Naja Kaouthia: two cases of Asiatic cobra envenomations.

Gautam Khandelwal

Kenneth D. Katz MD
Lehigh Valley Health Network, kenneth_d.katz@lvhn.org

Daniel E Brooks

Stephanie M Gonzalez

Colleen D Ulishney

Published In/Presented At

Khandelwal G, Katz KD, Brooks DE, Gonzalez SM, Ulishney CD. Naja Kaouthia: two cases of Asiatic cobra envenomations. J Emerg Med. 2007 Feb;32(2):171-4. doi: 10.1016/j.jemermed.2006.05.047. Epub 2007 Jan 17.

The Journal of Emergency Medicine, Vol. 32, No. 2, pp. 171–174, 2007

0736-4679/07 $–see front matter

ELSEVIER

doi:10.1016/j.jemermed.2006.05.047

Selected Topics: Toxicology

NAJA KAOUTHIA: TWO CASES OF ASIATIC COBRA ENVENOMATIONS

Gautam Khandelwal, MD,* Kenneth D. Katz, MD,*†‡ Daniel E. Brooks, MD,*†‡ Stephanie M. Gonzalez, MD,* and Colleen D. Ulishney, CSPI‡

*Department of Emergency Medicine, †Division of Medical Toxicology, University of Pittsburgh Medical Center, Presbyterian Hospital, and ‡Pittsburgh Poison Center, Pittsburgh, Pennsylvania

Reprint Address: Kenneth D. Katz, MD, UPMC Presbyterian, 200 Lothrop Street, Suite D-L45, Pittsburgh, PA 15213

□ **Abstract—Envenomation from cobra bites causes major morbidity and mortality in Asia and Africa but rarely in the United States. We describe two patients bitten by the Asiatic Cobra (*Naja Kaouthia*)—both successfully treated in the emergency department. Patient 1 was a 23-year-old woman bitten in the buttock by her cobra. Examination demonstrated two puncture wounds. She developed cranial neuropathy, respiratory failure, and coagulopathy 10 h later, necessitating endotracheal intubation and polyvalent antivenom administration. The patient recovered fully with minimal wound necrosis. Patient 2, a 44-year-old man, was bitten on the hand by his cobra. Examination revealed a puncture wound with progressive swelling. Edrophonium and monovalent antivenom were administered, and he recovered uneventfully. These cases emphasize the varied clinical presentations of the Asiatic cobra. Patient 1 developed delayed neurotoxicity, respiratory failure, and hematotoxicity with minimal wound necrosis, whereas Patient 2 experienced a more typical clinical course. © 2007 Elsevier Inc.**

□ **Keywords—*Naja Kaouthia*; envenomation; antivenom; neurotoxicity; necrosis**

INTRODUCTION

There are over 7000 poisonous snakebites in the United States each year, most involving the *Crotalidae* family, which includes rattlesnakes, copperheads, and water moccasins (1). Envenomations by members of the *Elapidae* genera, including the cobra, are a major cause of morbidity and mortality in Asia and Africa but rarely encountered in the United States. The few cases of cobra bites reported in the United States are secondary to human interaction with snakes at zoos, research laboratories, and private collections (1).

We describe two patients bitten by the Asiatic cobra (*Naja kaouthia*), both of whom were treated successfully by our Medical Toxicology service in the Emergency Department (ED). In addition, the clinical presentations encompassed a broad range of signs and symptoms, some atypical for cobra envenomation.

CASE REPORTS

Case 1

A 23-year-old woman without medical history presented to the ED approximately 3 h after being bitten in the left buttock by her pet Asiatic cobra. The patient had consumed alcohol and was feeding the snake when the bite occurred. The patient had never been envenomated nor received antivenom. At initial presentation the patient had no complaints. Her vital signs revealed a heart rate (HR) of 110 beats/min, blood pressure (BP) of 149/80 mm Hg, respiratory rate (RR) of 16 breaths/min, oral temperature of 37°C, and pulse oximetry of 98% on room air. Physical examination revealed an alert woman

Selected Topics: Toxicology is coordinated by *Kenneth Kulig*, MD, of Denver, Colorado

RECEIVED: 30 March 2005; FINAL SUBMISSION RECEIVED: 26 September 2005;
ACCEPTED: 9 May 2006

in no acute distress. Notable findings were two non-tender, 1-mm punctate lesions on the upper left buttock with minimal erythema.

Initial laboratory studies obtained approximately 2 h after presentation revealed the following: white blood cell (WBC) count 9.7 K/mm^3 (3.8–10.6), hemoglobin (HGB) 14.9 g/dL (12–16), platelet count (PLT) 246 K/mm^3 (156–369), creatinine (CR) 0.6 mg/dL (0.7–1.5), partial thrombin time (PTT) 33.8 s (24–33), prothrombin time (PT) 11.4 s (10–13), and international normal ratio (INR) 1.0. While the patient was waiting for intensive care unit (ICU) placement, 17 vials of South African Institute of Medical Research (SAIMR) polyvalent snake antivenom were procured from another city's zoo via fixed-wing transport.

The patient remained hemodynamically stable without complaint until approximately 10 h after the cobra bite, when the patient suddenly developed progressive ptosis, dysarthria, dysphagia, and upper extremity weakness. Rapid sequence intubation was performed and the patient was placed on mechanical ventilation. She received 25 mg of intravenous hydroxyzine, an epinephrine drip was readied at the bedside and then one ampule (10 mL) of SAIMR antivenom was administered over 10 mins. Nine additional vials of antivenom (90 mL) were subsequently added to 250 mL Normal Saline Solution (NSS) and administered at a rate of 50 mL/h. The patient tolerated the antivenom infusion without incident.

Approximately 12 h after the development of neurological symptoms, the patient was alert and following commands with a normal physical examination. Abnormal laboratory studies approximately 17 h after the initial blood work included the following: WBC 29.0 K/mm^3, PT 19.6 s, INR 1.5, and PLT 71.0 K/mm^3. The patient was extubated the following morning and transferred to a monitored floor. The WBC count increased to a peak of 35.9 K/mm^3 on hospital day 2 and eventually declined to 16.3 K/mm^3 on the day of discharge. There was no clinical evidence of infection. The PLT count reached a nadir of 52 K/mm^3 on hospital day 3. The PT normalized on hospital day 3 to 10.6 s. The HGB count remained normal throughout her hospital stay. Other abnormal studies included a D-dimer $>$ 1000 ng/mL (68–494), fibrin degradation products $>$ 20 μg/mL (normally undetectable), thrombin time of 33.4 s (16–22) and reptilase time of 27.1 s (15–22) on hospital day 2. The patient never demonstrated signs or symptoms of bleeding. Serial examinations of the wound revealed a minimally tender, quarter-sized area of necrosis. The patient did not require any further antivenom and was discharged in good condition on hospital day 3. The patient remained well, without evidence of serum sickness or other sequelae with follow-up at 1, 2 and 3 weeks. Her wound was clinically inconsequential and required no debridement.

Case 2

A 44-year-old male snake-breeder with a past medical history significant for prior rattlesnake envenomation requiring antivenom and fasciotomy, presented to the ED approximately 1 h after being bitten on the left hand by an Asiatic cobra. The patient stated that he transiently felt dizzy, experiencing numbness in the extremities immediately after the bite, but that these symptoms had resolved before arrival. At presentation the patient complained of pain in the left hand; vital signs were normal. Physical examination was significant only for a small puncture wound on the dorsum of the left hand's first web space, without edema or necrosis.

An intravenous (i.v.) line was established. *Naja kaouthia*-specific monovalent antivenom (Queen Saovabha Memorial Institute [QSMI]) was procured from an outside facility. Initial laboratory studies obtained approximately 2 h after presentation were: WBC 15.3 K/mm^3, HGB 14 g/dL, PLT 207 K/mm^3, CR 0.9 mg/dL, PTT 29.6 s, PT 11.6 s, and INR 1.0. On re-examination 1 h later, there was increased edema at the bite-site measuring approximately 2 cm. He was initially treated with 30 mg of pyridostigmine orally, and subsequently received five vials of QSMI antivenom (diluted in 500 mL of NSS) over 1 h due to progressive wound pain and edema. The patient developed a 5-mm hive on the left side of the neck during antivenom infusion and was given 50 mg of diphenhydramine orally. The patient tolerated the infusion without further incident, and was subsequently transferred to the ICU.

The patient recovered well while in the hospital and demonstrated no neurotoxicity or wound necrosis. Repeat studies on hospital day 2 were: WBC 6.0 K/mm^3, HGB 13.3 g/dL, PLT 202 K/mm^3, PTT 30.5 s, PT 12.1 s, and INR 1.1. The patient was discharged on hospital day 2, and remained asymptomatic without evidence of serum sickness or deterioration at follow-up in 1 week.

DISCUSSION

Cobra venom is composed of many proteins that exert neurotoxic, cardiotoxic, and hemotoxic properties (1). In most cases the neurotoxic effects are most prominent and are caused by postsynaptic motor end plate blockade of acetylcholine receptors, an effect similar to that seen in curare poisoning (2). This prevents nerves from stimulating muscle contraction and leads to paralysis (3). Cobra envenomation typically presents with cranial nerve

palsies manifested by ptosis, opthalmoplegia, dysphagia and dysarthria. This is often followed by increasing somnolence and confusion, flaccid paralysis, and finally, respiratory compromise and coma (4).

Cardiotoxicity after cobra envenomation is uncommon. In one series of 46 patients envenomated by cobras in India, four patients developed hypotension and cardiac arrest (5). The proposed mechanism of action involves altered calcium transport across cellular membranes, leading to conduction disturbances (1).

The hemotoxicity of cobra venom arises from multiple proteins (including hemolysin, proteases and Hyaluronidase) that are thought to activate the complement system and lead to the consumption of clotting factors. Furthermore, these agents produce enzymatic destruction of endothelium and connective tissue and are responsible for local tissue necrosis.

The mainstay of treatment for cobra envenomation is aggressive supportive care (mechanical ventilation and hemodynamic support) and the administration of antivenom. Indications for the use of antivenom include systemic manifestations of envenomation such as the development of neurotoxicity or cardiotoxicity (1). Isolated edema or necrosis at the bite site is not considered an indication for antivenom, but it should be available in case of systemic toxicity (6). The few reported successful treatments of cobra-induced neurotoxicity indicated that 10 vials (100 mL) of antivenom were adequate for reversal of the symptoms (2,6). One study also suggested that patients who received 100 mL of antivenom had a significantly decreased duration on a mechanical ventilator as compared to patients who received 50 mL (2). Because cobra venom acts at post-synaptic neuromuscular receptors, cholinesterase inhibitors such as neostigmine and edrophonium also have been used successfully to treat the neurotoxic effects (4,7). However, their effects are short-lived and are not expected to maintain clinical stability in the event of progressive neurotoxicity.

Our first patient's case is unique for several reasons, including: delayed onset of neurotoxicity, transient thrombocytopenia, minimal wound necrosis, and the successful use of polyvalent antivenom. She manifested neurotoxicity approximately 10 h after being envenomated, in contrast to a case series of three patients who developed neurologic symptoms from 3 min to 4 h after *Naja kaouthia* envenomation (8). Other studies have reported the mean time of neurotoxic effects occur from 1 to 6 h after a cobra envenomation (1,4).

Our hypothesis for the delayed onset of neurotoxicity in this case is related to the location of the bite. Unlike a bite on the extremities leading to almost immediate venom deposition in the systemic circulation, our patient was bitten in the buttock, which has a relatively greater volume of adipose tissue. This may have led to slower systemic absorption of the venom and delayed onset of neurotoxicity.

The patient also demonstrated thrombocytopenia and coagulopathy, with a decrease in platelet concentration from 246 to 52 K/mm^3, and an increased PT to 19.6 s. Even though the patient failed to develop bleeding complications, no other case of cobra envenomation describes this phenomenon.

Finally, this is the first reported successful use of a polyvalent antivenom for the acute treatment of a *Naja kaouthia* envenomation. The results, however, were expected based on experiences with the use of other species' polyvant antivenoms. CroFab, derived from snakes of the *Crotalidae* family, has been used successfully for treatment of envenomations from other species. Similarly, Wyeth product, another polyvalent antivenom, works against species whose venom is not used in the manufacturing process. Successful use of polyvalent antivenom has also been demonstrated in scorpion and black widow (*Latrodectus mactans*) spider bites. In a review of scorpion bites in Saudi Arabia, a polyvalent antivenom was used to treat envenomation in pediatric patients (9). Furthermore, there are several equine-derived *Latrodectus* antivenoms, each targeted against one species' venom. In the United States, the antivenom is targeted against *L. mactans*, yet it is effective in treating envenomation from all North American species (10). The presence of the common, active venom component (alpha-latrotoxin) in all species allows for clinically useful cross-neutralization of venoms between different species, even those from different continents (11–13).

Our second cobra victim had a relatively more common presentation of a localized wound, which progressed during ED observation. Although not an absolute indication for antivenom administration, it was felt that because there was clinical evidence of envenomation, neurotoxicity might develop. Physostigmine was given to the second patient as a precaution to bridge the time gap so that antivenom could be prepared and eventually administered. However, the patient never demonstrated neurotoxicity.

Information about antivenoms and recommendations for treatment can be obtained by contacting your regional poison control center (800-222-1222). Poison centers and major zoos maintain the *Antivenom Index* (14), a catalog published by The American Zoo and Aquarium Association, which outlines the antivenoms available for treatment of both exotic and native snake bites.

CONCLUSION

We present our experience with two *Naja kaouthia*-envenomated patients who presented with significantly

different clinical courses despite being envenomated by the same species. The patients developed neurologic symptoms but responded well to supportive care and use of both species-specific and polyvalent antivenoms.

REFERENCES

1. Britt A, Burkhart K. *Naja naja* cobra bite. Am J Emerg Med 1997;15:529–31.
2. Pochanugool C, Limthongkul S, Wilde H. Management of Thai cobra bites with a single bolus of antivenin. Wilderness Environ Med 1997;8:20–3.
3. Nedergaard OA. Curare: the flying death. Pharmacol Toxicol 2003; 92:15–5.
4. Gold BS, Pyle P. Successful treatment of neurotoxic king cobra envenomation in Myrtle Beach, South Carolina. Ann Emerg Med 1998;32:736–8.
5. Stueven H, Aprahamian C, Thompson B, Horwitz L, Darin J. Cobra envenomation: an uncommon emergency. Ann Emerg Med 1983;12:636–8.
6. Gold BS. Neostigmine for the treatment of neurotoxicity following envenomation by the Asiatic cobra. Ann Emerg Med 1996;28: 87–9.
7. Watt G, Meade BD, Theakston RD, Padre LP, Tuazon ML. Comparison of Tensilon and antivenom for the treatment of cobra-bite paralysis. Trans R Soc Trop Med Hyg 1989;83:570–3.
8. Bernheim A, Lorenzetti E, Licht A, Markwalder K, Schneemann M. Three cases of severe neurotoxicity after cobra bite (*Naja kaouthia*). Swiss Med Wkly 2001;131:227–8.
9. El Aminn EO, Berair R. Scorpion stings in children. Saudi Arabia experience. Arch Pediatr 1995;2:766–73.
10. Isbister G, Graudins A, White J, Warrell D. Antivenom treatment in arachnidism. J Toxicol Clin Toxicol 2003;41:291–300.
11. Daly F, Hill R, Bogdan G, Dart R. Neutralization of *latrodectus mactans* and *L. hesperus* venom by redback spider (*L. hasseltii*) antivenom. J Toxicol Clin Toxicol 2001;39:119–23.
12. Graudins A, Padula M, Broady K, Nicholson G. Red-back spider (l*atrodectus hasseltii*) antivenom prevents the toxicity of widow spider venoms. Ann Emerg Med 2001;37:154–60.
13. Wiener S. Red back spider antivenene. Med J Aust 1961;48:41–4.
14. Boyer DM, ed. Antivenom Index, 1999 Revision. The American Zoo and the American Association of Poison Control Centers, 1999.