was found by the owner paralysed in its yard. The dog was immediately presented to the veterinary hospital. On initial physical examination the dog was tetraparetic, obtunded, exhibiting ptosis and had a mild respiratory effort. A blood sample was collected from a peripheral vein and an ACT test performed but no clot formed. A commercial snake venom detection kit (SVDK, Seqiris, Parkville, Australia) performed on a serum sample showed a positive result for brown snake venom. This confirmed the suspected diagnosis of brown snake envenomation. Two vials of antivenom C were administered by slow intravenous infusion without complications. The dog's respiratory effort continued to deteriorate over the next two hours. Thoracic radiographs were performed then which showed a generalised alveolar pattern and pulmonary haemorrhage was suspected. The dog was placed on masked supplemental oxygen and one unit of FFP was administered. The dog continued to deteriorate, was hypoxaemic and hypercapnic with a PCO2 of 75 mmHg measured on venous blood gas. Anaesthesia was induced, endotracheal intubation performed and mechanical ventilation commenced 6 h post-admission. At 36 h post-admission the dog was successfully weaned off the ventilator. At this time, the dog still required supplemental oxygen and one unit of FFP was started. Endotracheal intubation was performed with no further drug administration, a significant amount of blood was suctioned from the endotracheal tube and trachea. Shortly after the dog went into respiratory arrest and manual positive pressure ventilation commenced. The prognosis was considered poor at this stage and the owner elected to euthanise the dog.

2.6. Case 6

A two-year-old 56 kg desexed female Great Dane dog presented to the veterinary hospital after the owner reported finding a dead brown snake in the dog's yard. The snake was identified by scale count as an eastern brown snake. On presentation, the dog was ambulatory, a soft cough with mild haemoptysis was noted, other vital signs were within normal limits. A blood sample was collected from a peripheral vein and an ACT test performed but no clot formed. A diagnosis of brown snake envenomation was made and two vials of antivenom C were administered intravenously over 5 min without adverse reaction. The dog was also administered 0.02 mg/kg of acepromazine (ACP 2 Injection, Ceva Animal Health Pty Ltd, Australia) and 0.2 mg/kg of butorphanol (Butorgesic, Ilium, Australia) intravenously for anxiolytic effects. The dog was given supplemental oxygen via face mask. Over a 20 min period the dog's respiratory status had markedly deteriorated, hypoxaemia and haemoptysis progressed. A bolus infusion of one unit of FFP was started. Endotracheal intubation was performed with no further drug administration, a significant amount of blood was suctioned from the endotracheal tube and trachea. Shortly after the dog went into respiratory arrest and manual positive pressure ventilation commenced. The prognosis was considered poor at this stage and the owner elected to euthanise the dog.

2.7. Case 7

A 15-month-old 30 kg desexed female Labrador dog was found by the owner in the yard playing with a brown snake. The snake was brought into the hospital and positively identified as an eastern brown snake by scale count (Cogger, 1978). On initial physical examination the dog had frank blood on its paws, no visible skin haemorrhage, pale oral mucous membranes and ptosis. A blood sample was collected from a peripheral vein and an ACT test performed but no clot formed. One vial of antivenom C was administered by slow intravenous infusion. Two hours later, the dog developed haemoptysis and thoracic radiographs were taken which showed a generalised alveolar pattern in the dorsal lung lobes. The dog continued to decline into a fulminant pulmonary haemorrhage, endotracheal intubation was performed and manual positive pressure ventilation initiated. A poor prognosis for survival was given at this time and the owner elected to euthanise the dog.

2.8. Case 8

A four-year-old 21 kg non-desexed female American Staffordshire Terrier was found by the owner to be quieter than usual and passing mucoid diarrhoea. The owner later found a dead brown snake in the yard. The dog was presented to the veterinary hospital with the snake which was positively identified by scale count as an eastern brown snake (Cogger, 1978). At initial physical examination, the dog was ambulatory but mildly weak with suspected snakebite bite wounds on the skin on either side of its neck that were actively haemorrhaging. A blood sample was collected from a peripheral vein and an ACT test performed but no clot formed. Two vials of antivenom C were administered by slow intravenous infusion without any adverse reaction. Two hours after hospital admission the dog became dyspnoeic and masked oxygen supplementation was commenced. Radiographs of the thorax showed diffuse pulmonary infiltrates that were considered likely due to pulmonary haemorrhage. A third vial of antivenom C was administered intravenously. A transfusion of one unit of FFP was then commenced. However, 4 h after admission the dog experienced a catastrophe fulminant pulmonary haemorrhage, general anaesthesia was induced, endotracheal intubation performed and positive pressure ventilation initiated. A unit of packed canine red blood cells and a second unit of FFP was transfused. The dog was subsequently placed on a mechanical ventilator. A fourth vial of antivenom C was administered followed by another unit of FFP. A SVDK (Seqiris, Parkville, Australia) was performed at 6 h post-admission which returned a mild positive for brown snake venom and a fifth vial of antivenom C was administered. At 7 h post-admission, a blood sample was collected and the PCV was 22% and TP 40 g/L. An ACT test was performed at this time, but no clot formed. Due to the decreased PCV and TP further half unit of packed red blood cells and one unit of FFP was administered. By 10 h post-admission the dog had deteriorated further and had developed cardiac arrhythmias, severe haematochezia and haematemesis. Despite being on 100% oxygen and on a mechanical ventilator blood oxygen saturation was only 75%. Due to the likely poor prognosis the dog was euthanised at the owner's request.

2.9. Case 9

A 5-year-old 5.5 kg desexed female Miniature Fox Terrier dog was found in the yard with a brown snake. At initial examination, the dog...
had a bleeding wound on the right side of its thorax. A blood sample was collected from a peripheral vein and an ACT test performed but no clot formed. The PCV at this time was 40%. The dog was administered 0.02 mg/kg of acepromazine (ACP 2 Injection, Ceva Animal Health Pty Ltd, Australia) and 0.2 mg/kg of butorphanol (Butorgesic, Ilium, Australia) subcutaneously for their sedative effects. An intravenous catheter was placed and 1 h post-admission the dog developed profound paralysis and hypotension. It was intubated and manually ventilated for the duration of the antivenom administration. Urine was collected and a SVDK performed which showed a strong positive for brown snake venom. At the time, haemoglobinuria was noted. The dog was administered four vials of antivenom C. During that time, it developed bradycardia of 40 beats per minute occurred, 0.01mg/kg of adrenaline (Aspen Australia, St Leonards, Australia) was administered intravenously and normocardia resumed. At the end of the fourth vial, adrenaline (Aspen Australia, St Leonards, Australia) was administered four vials of antivenom C. During that time, it de

Ventilated for the duration of the antivenom administration. Urine was collected from a peripheral vein and an ACT test performed but no clot formed. The SVDK was performed on a urine sample which showed a strong positive for brown snake venom. Despite masked oxygen supplementation, its oxygen saturation was measured at 80%. Anaesthesia was induced with 2 mg/kg of alfaxan (Alfaxan, Jurox Pty Ltd, Australia) intravenously and the dog intubated. The dog was placed on the mechanical ventilator, and fifth vial of antivenom C was administered. Its PCV was remeasured 26 h post-admission and had further declined to 9%. Due to the likely poor prognosis the dog was euthanised at the owner's request.

2.10. Case 10

A 2-year-old 46 kg desexed male Rhodesian Ridgeback cross dog was found by the owner, collapsed and haemorrhaging from its mouth. It was last seen normal 10 h prior. At initial examination, the dog presented with tachycardia, weak femoral pulses, melaena, respiratory distress and haemoptysis. An intravenous catheter was placed, and the dog administered a 1 L bolus of an isotonic crystallized blood oxygen was provided while the diagnostic tests performed. A blood sample was collected from a peripheral vein and an ACT test performed but no clot formed. The SVDK was performed for brown snake venom. The dog was intubated with a vial of antivenom C. It continued to cough with overt haemoptysis and its oxygen saturation also continued to deteriorate. Anaesthesia was induced with 2 mg/kg of alfaxalone (Alfaxan, Jurox Pty Ltd, Australia), endotracheal intubation and manual ventilation commenced. The response to positive pressure ventilation was poor with an oxygen saturation not exceeding 82%. The dog was euthanised at the owner's request due to the likely poor prognosis at 1 h post-admission.

3. Materials and methods

All cases occurred in south-eastern Queensland over a period of 7 years from 2011 to 2018 and were treated at the Animal Emergency Service (Underwood and Carrara, Australia), Pet Intensive Care Unit (Underwood, Australia), and Veterinary Specialist Service (Underwood and Carrara, Australia). All FFP used was from in-house canine donors that had previously had citrated plasma collected and frozen; one unit of FFP contains approximately 200–250 mL of citrated plasma. Antivenom A = experimental caprylic acid fractionated equine whole IgG tiger-brown snake antivenom 8000 units (Padula and Leister, 2017). Antivenom B = Multi-brown snake antivenom 1500 units; Australian Veterinary Serum Laboratories, Lismore, Australia. Antivenom C = Tiger and multi-brown snake antivenom 7000 units; Summerland Serums, Dalwood, Australia. One unit of antivenom is defined as the amount that will neutralise the lethal effects in mice of 0.01 mg of venom. Serum concentration of brown snake venom antigen and brown snake venom antivenom were retrospectively determined on frozen samples by ELISA as described previously (Padula and Leister, 2017). ACT tests were performed using commercial tubes (MAX-ACT™, Helena Laboratories, Mt Waverly, Australia); this method has previously been validated for use in dogs with the normal reference range of 60–90 s adopted (See et al., 2009). Briefly, 2 mL of whole blood was rapidly transferred to the commercial ACT tube. The tube was immediately placed into a single well whole blood coagulation monitoring instrument designed to accurately measure the ACT in seconds (Hemochron 401, Edison, New Jersey). When a clot was formed the specific time was recorded in seconds, but for all ACT tests over 1500 s the results are reported here as ‘no clot’.

4. Discussion

This case series is the first report describing fulminant pulmonary haemorrhage in dogs following P. textilis envenomation and reinforces the potential for VICC to result in fatal complications with only 30% (3/10) of affected dogs surviving. In comparison, a previous report by the same authors found that 81% (13/16) dogs survived following treatment for confirmed brown snake envenomation with 13% (2/16) euthanised for direct financial reasons (Padula and Leister, 2017). The consistent clinical findings in these cases of pulmonary haemorrhage were the early onset (median 2 h) of haemoptysis, presence of VICC, and respiratory distress. Whilst pulmonary haemorrhage is infrequently observed in dogs following envenomation, this case series demonstrates that when it does occur the consequences can be fatal. The authors estimate that in their experience in southeast Queensland 1–2% of dogs presenting for eastern brown snake envenomation will develop haemoptysis and potentially fatal fulminant pulmonary haemorrhage, with approximately 100 cases treated each year during the timeframe of this study.

Haemoptysis was seen in 90% (9/10) of the cases with the onset time at between admission and 6 h post admission. Thoracic radiographs were performed on six patients and all demonstrated a diffuse alveolar pattern. The combination of severe coagulopathy, evidence of active bleeding from other sites (in some cases) and haemoptysis make pulmonary haemorrhage the most likely cause for the alveolar infiltrates on thoracic radiographs. Other differentials that could be considered include severe pneumonia. The principle procoagulant activator of P. textilis venom is a high molecular weight enzyme (group C prothrombin activator) with antigenic similarity to that found in the Coastal taipan (Oxyuranus scutellatus) (Masci et al., 1988). VICC is a venom-induced activation of the clotting pathway by prothrombin activators, converting prothrombin to thrombin. This process initially results in rapid clot formation followed by severe factor deficiencies due to consumption of coagulation factors and activation of fibrinolysis pathways. Though unclear, we hypothesise that the proposed mechanism of haemoptysis is due to massive acute pulmonary thromboembolism after activation of group C prothrombin activators and the initial procoagulant effect of P. textilis (Padula and Leister, 2017). Pulmonary embolism in humans is reported to cause haemoptysis. Intravenous injection of 7 μg/kg of the purified procoagulant enzyme was lethal to rats within minutes, but pre-injection with heparin prevented this lethal effect, suggesting death was the result of intravascular coagulation (Masci et al., 1987). Further investigation is warranted to gain a better understanding of the pathophysiology leading to the fulminant pulmonary haemorrhage demonstrated in these cases.

All cases in this series of ten dogs were promptly treated with antivenom. Previous studies have demonstrated that antivenom is able to...
bind to procoagulant toxin in vitro and neutralise these to variable extents, thereby preventing any procoagulant effects (Padula and Leister, 2017). Antivenom effectiveness for reversal of VICC is limited once the clotting pathway is activated and clotting factors already consumed. Procoagulant toxins act in the central compartment, making their onset of action relatively rapid (Maduwa and Isbister, 2014). The prothrombin activator toxin works so rapidly that antivenom cannot be practically administered in time to prevent VICC (Isbister et al., 2010). Clotting factor resynthesis and full recovery of clotting function may take up to 48 h. Hence, factor replacement has been suggested; although there is concern that the provision of these clotting factors may worsen the problem if procoagulant toxins are not neutralised (Isbister et al., 2013). A human study analysing the use of FFP in treatment of VICC in cases of Australian snakebite showed that the administration of FFP within 4 h of antivenom administration results in more rapid restoration of clotting function in the majority of patients. This was however not associated with more rapid hospital discharge and the numbers were too small to determine whether the administration of FFP could reduce the risk of major haemorrhage. The study also mentions that ongoing factor consumption after antivenom administration may be attributed to the presence of active clotting factors in the initial period of resolution of VICC. It states that administration of FFP within 6–8 h of the bite should only be given if there is severe clinical bleeding (Isbister et al., 2013). Though this result argues the support for the cautious use of FFP in snakebite patients, its limitations lie with the lack of similar veterinary studies in support of this finding as well as its small sample size.

All dogs in this case series demonstrated no clot forming on an ACT test which supports VICC. In a human study of factor deficiencies in VICC, international normalised ratio (INR), aPTT, coagulation factors: I, II, VII, VIII, IX, X, von Willebrand factor antigen and D-dimer concentrations were measured. The results showed an absence of detectable fibrinogen, absent or low factor V and VIII, unrecordably high INR, aPTT, very high D-dimer but only a partial reduction in the concentration of factor II and X (Isbister et al., 2010). For a conclusive diagnosis of VICC, PT, aPTT, D-dimer and fibrinogen levels should be tested. However, a practical approach adopted by veterinarians when eastern brown snakebite is strongly suspected is to perform the simple, low cost ACT test. The authors previous work on brown snake envenomation in dogs demonstrated VICC was presented in all cases of confirmed envenomation (Padula and Leister, 2017). Fatal complications from VICC in humans envenomed by P. textilis have included cerebral haemorrhage in six cases (Tibballs, 2005). In a series of 552 human snakebite cases with VICC in Australia over a 10 year period, cerebral haemorrhage was diagnosed in 1% within 1–12 h of the bite despite all patients receiving antivenom and FFP (Berling et al., 2015). The administration of FFP to human snakebite cases presenting with VICC was examined in clinical trial conditions in 70 patients and found to shorten the time to restoration of normal clotting times, but had no effect on duration of hospital stay (Isbister et al., 2013). However, due to the rarity of the potentially fatal VICC complications (ie cerebral haemorrhage) much greater numbers of patients are required to study how effective FFP is for preventing fatal cerebral haemorrhage. In this series cases 1, 2, 3, 5, 6, 8 and 9 (70%; 7/10) received FFP and out of these only cases 1, 2 and 5 (30%; 3/10) survived. Cases 1, 2, 5 and 9 received FFP at approximately 4 h post admission while cases 3, 6 and 8 received FFP in less than 2 h post-admission. Though the reasons were unclear, a previous human study had demonstrated that those receiving FFP early had evidence of factor consumption after it was administered. However, all these patients had received antivenom prior to the FFP suggesting that the active clotting factors were endogenous ones activated in the initial consumptive provies and not the procoagulant toxin (Isbister et al., 2013). The administration of FFP isn't without risk and immunologic and non-immunologic reactions (including transfusion related acute lung injury) can occur ranging from mild to potentially fatal.

Measurement of the concentration of brown snake venom antigen in serum was made in two cases and the results were much higher than typically reported in humans (Allen, 2012). The dose of venom and, or, rate of administration may play a role in the pathology that subsequently ensues. The venom of P. textilis contains both presynaptic and postsynaptic neurotoxins, along with potent procoagulants (Padula et al., 2016). The venom of P. textilis is highly lethal when injected into mice, with a reported LD50 of 0.053 mg/kg (Broad et al., 1979). Mice die from progressive respiratory paralysis with five lethal doses. Pre-mixing of venom and brown snake antivenom prevents death. Venom from the coastal taipan (Oxyuranus scutellatus) when injected at low doses into mice caused respiratory paralysis (ie 4 LD); but larger doses (ie 500 LD) resulted in rapid death from pulmonary thrombi (Herrera et al., 2012). Coastal taipan venom contains a serine protease prothrombin activator like that found in P. textilis (Isbister, 2009). Post mortem examinations were offered to 2 clients but were declined at the time. Antemortem computed tomography with pulmonary angiography is considered the gold standard for diagnosis of pulmonary thromboembolism and would help to further understand the pathophysiology of these fulminant haemorrhages.

Pulmonary haemorrhage may be more likely in dogs envenomed by eastern brown snakes in Queensland. Fulminant pulmonary haemorrhage was not reported in 104 dogs and 45 cats envenomed near Melbourne in southern Australia although only three cases were from brown snakes (Indrawirawan et al., 2014). Although underlying pre-existing lung pathology could not be ascertained in the ten cases described, it is possible that pre-existing pathology may potentiate haemorrhage in the presence of VICC. Pre-existing hypertension in humans was present in brown snake envenomed patients that developed fatal cerebral haemorrhage (Berling et al., 2015). Significant geographical differences in the procoagulant activity and venom yields between P. textilis specimens collected from Queensland and South Australia have been described (Fligt et al., 2006; Skejic and Hodgson, 2013). Queensland brown snakes yielded more dry venom mass per milking (6.7 v 30.2 mg), demonstrated greater procoagulant activity and were larger snakes overall (mean length 140.9 v 110 cm) (Fligt et al., 2006; Mirtschin et al., 2002). In laboratory studies, the venom of P. textilis has been shown to have profound in vivo cardiovascular and coagulopathic effects in dogs. Intravenous injection of 2.5–10 μg/kg of P. textilis venom into anaesthetised dogs resulted in uncontrollable blood within 5–10 minutes, massive cardiovascular depression and severe hypotension (Tibballs et al., 1991).

In conclusion, this case series of eastern brown snake envenomed dogs that presented with VICC highlight the potential for occasional cases to develop fulminant and potentially fatal pulmonary haemorrhage. Further investigation is needed to gain a better understanding of the pathophysiology of fulminant pulmonary haemorrhage following brown snake envenomation.

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