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Case report

Suspected anaphylaxis and lack of clinical protection associated with envenomation in two dogs previously vaccinated with Crotalus atrox toxoid

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ABSTRACT

Objective: to describe the clinical presentation of two canines present in anaphylactic shock secondary to rattlesnake envenomation. In both cases, there was no previous documented previous envenomation event and the initial sensitization required for anaphylactic response is believed to be secondary to Crotalus atrox toxoid vaccine.

Case description: In the first case, a 12-year-old golden retriever present for collapse, severe hematochezia, and vomiting after first time envenomation from a suspected western diamondback rattlesnake. The patient presented in severe hypovolemic shock and required aggressive fluid therapy, antivenom, anti-emetics, and pain management. The patient made a full recovery within 24 hours. In the second case, an 8-year old English setter presented for acute collapse, vomiting, and facial swelling after suspected first time envenomation from a suspected Prairie rattlesnake. The patient presented in severe hypovolemic shock with cardiac arrhythmias and required aggressive fluid therapy, antivenom, pain control, anti-emetics, and antibiotics. The patient made a full recovery after three days of hospitalization. Both patients had been previously vaccinated with the *C. atrox* vaccine.

Conclusion: This case report documents suspected anaphylaxis in two canine patients after first time envenomation by a rattlesnake. Both patients were previously vaccinated by the *Crotalus atrox* toxoid, which is hypothesized to be the initial inciting trigger.

1. Introduction

There are approximately 8000 venomous snakebites occurring in the human population in the United States each year (Gold, 2004) and are a significant clinical problem for the small animal veterinarian. The majority of venomous bites sustained in the United States are from the family *Viperidae,* subfamily *Crotalinae,* which includes rattlesnakes, copperheads, and water moccasins. It is thought that the eastern and western diamondback rattlesnakes (*Crotalus adamanteus, Crotalus atrox,* respectively) are responsible for the most morbidity and mortality due to their venom potency and widespread geographic distribution (Juckett and Hancox, 2002).

Venom from a rattlesnake contains multiple substances, including small peptides and enzymes that contribute to multisystemic disease, with hematologic/coagulopathic abnormalities, local tissue necrosis/inflammation, and in some cases, neurologic impairment (Armentano and Schaer, 2011). The mainstays of therapy for rattlesnake envenomation include fluid resuscitation, antivenom administration, and pain management.

In rare instances, patients can present in anaphylactic shock with venom playing the role as the trigger leading to immunologic reaction and mast cell degranulation (Hogan and Dire, 1990). In most instances, this is noted in patients with a previously known envenomation event. In this case series, two patients presented for rattlesnake envenomation in concurrent anaphylactic shock with no previous sensitization event. It is hypothesized in both patients

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that the previous sensitization event was from repeat vaccinations with *C. atrox* toxoid vaccine.

2. Case report

2.1. Case 1

A previously healthy 12-year old female spayed golden retriever presented to the emergency service in Maricopa County, Arizona for rattlesnake envenomation. The owner witnessed a rattlesnake bite to the left rostrolateral muzzle immediately prior to collapse and approximately 30 minutes prior to emergency room presentation. The dog suffered acute collapse, vomiting, and hematochezia within minutes of the bite. The patient suffered no previous rattlesnake envenomation. Three prior injection of the *C. atrox* toxoid vaccine were administered one year apart, with the last vaccination given one year prior to this envenomation (March 2012, March 2013, April 2014).

Physical examination showed marked obtundation, lateral recumbency, and inability to stand, tachycardia (200 bpm), weak femoral pulses, muddy mucous membranes with a prolonged capillary refill time (CRT) > 3 seconds, tachypnea (60bpm) and a rectal temperature of 101.8F (39.7C). Doppler blood pressure was measured at 60 mmHg and electrocardiogram identified a narrow complex tachycardia. Two small puncture wounds with mild hemorrhage and minimal swelling were noted on the left rostolateral muzzle. Retching with rhythmic abdominal contractions and multiple episodes of large volume hematochezia occurred during initial assessment.

The dog was treated with oxygen delivered via loose fitting facemask, shock fluid therapy in titrated aliquots that consisted of the following during the emergency phase of resuscitation: 60mL/kg of Normosol-R,[1] 3mL/kg of 7.1% NaCL,[2] and 5ml/kg of Vetstarch.[3] Fluid therapy was continued following optimized endpoints of resuscitation at 4.8mL/kg/hr of Normosol-R[1] and 1.6mL/kg/hr of Vetstarch.[3] Hydromorphone[4] (0.1mg/kg intravenous) was administered for analgesia. The dog was admitted to the intensive care unit for ongoing care and two vials of F(ab′)2 Antivenom, Crotalidae polyvalent, equine origin[5] (Venom Vet) were administered over two hours. A single dose of maropitant citrate[6] (1mg/kg) and pantoprazole[7] (1mg/kg) were administered. Fentanyl[8] was provided as a constant rate infusion of 3 μg/kg/hr.

While resuscitation efforts were underway, the following diagnostics were obtained: venous blood gas and electrolytes, complete blood count, biochemistry profile, prothrombin time, activated partial thromboplastin time, and blood smear analysis. Initial venous blood gas showed a lactic acidosis (pH 7.33, reference interval [7.34–7.42], Lactate 7.5mmol/L, reference interval [0.3–3.4]). Packed cell volume measured 56%, reference interval (37–55%) and total plasma protein of 42g/L, reference interval (52–82g/dL). The serum biochemistry panel showed a hypoalbuinemia (1.6g/dL, reference range [2.2–3.9]) and hypoglobulinemia (1.9g/dL, reference range [2.5–4.5]). Automated machine complete blood count was within normal limits. Citrate whole blood prothrombin time (PT) was mildly prolonged at 19s [11–17 seconds] and activated partial thromboplastin time (aPTT) was markedly prolonged at >300 seconds [72–102 seconds]. A blood smear analysis showed moderate thrombocytopenia (129 K/μL, reference interval [200–500 K/μL]) with estimated 75% echinocytes and occasional spherocytes. An abdominal focused assessment with sonography for trauma (AFAST) was performed by the author during stabilization (Lisciandro, 2011), showing a double walled gallbladder with no peritoneal free fluid (Quantz, 2009). No pleural or pericardial effusions were appreciated on thoracic focused assessment with sonography for trauma.

A repeat aPTT two hours following completion of antivenom administration showed a mildly prolonged aPTT (110 seconds, reference interval [72–102 seconds]). A blood smear analysis showed no echinocytes or other red blood cell abnormalities. PCV was 42% and total plasma protein was 30g/dL. Venous blood gas and electrolytes were measured 18 hours post presentation, with no abnormalities. A blood smear again evaluated, showing no echinocytes and adequate platelets. PCV was 42% and total plasma protein was 42g/dL with clear serum.

The tachycardia and hypotension resolved at approximately 90 minutes following emergency presentation, with Doppler systolic blood pressure remaining ≥100 mmHg for the duration of hospitalization. Large volume hematochezia persisted for approximately 6 hours following admission, tapering off to smaller volumes throughout remainder of hospitalization. Occasional runs of wide complex pre-mature beats at an accelerated rate of 140 bpm were noted on the electrocardiogram approximately 12 hours following presentation. Specific treatments for this arrhythmia were not pursued and the arrhythmia was much less frequent at the time of discharge to home. The dog was walking and eating with no vomiting, retching, or regurgitation approximately 12 hours following presentation. The dog was discharged to home at 24 hours post presentation on the following medications with instructions to follow up: Gabapentin[9] (6mg/kg every 12 hours), Tramadol[10] (3-4-5mg/kg every 8 hours), and Proviable[11] once daily. The owner was contacted three weeks post discharge and noted that the patient was doing well.

2.2. Case 2

An eight year old, male intact English setter presented to the emergency service in Fort Collins, CO for acute collapse following suspect rattlesnake envenomation. The rattlesnake envenomation was not witnessed, however, two black puncture wounds were noted on the oral mucosa during the physical examination and the dog was out hiking in an area with known rattlesnake encounters. The dog vomited a large amount and then collapsed following the presumptive envenomation. The dog had a previous documented episode of facial swelling after being in the yard approximately two years prior, which required no medical intervention at this time. It is suspected that this prior event was mild facial edema secondary to an insect sting, as rattlesnakes had not been witnessed in the yard of this home and the dog did not develop any other signs consistent with a rattlesnake envenomation at that time. Two prior injections of the *C. atrox* toxoid vaccine were administered one year part, with the last vaccination given 3 months prior to this suspected envenomation (April 2014, April 2015).

The presenting physical examination showed a sinus tachycardia, lateral recumbency, pale mucous membranes with a CRT > seconds, obtunded mentation, moderate unilateral swelling of the rostral muzzle with a well-demarcated 5 cm × 3 cm region of

[1] Normosol-R, Hospira, Inc. Lake Forest, IL.
[2] 7.2% NaCL, MWI. Boise, ID.
[3] Vetstarch, Abbott Laboratories. North Chicago, IL.
[4] Hydromorphone, West-ward. Eatontown, NJ.
[5] Venom Vet, Instituto Biologico. Argentino S.A.I.C.
[6] Maropitant citate injectable, Zoetis. Parsippany, NJ.
[7] Pantoprazole, Zycomed GmBH. Konstanz, Germany.
[8] Fentanyl, West-ward. Eatontown, NJ.
[9] Gabapentin, Amneal Pharamceuticals. Paterson, NJ.
[10] Tramadol, Amneal Pharmaceuticals. Paterson, NJ.
[11] Proviable. Nutramax Laboratories. Lancaster, SC.