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Case report

Severe neurotoxicity requiring mechanical ventilation in a dog envenomed by a red-bellied black snake (*Pseudechis porphyriacus*) and successful treatment with an experimental bivalent whole equine IgG antivenom

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ABSTRACT

Snakebite in dogs from *Pseudechis porphyriacus* (red-bellied black snake; RBBS) is a common envenomation treated by veterinarians in Australia where this snake occurs. This case report describes the successful treatment of a clinically severe RBBS envenomation in a dog with an experimental bivalent equine whole IgG antivenom and mechanical ventilation, following its presentation in a cyanotic state. The cause of the cyanosis and respiratory distress was considered due to paralysis from neurotoxins in RBBS venom. The dog was treated with two vials of bivalent antivenom, each containing sufficient antivenom to neutralise the lethal effects of 40 mg of tiger snake (*Notechis* sp) and 40 mg of brown snake (*Pseudonaja* sp) venom. Hypoxaemia ($Sp0_2$ of 75%) and hypercapnia ($PaCO_2$ of 61 mmHg) indicated the need for mechanical ventilation (MV) to prevent imminent death. The dog was anaesthetised using total intravenous anaesthesia and MV used for 18 h. Following discontinuation of MV, it resumed spontaneous breathing thereafter and made a complete recovery. Serum biochemistry revealed a significant myopathy with elevated CK and AST levels, peaking approximately 48 h post-treatment. Elevated liver enzymes, suggestive of hypoxic liver injury, were detected during the period of hospitalisation. The dog represented approximately one week after hospital discharge because of inappetence and mild hepatopathy, which resolved spontaneously by 30 d post-treatment. A mild coagulopathy was initially present which resolved within 24 h following antivenom treatment. At initial presentation, RBBS venom antigen was detected by sandwich ELISA in urine and serum. Free RBBS venom antigen was not detected post-antivenom treatment. Human cases of RBBS requiring ventilatory support are rare. This unusual case of RBBS envenomation in a dog highlights its potential clinical severity in dogs, and the need for early, aggressive, MV to achieve a successful outcome in cyanosed and clinically severe cases.

1. Introduction

The Australian red bellied black snake (RBBS), *Pseduechis porphyriacus*, is a common cause of snakebite in dogs and cats in geographical regions of Australia where the snake is found (Padula et al., 2016). Envenomation typically results in clinical signs of myopathy, haemolysis, pigmenturia and local tissue swelling (Ong et al., 2015; Padula et al., 2016). Simple supportive care and antivenom treatment are highly effective in the majority of cases (Padula and Winkel, 2016a). However, previously described complications of RBBS envenomation in dogs include renal failure (Heller et al., 2006), severe anaemia with spherocytosis (Trigg and McAlees, 2015) and local tissue destruction (Padula and Winkel, 2016a). Severely RBBS envenomed animals that present with respiratory distress and cyanosis are less commonly observed, and death is likely to occur in these cases unless ventilation is supported. There are no detailed published case reports of successful treatment of severe RBBS envenomed dogs requiring mechanical ventilation (MV). This case report describes the successful treatment of a clinically severe RBBS envenomed dog with bivalent

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antivenom and MV.

The venom of the RBBS contains a range of toxic substances including neurotoxins (Hart et al., 2013; Ramasamy et al., 2005); however, neurotoxicity is rarely reported in envenomed humans (Churchman et al., 2010; Pearn et al., 2000). The evidence for neurotoxins in *Pseudechis* sp. is derived from *in vitro* studies using chicken and rat nerve-muscle extracts in organ baths. Venom from all seven species within the *Pseudechis* genus (*P. australis* (mulga snake), *P. colletti* (Collett's snake); *P. guttatus* (spotted black snake); *P. papuanus* (Papuan black snake); *P. porphyriacus* (red-bellied black snake) and *P. pailsii* (eastern pygmy mulga) were demonstrated to have neurotoxic properties *in vitro* (Ramasamy et al., 2005). In these studies, the prior administration of tiger snake (*Notechis* sp) or black snake antivenom to the organ bath perfusion solution prevented the venom induced inhibition of twitch height. The subsequent addition of antivenom, following incubation with venom, resulted in only partial reversal of venom effects with a 20–28% restoration in twitch height (Ramasamy et al., 2005).

When considered necessary, and due to its cross-reactivity, monovalent tiger snake antivenom is usually administered to animal or human patients suffering RBBS envenomation. Due to the relatively high incidence of adverse reactions in humans to equine antivenom, antivenom is preferentially administered only to cases considered severe enough to benefit (Churchman et al., 2010). Tiger snake antivenom is used because of the smaller volume in each vial and it is also a lower cost product than monovalent black snake antivenom. A larger volume monovalent black snake antivenom, prepared against *Pseudechis australis,* is available within Australia, and may be used in some cases of RBBS. However this product is a polyvalent antivenom due to the production methods used (O'Leary and Isbister, 2009).

The limited published reports of RBBS envenomed dogs suggest that neurotoxicity does occasionally occur and when present may be severe enough to require lifesaving MV for treatment. This case report describes a clinically severe RBBS envenomation in a dog and treatment with antivenom and mechanical ventilation to achieve a successful outcome.

2. Case report

A 25 kg seven-year-old, desexed male, Staffordshire bull terrier, presented for veterinary treatment because of excessive salivation, neck ventroflexion and generalised weakness. Two hours prior to presentation the owner had observed the dog to have vomited. A dead RBBS was later found by the owner in the dog's yard in suburban Brisbane. At initial clinical examination the dog had mydriasis, absent palpebral reflexes, absent gag reflex, cervical neck ventroflexion and was non-ambulatory. Systolic, diastolic and mean arterial blood pressure were 122, 77 and 92 mmHg respectively. A moderate sized oedematous swelling of the right lip commissure was noted (Fig. 1). A cephalic intravenous catheter was immediately placed and blood samples collected for baseline diagnostics. Due to multiple regurgitations, hypoxaemia despite oxygen supplementation, poor respiratory excursion and poor laryngeal function, treatment was initiated immediately, general intravenous anaesthesia (2 mg/kg, Alfaxan, Jurox, Australia) induced, and orotracheal intubation was performed.

Snake envenomation was suspected and the diagnosis was rapidly confirmed by a positive SVDK (CSL, Parkville, Australia) test result for black snake immunotype on urine. RBBS venom antigen was subsequently detected by ELISA in frozen urine and serum samples collected at initial presentation, immediately prior to antivenom administration (Table 2). RBBS venom antigen was not detectable in serum collected 3 h post-antivenom, but was detectable at a much lower concentration in urine at this same time point. Serum antivenom concentration at 3 h post-administration, and over the following 48 hours, appeared adequate for neutralisation of RBBS venom concentration detected. Antivenom was detectable in very low concentration in urine relative to serum concentration. The specificity of the antivenom ELISA appeared good with undetectable equine antivenom (IgG) in the urine and serum prior to treatment.

Fig. 1. Unilateral facial swelling following RBBS envenomation (arrow shows bite location).

Initial blood gas analyses were performed (Table 1) and revealed a mild acidaemia due to moderate respiratory acidosis, mild metabolic acidosis due to mild hyperlactataemia, and a stress hyperglycaemia. A 10 mL/kg intravenous bolus of Hartman's solution was initially given and intravenous fluids continued at twice maintenance to aid diuresis and urine production. Blood samples were collected and an activated clotting time (ACT) performed which returned an abnormally long clot formation time (150 sec; normal <85). A mild coagulopathy was initially present with prolongation of both the PT (25s; normal 8–12) and activated clotting time (151 s; normal <85 s). Both coagulation parameters had returned to normal ranges by 24 h post-antivenom. Clinically significant bleeding was not observed at any stage. Serial haematology profiles revealed anaemia and presence of numerous spherocytes and other red cell morphological abnormalities on blood film (Table 3). A moderate anaemia was present initially evidenced by reduced haemoglobin, haematocrit and red cell count, but did not reach critically low levels. Red cell numbers had returned to normal by 30 days post-treatment but spherocytes remained present. Neutrophil numbers were moderately increased during the period of hospitalisation.

One vial of bivalent tiger-brown snake antivenom as