

CASE REPORT

Treatment of the first known case of king cobra envenomation in the United Kingdom, complicated by severe anaphylaxis

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Summary

We report the first known case of envenomation following snake bite by a king cobra in the UK. The patient required tracheal intubation and ventilation. Treatment with king cobra antivenom resulted in anaphylaxis (bronchospasm and hypotension), requiring adrenaline infusion. The patient's trachea was extubated 11 h after administration of antivenom.

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The king cobra (*Ophiophagus hannah*) is the world's longest venomous snake, growing up to 5.5 m (18.5 ft). It also has one of the longest lifespans, living up to 25 years. To our knowledge (PubMed search 1966–2006), confirmed by consultation with the Liverpool School of Tropical Medicine, there has never been a reported case of king cobra snake bite in the United Kingdom. Worldwide, the most recently reported cases of non-native bites by this snake have been in the USA, and followed king cobra bites to the keepers of imported snakes [1]. We describe the case of a 22-year-old shop worker who was bitten whilst feeding a king cobra in a specialist reptile outlet in Bristol, UK.

Case report

A 22-year-old man presented to the Accident and Emergency Department within 20 min of receiving a bite from an adult king cobra to the lateral aspect of his left index finger (Fig. 1). Initial first aid had included a pressure dressing around the wrist. The patient was a known asthmatic who used inhalers, but was otherwise well. He had no previous history of snake bites or allergies.

On arrival, he was found to be lucid (Glasgow coma score 15), with normal vital signs, except for a tachycardia of 124 beats.min⁻¹. His initial complaint was of a feeling of 'dizziness'. On examination there were double punc-

ture marks to the lateral aspect of his left index finger between its mid and distal phalanges. The index finger was swollen. There were superficial glass lacerations, sustained coincidentally, to his middle finger.

Within 10 min of arrival, he developed bilateral eyelid ptosis. Cranial nerve dysfunction is an early manifestation of envenomation after king cobra snake bite, so further problems were anticipated [1]. Intravenous access was obtained, routine bloods were taken and 1000 ml saline 0.9% was given. Toxbase and the Liverpool School of Tropical Medicine were contacted for further advice, and the specific antivenom was urgently ordered from Guy's and St Thomas's Hospital Poisons Unit in London. Treatment of the affected limb included pressure bandaging of the entire limb to the shoulder, to prevent lymphatic drainage of large molecular weight toxins proximally whilst still maintaining arterial flow [2].

Within 30 min of arrival, the patient complained of shortness of breath and was unable to swallow saliva. Therefore, following pre-oxygenation, the patient's trachea was intubated after a rapid sequence induction with 150 mg propofol and 100 mg suxamethonium. He received 10 mg vecuronium once correct positioning of the tracheal tube was confirmed and was commenced on titrated infusions of 10 mg.ml⁻¹ propofol and 1 mg.ml⁻¹ morphine. Approximately 2 h after arrival he was transferred to the Intensive Care Unit (ICU), and invasive



Figure 1 Patient's left index finger showing snake bite.

arterial monitoring, large bore intravenous access and urinary and nasogastric catheters were placed. At this stage the patient had a normal electrocardiogram and chest X-ray and apart from neutrophilia, all blood tests were normal.

On the ICU, oxygenation and ventilation were adequate, but cardiovascular monitoring displayed developing hypertension with a systolic blood pressure of 200–220 mmHg. The pulse rate became erratic in the range of 45–85 beats.min⁻¹, although sinus rhythm was maintained. Six hours after the patient had been bitten, king cobra specific equine antivenom was delivered from London (20 vials of monospecific freeze-dried antivenom for *Ophiophagus hannah* envenomation; manufactured by Queen Saovbha Memorial Institute 1871 RAMA IV Road, Bangkok 10330, Thailand). This was reconstituted in 200 ml water for injections and made up to 500 ml with saline 0.9%, and infused at an initial rate of 2 ml.h⁻¹. After 15 min, with no adverse reactions, the infusion was increased to 999 ml.h⁻¹ to administer the full dose within 30 min as recommended by the manufacturer.

Five minutes after the change in infusion rate, the patient's blood pressure increased further, peaking at a systolic pressure of 250 mmHg. At this point labetalol in 10-mg boluses was given to a total of 30 mg. Shortly after this, two maculopapular spots developed on the patient's chest, and he was given 200 mg hydrocortisone, 10 mg chlorphenamine and 50 mg ranitidine intravenously. Within 10 min the rash became a florid urticarial reaction, eventually involving the whole chest, flanks and upper thighs. The patient developed severe bronchospasm (peak airway pressures 40–50 cmH₂O, achieving tidal volumes of only 300–350 ml) and arterial oxygen saturation measured by pulse oximetry dropped to 80% with an F_IO₂ of 1.0. Within 1 min of the fall in saturation, the systolic blood pressure fell to 80 mmHg. The antivenom infusion was stopped as anaphylaxis to the antivenom was felt probable.

Adrenaline was given intravenously in 10-µg boluses up to 100 µg, and an intravenous infusion was started at

0.1 µg.kg⁻¹.min⁻¹. A rapid bolus of 500 ml hydroxyethylstarch 6% was given and bronchodilators administered. Thirty-five minutes after the reaction to the antivenom had started, and with treatment for anaphylaxis continuing, the bronchospasm and hypotension had resolved, and the rash had virtually disappeared. After further advice from Liverpool, the antivenom infusion was recommenced at the slower rate of 100 ml.h⁻¹. An infusion of 200 mg hydrocortisone over 24 h was also started. Although the rash became visible again, no other serious reaction was noted. The antivenom infusion was completed 9.5 h after the bite. Shortly after this, the adrenaline infusion was stopped (after a total of 2 h), but the hydrocortisone infusion was continued.

Once the antivenom infusion had finished, the lymphatic pressure dressings were removed. When the sedation was reduced to allow assessment of neurological function, approximately 17 h after the bite, it became apparent that motor function had been regained. The patient was able to lift his head from the pillow, there was no ptosis, limb power was strong, tidal volumes were > 10 ml.kg⁻¹, and he had a good cough reflex. Residual sedation was stopped, and the patient's trachea was extubated. He was discharged to the care of the plastic surgeons 24 h after the bite, for continuing management of isolated ischaemia of the bitten finger.

Discussion

The king cobra (Fig. 2) lives in much of mainland India, southern China, Malaysia and the Philippines, and

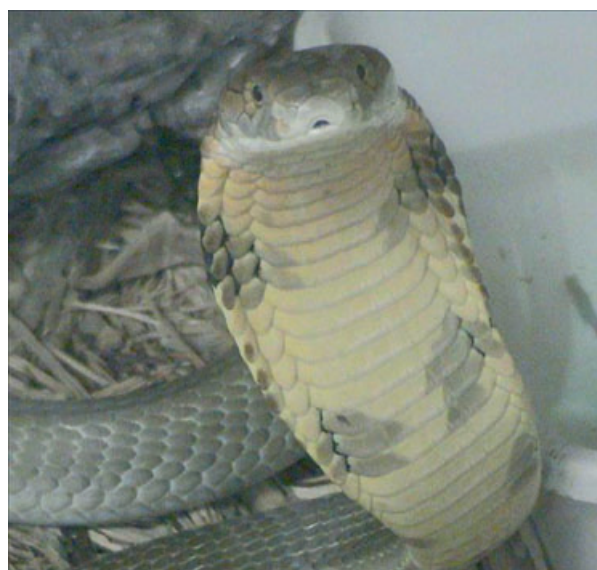


Figure 2 The king cobra *Ophiophagus hannah*.

throughout the dense highland forests of south-eastern Asia, but not Sri Lanka. In the mountainous regions of India, king cobras have been known to live in altitudes exceeding 2000 m (6500 ft) above sea level. The snake has a preference for living in areas dotted with lakes and streams and is an excellent swimmer. Although called a cobra it does not belong to the same genus (*Naja*) as 'true' cobras. The king cobra is peculiar in that it feeds almost exclusively on other snakes, reflected in its genus name of *Ophiophagus* (snake eater). The king cobra is known to attack larger snakes, including pythons. In spite of its fearsome reputation, the king cobra is generally a shy creature, avoiding confrontation with humans as much as possible.

Snake venom contains a variety of components which is species-dependent. These may include neurotoxins, myotoxins, cardiotoxins, haemolysins, anticoagulants and enzymes such as proteinases, phospholipases, hyaluronidase and kinin-releasing enzymes. The various toxins are predominantly large molecular weight proteins that, following a bite, are transported via the lymphatic system to the central circulation. In most elapid snakes the volume of venom injected is under voluntary control, leading to a variable degree of clinical effects following envenomation [3]. The main constituent of king cobra venom is a postsynaptic neurotoxin, and a single bite can deliver up to 400–500 mg of venom. The toxicity of venom is measured in terms of the lethal dose for mice, and the LD₅₀ for mice for king cobra venom is 1.91 mg.kg⁻¹, so that one bite may contain up to 15 000 LD₅₀ mice doses. In comparison, the world's most venomous snake, the Australian elapid small-scaled snake (*Oxyuranus microlepidotus*), can deliver up to 100 mg of venom with an LD₅₀ for mice of 0.01 mg.kg⁻¹, giving up to 500 000 LD₅₀ mice doses per bite [4].

In 1970–77, 17 people in Britain were victims of 32 bites by foreign venomous snakes [5]. *Crotalus atrox* (western diamondback rattlesnake) caused eight of these bites, *Bitis arietans* (puff adder) five, and the remaining 19 bites were caused by 12 different species. All the victims were bitten whilst handling the snakes and 24 bites were incurred by individuals in their own homes. Poisoning was negligible in 17 of bites, but life-threatening in at least two cases. Local necrosis developed in six cases, resulting in prolonged illness in five people.

In the western world where the private collection of venomous snakes has increased [6–8], envenomations also result from human interaction with cobras in zoos and research laboratories. In one paper from the USA covering the period 1977–95 [9], 54 consultations regarding bites by venomous snakes not native to the USA were summarised. At least 29 non-native snake species were involved, with cobras making up 40% of

the group. There was one fatality. A high percentage of venomous snake bites in the United States involve deliberate interaction with snakes. King cobra bites are considered more serious than bites from other cobra species because of the greater volumes of injected venom and the more rapid onset of neurotoxic symptoms. However, even in the USA, bites from king cobras are rare [1, 8]. An earlier series from the USA reported that cobras inflicted 18 out of 85 bites by non-native snakes [10]. Comparable figures are unavailable for other nations, although it has been reported that only three cobra bites among 32 bites inflicted by non-native venomous snakes occurred in Britain [5] (rattlesnakes were most often implicated in this series).

Comprehensive stocks of antivenoms for treating bites by foreign venomous snakes are held by the National Health Services in Liverpool and London. Antivenom is generally indicated in two situations:

- 1 for potentially serious systemic poisoning, as evidenced by hypotension, electrocardiographic changes, neutrophilia, and acidosis (after viper or elapid bites); abnormal bleeding or non-clotting blood after viper bites; and ptosis or glossopharyngeal palsy after elapid bites;
- 2 for bites from snakes whose venom causes local necrosis, to prevent or minimise complications [5].

For effective antivenom treatment, intravenous infusion is required.

Antivenom is produced using horse serum, with resultant antigenic problems that result in a high incidence of adverse reactions. Antivenom may be 'specific' – that is, acting against one specific snake venom – or 'polyvalent', usually containing antivenom to a number of different venomous snakes indigenous to a particular region. When the species of the offending snake is known (as in this case), specific antivenom should be used as there is a greater incidence of adverse reactions to antivenom when polyvalent antivenom is used [11, 12]. The aim of treatment with antivenom is to neutralise all circulating venom and all venom that will reach the circulation. The dose depends on the amount of venom present, and if, after administering antivenom, there are still signs of progressive envenomation, more antivenom must be given.

The prophylactic use of hydrocortisone and antihistamines before infusion of antivenom serum to reduce the occurrence or severity of allergic reactions has been recommended [13]. However, antihistamines counter only the effects of histamine release and hydrocortisone takes time to act. In the development of acute adverse reaction following antivenom administration, their use is therefore of limited immediate benefit. Adrenaline is the drug of choice in anaphylaxis and a role has been proposed in preventing reactions to antivenom serum.

There is evidence from both retrospective studies [12] and a well controlled double-blinded randomised placebo study [13] that the subcutaneous administration of 0.25 ml adrenaline 1 : 1000 immediately before injection of antivenom reduces the incidence of adverse reactions from ~40% to 10% without additional adverse effects attributable to adrenaline.

Our patient did not receive antihistamines, steroids or adrenaline as pretreatment. Treatment with adrenaline before administering the antivenom was not appropriate as the patient was hypertensive and requiring labetalol. Pretreatment with adrenaline has been questioned in snake bite victims because of the risk of coagulopathy with certain snake envenomations that, with adrenaline-induced hypertension, could result in fatal haemorrhage. However, of seven cases of fatal intracerebral haemorrhage after snake bite documented in Australia, only three had received adrenaline pretreatment [14], and in a study by Heilborn et al. [15] eight patients receiving 0.5 mg adrenaline administered in this way showed only transient increases in systolic blood pressure, while diastolic blood pressure fell.

We feel that several important aspects are raised by our case. Firstly, the number of exotic non-native and venomous snakes kept in private collections in the United Kingdom is increasing. The availability of specific antivenom is limited and takes time to arrive, emphasising the need for early intervention – in our case, tracheal intubation and ventilation to combat the effects of the neurotoxin. Secondly, although experience in the UK is limited, there are experts available 24 h a day for advice and logistical help with antivenom acquisition and administration (for example, The National Poisons Information Service (0870–600 6266) and Toxbase (www.spib.axl.co.uk)). This help is essential and must be sought early. Finally, this is one of the few situations where, despite the development of severe anaphylaxis to an intravenous infusion, the antigenic agent should be recommenced to complete the treatment once stability has returned and appropriate safeguards have been taken.

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