ORIGINAL ARTICLE

Five-year experience with Chinese cobra (*Naja atra*)–related injuries in two acute hospitals in Hong Kong

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Objective To review the clinical features and management of patients with injuries related to the Chinese cobra (*Naja atra*).

Design Retrospective study.

Setting Two acute hospitals in Hong Kong.

Main outcome measures The nature of injuries, envenoming features, complications, response to antivenom therapy, and outcome.

Results Eighteen patients were recruited during the 5-year study period. Fifteen of them were snake-bitten, the remaining three suffered ocular injuries. Of the 15 patients with cobra bites, 14 (93%) presented with local swelling. No patient developed severe neurotoxic symptoms. Two patients had laboratory features of haemolysis. Fourteen patients received antivenom therapy and five of them subsequently underwent surgical interventions for extensive local tissue damage and necrosis. There was no fatality.

Conclusion Bites from Chinese cobra result in serious local complications with extensive tissue necrosis and minimal neurotoxic symptoms. There is an apparent trend of favourable outcomes following the early administration of antivenom to patients without early signs of irreversible tissue damage. Further research is needed to evaluate the effectiveness of early antivenom use in Chinese cobra bites in order to minimise extent of tissue damage.

Introduction

Snake envenomation is not an uncommon medical emergency in Hong Kong. Little information about local cobra (*Naja atra*) envenomation has been reported however. Only three local cases could be found in the literature.[1,2] Two of these were described incidentally in a case series about the bamboo snake (*Cryptelytrops albolabris*), which is responsible for 95% of snake envenomations in this region. Both patients had local symptoms, one of whom developed skin necrosis treated by repeated debridement and a skin graft.[1] The third case entailed a fatal *N atra* bite in another case series.[2] The patient developed compartment syndrome over his injured limb complicated by extensive skin necrosis and necrotising fasciitis. The cause of his death was septicaemia complicated with acute renal failure, thrombocytopenia, and coagulopathy. Although cobra bites in Hong Kong are seldom fatal, such envenomations cause many deaths in the agricultural areas of some South Asian countries.[3] Envenomation syndromes due to cobras in Asia vary depending on locality. Researchers reported region-specific clinical presentations due to Asiatic cobra species ranging from potentially fatal neurotoxicity but with minimal local symptoms, to extensive local tissue necrosis without neurotoxicity.[4-6] We report here the clinical presentation and management of patients with *N atra*–related injuries seen in our institutions during the past 5 years. In particular we set out to document the liability to complications from Chinese cobra bites (including neurotoxic symptoms and local tissue necrosis) encountered locally in comparison to envenomation due to other Asiatic cobra species.

Key words
Antivenins; Cobra venoms; Emergency treatment; Necrosis; Snake bites

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Methods

Patients

The study was conducted in the accident and emergency departments (AEDs) of Tuen Mun Hospital and Pok Oi Hospital. These are the two acute hospitals located in non-urban areas of Hong Kong with a significant burden of snake-bite incidents. All patients who attended the two hospitals for Chinese cobra–related injuries from 1 April 2004 to 31 March 2009 were included.

TABLE 1. Frequency of patients presenting with cobra bites

	No. of patient injuries
According to month	
January	0
February	0
March	1
April	1
May	1
June	0
July	1
August	6
September	2
October	4
November	2
December	0
According to time of injury	
0000-0559	1
0600-1159	5
1200-1759	8
1800-2359	4
According to body part involved	
Upper limb	5
Lower limb	10
Eye	3
According to location	
Indoors	8
Outdoors	10

香港兩間急症醫院處理與眼鏡蛇有關的受傷病例的五年經驗

目的 探討與眼鏡蛇有關的受傷病例，其臨床症狀與處理方法。

設計 回顧研究。

安排 香港兩間急症醫院。

主要結果測量 受傷類別、毒液特徵、併發、對抗毒治療的反應及結果。

結果 研究期間共有18位病人，其中15位被蛇咬傷，其餘3位被蛇的毒液傷及眼部。15位被眼鏡蛇咬傷的病人中，14位（93%）的傷口出現腫脹。病人均沒有嚴重的神經中毒症狀，兩位病人的檢驗結果顯示有溶血。14位病人接受抗毒治療，其中5位最終須進行手術以治療擴大性的傷口組織受損及壞死。沒有死亡案例。

結論 被眼鏡蛇咬傷的病人會引致嚴重的傷口組織併發，繼而有擴大性的組織壞死，及出現輕微的神經中毒症狀。縱使病人未有出現不能逆轉的組織受損，盡早使用抗毒治療有明顯較好的治療結果。需要進一步研究及早使用抗毒治療是否可以減低被眼鏡蛇咬傷的組織受損程度。

Snake identification

The species of snake was confirmed by examination of the specimen (dead or alive), opinion sought from local experts (ie advice from the Kadoorie Farm and Botanical Gardens), identification by the patient with the snake photo handbook, or the combination of typical clinical features and patients' descriptions of the appearance of the snakes.

Evaluation

For each incident, demographic data, its timing and location, interval between injury and arrival at the AED (bite-to-door time), envenoming symptoms, local complications, antivenom therapy (number of vials and bite-to-needle time) and response, any surgical intervention, and length of hospital stay were retrieved from the clinical records.

Results

During the study period, there were a total of 18 confirmed cases of *N atra*–related injuries. For six incidents, the dead snake specimen was available for identification. Ten patients were able to identify the snakes to be Chinese cobra clearly, using the snake photo handbook. Two others were bitten by snakes of similar appearance and developed typical clinical features of Chinese cobra–bite poisoning. On the other hand, four patients with suspected Chinese cobra injuries were excluded, because their wounds lacked typical clinical features, despite the Chinese cobra having been described or identified by the respective patients.

Time of occurrence and mode of injuries

Among the confirmed cases, 15 endured cobra bites, whilst three suffered ocular injuries from cobra-venom spat into their eyes. One patient was bitten by a cobra in mainland China, but all the others were local cases. Of the 18 incidents, 14 (78%) occurred in the summer and early autumn period (between August and November), 13 (72%) ensued in the daytime (06:00-17:59), and eight (44%) occurred indoors. Most of the cobra bites involved the lower limbs (Table 1). All but two patients arrived at the hospital within 2 hours of presentation.

Local and systemic complications from cobra bites

Eleven of the 15 patients with cobra bites complained of paraesthesia over the wounds and in three of them, the paraesthesias progressed over the entire forearm

TABLE 2. Clinical features of patients with *Naja atra* bites

Patient No.	Sex/age (years)	Injured area	Neurotoxicity‡	Initial local symptom§	Bite-to-needle time (hours)
Without surgical intervention					
1*	M/34	Right ankle	+	P, E	3
2	F/44	Right little finger	++	-	3
3	F/44	Left foot	+	S, E	4
4	F/44	Right thumb	++	P, E	6
5	M/51	Right thumb	++	P, E	3
6	F/67	Right thumb	+	S, E	3
7	F/20	Left 5th toe	+	S, E	7
8	M/44	Right 3rd toe	+	S, E	12
9	M/48	Right thumb	-	S, E	2
10	F/9	Left foot	-	P, E	4
With surgical intervention					
11	F/78	Right 4th toe	-	S, E	2
12	M/58	Left ankle	-	P, E	25
13	F/26	Left 5th toe	+	S, E	1
14	F/84	Left ankle	+	S, B	2
15†	M/59	Right leg	+	S, B, N	-

* This patient was discharged against medical advice and the outcome was unknown
† No antivenoms therapy because of delayed presentation
‡ Neurotoxicity: + = paraesthesia over bitten area, ++ = progressive paraesthesia of the affected limb
§ Extension of swelling: P = pain without obvious swelling, S = extensive swelling well beyond the bitten area; local skin condition: E = erythema, B = bruising or discolouration of skin; N = necrosis

although the bite was on the fingers and thumb. No patient developed severe neurotoxic symptoms (limb weakness, respiratory muscle paralysis, or apnoea), but on presentation two had gastro-intestinal symptoms (including nausea and vomiting). Of the 15 patients, 14 presented with swelling over bitten areas (Table 2), around half of whom (6/14) developed necrosis over the injured area and five were treated by debridement (Table 3). Three patients treated by debridement received a skin graft or skin flap for wound repair due to the extensive area involved. Two patients developed laboratory features of haemolysis with a reduction in haemoglobin (Hb) level, elevated blood bilirubin and lactate dehydrogenase (LDH) levels. One patient developed a coagulopathy associated with the wound infection. Electrocardiograms (ECG) performed on 13 patients revealed no obvious abnormalities. Moreover, none of the 15 patients developed cardiovascular instability (hypotension or bradycardia), and there was no mortality.

Antivenom therapy and clinical outcome

The antivenom we used was manufactured by the Shanghai Institute of Biological Products and each vial contained 1000 IU. The recommended dose on the product insert for Chinese cobra bite was 2000 IU, but the indications were not clearly documented. Fourteen of the 15 patients with cobra bites were given antivenom. Local pain and swelling were the indications we adopted for antivenom in 13 patients. The remaining patient (case 2) had progressive paraesthesia over her injured limb; her symptoms improved soon after the administration of antivenom. The median time lag to antivenom administration after the snakebites was 3 hours (range, 1-25 hours). Treatment was discontinued once there was cessation of progressive swelling or neurotoxic symptoms. The number of vials given ranged from 1 to 21. In our patients, no allergic reaction or adverse effect was encountered after using antivenom. All patients with cobra bites were frequently reassessed (every 2 to 4 hours). The decision to administer additional antivenom doses was made by individual emergency physicians, based on the perceived clinical response to treatment. The timing of repeated antivenom doses ranged from 2 to 12 hours, depending on the perceived progress of symptoms and availability of antivenom.

Patients who recovered without tissue necrosis received at least two vials of antivenom. For patient 6

TABLE 3. Details pertaining to patients having surgical interventions

Case No.	Operations	Extension of necrosis (depth)	Bacterial growth	Length of stay (days)
11	Repeated debridement x 3 + skin graft	3rd, 4th and 5th toe, to lateral malleolus (subcutaneous tissue)	*Klebsiella* spp, *Acinetobacter* spp, *Enterobacter* spp, *Enterococcus* spp, and *Peptostreptococcus*	3+22*
12	Debridement + skin flap and graft	Anterolateral aspect of distal 1/3 of leg to lateral dorsum of foot (subcutaneous tissue)	*Enterococcus* spp	31
13	Repeated debridement x 2 + skin graft	Extended to dorsum of foot (subcutaneous tissue)	*Enterococcus* spp and *Clostridium perfringens*	29
14	Bedside debridement under local anaesthesia x 4	Lateral aspect of foot (subcutaneous tissue)	*Enterococcus* spp and *Acinetobacter* spp	6+7+64*
15	Bedside debridement under local anaesthesia†	Shin (subcutaneous tissue)	*Acinetobacter* spp	3

* Repeated admission for wound care
† Debridement on follow-up

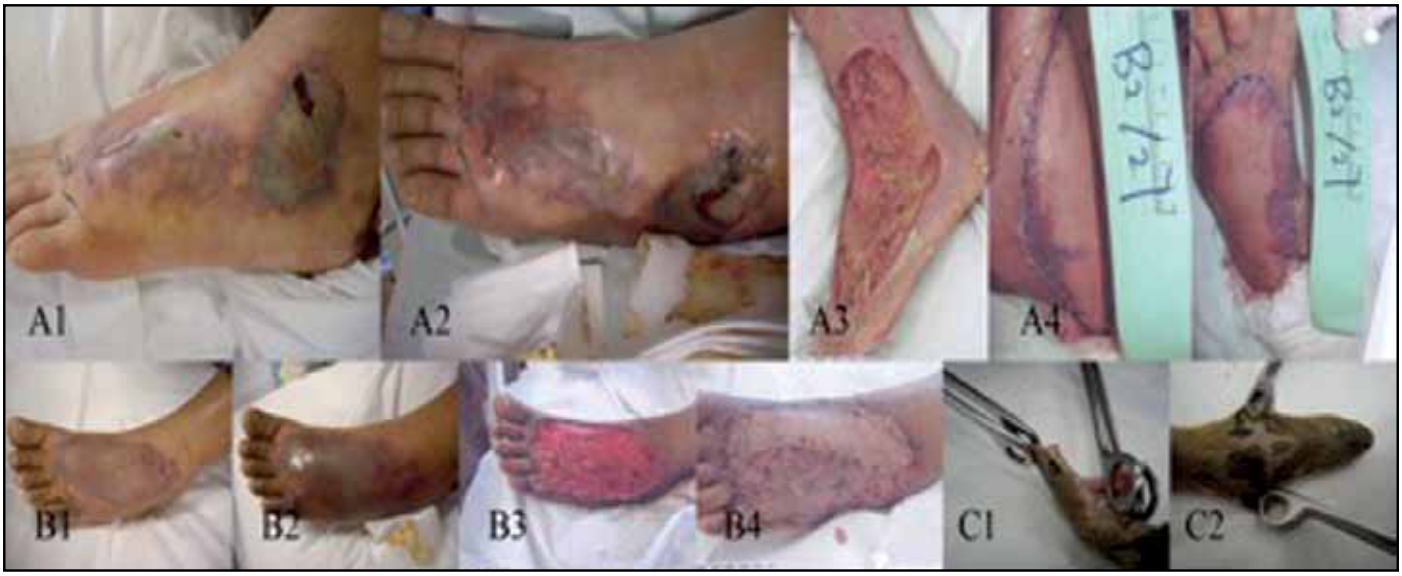

FIG 1. Clinical photos of local complications in two patients after *Naja atra* bites and photos of a dead specimen of *N atra*
(A1 to A4) Extensive tissue necrosis involving the dorsum of left foot after cobra bite over the left ankle of patient 12 with subsequent debridement and skin flap performed
(B1 to B4): Skin necrosis involving the whole dorsum of the left foot of the patient in patient 13 after cobra bite over the fifth toe. Debridement of necrotic skin and skin graft was done
(C1 to C2): A dead specimen of a *N atra* with the fangs and hood shown

with a cobra bite over her right thumb and progressive swelling across the wrist, 21 vials of antivenom were used in total. The local swelling subsequently subsided, and was followed by only a small area of necrosis, which healed without surgical interventions. The outcome of patient 1 was unknown, as he was discharged against medical advice.

Five patients developed extensive tissue necrosis treated by surgical interventions. Among these, patient 15 did not receive antivenom due to delayed presentation (22 hours post-injury) and tissue necrosis at presentation. The other four each received 1 to 18 vials of antivenom therapy (Table 3).

In patient 12, administration of antivenom was delayed due to difficulty in snake identification. Further enquiries about the snake's appearance and review of the clinical features confirmed the *N atra* bite. The first dose of antivenom was therefore given 25 hours post-injury. Although the swelling ceased progressing after 12 vials of antivenom, the local skin condition deteriorated and extensive tissue necrosis ensued, despite administration of a total of 18 vials (Fig 1).

Patients 11, 13, and 14 developed extensive tissue necrosis for which surgical interventions were carried out, although their antivenom therapy was started within 4 hours of injury (Tables 2 and 3). Patient 11 had cobra bite over her right fourth toe and was admitted into medical ward for further management after one vial of antivenom given in the AED. There was no obvious progression of swelling during her stay in medical ward. She was subsequently discharged on day 3. However, extensive swelling was noticed when the patient was followed up in the out-patient clinic on day 10 post-injury. She was admitted into the orthopaedic ward for further management.

Patient 13 presented with a cobra bite on her left little toe. The contents of two vials of antivenom were given about 1 hour after envenomation. The patient had progressive pain and swelling across her left ankle during reassessment. Another six vials of antivenom were used 13 hours post-injury, but with no improvement. Subsequently, skin necrosis developed despite a total of 20 vials antivenom being used (Fig 1).

Patient 14 presented with swelling and dark discolouration of the wound 1 hour after a cobra bite over her left ankle. A total of six vials of antivenom were given. Despite the apparent cessation of the progression of swelling, blisters formed that were subsequently followed by ulceration and necrosis, for which repeated surgical debridement was performed. Very likely due to her prolonged immobilisation, she stayed in the orthopaedic ward for around 2 months for rehabilitation.

Length of stay

Most of the patients with cobra bites (11/15) had short hospital stays (1-4 days). Four patients (6, 12, 13, and 14) had repeated admissions or a prolonged stay for wound care (Table 3).

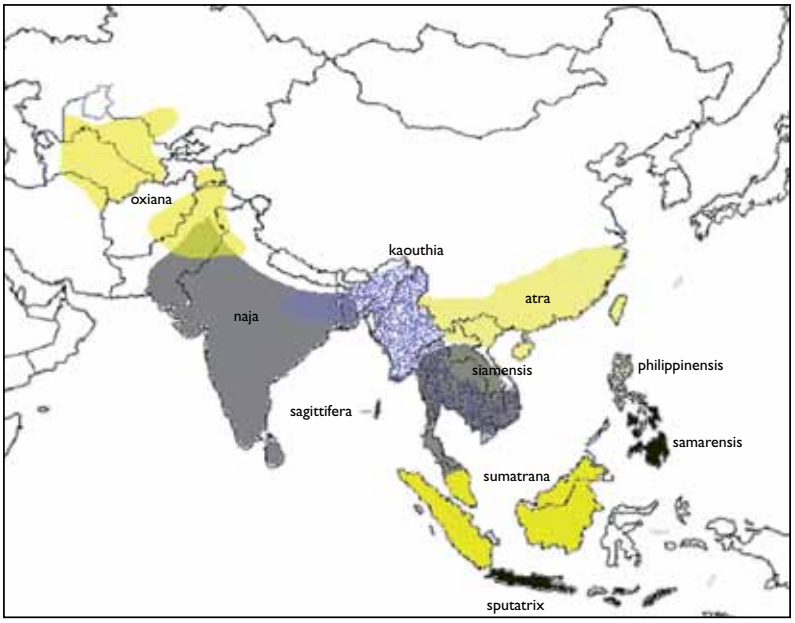

FIG 2. Geographic distribution of Asiatic cobras[9]

Discussion

Time of occurrence

The seasonal distribution (mainly in summer and early autumn) of cobra-related injuries in our study had a similar pattern to that described in a previous local epidemiological study on snake bites.[7] The Chinese cobra is active day and night.[8] However, the majority of incidents in our series happened during daylight. The cobra bite incidents were not related to any particular type of human activity.

Overview of the medical significance of Chinese cobra and other Asiatic cobra species

The Chinese cobra (*N atra*), also known as Formosa Island cobra, is a native of Hong Kong that also inhabits Northern Laos, northern Vietnam, southern China, and Taiwan (Fig 2[9]). In Taiwan, over the years *N atra* has caused significant injuries (even neuromuscular junction blockade resulting in severe neurotoxicity) and deaths.[10,11] Apart from *N atra*, most other Asiatic cobras are also considered to be medically important, often biting humans and giving rise to significant morbidity and mortality, especially in South Asia.[12] In the past, all Asiatic cobra populations were regarded as a single species, *N naja*. However, there is much diversity among cobras inhabiting different parts of Asia in terms of morphology, and most importantly, venom composition. Recent revisions of the taxonomy of Asiatic cobras based on an analysis of their morphological characters,[13] combined with the mitochondrial DNA sequence of their evolutionary lineages, have revealed the existence of at least 10 distinct species of Asiatic *Naja* (Fig 2).[9] Their bites in general cause local and neurological complications, but difference in venom composition accounts for geographical variations in clinical features following cobra bites (Table 4[4,6,11,14]). Apparently, bites from the same cobra species in different regions may also present differently.[15] Cobra venoms comprise a complex mixture of enzymatic and non-enzymatic proteins, peptides, and other organic compounds. Analysis of the proteomic profile of *N atra* venom showed that cardiotoxins, neurotoxins, haemotoxins, and phospholipase A_2 contributed 68%, 11%, 3%, and 15% of the proteins, respectively.[16] In addition to the common local and neurological effects of cobra venom exposure, cardiovascular and haematological disturbance may ensue.

Neurotoxicity

The neurotoxin (the primary lethal component in cobra venom) blocks acetylcholine receptors in the postsynaptic regions of motor end plates without affecting the release of acetylcholine in presynaptic terminals.[17] Phospholipase A_2 in cobra venom was shown to have additional neuromuscular blocking activity in vitro.[18] The clinical manifestations of neurotoxicity include: ptosis, ophthalmoplegia, dysphagia, flaccid paralysis, respiratory paralysis, and coma.[19] A Taiwan study on *N atra* bites reported neurotoxicity with muscle weakness in 15% (4/27) of the patients.[11] However, in our series profound

TABLE 4. Geographical variation of clinical features following Asiatic cobra bites

Cobra species	Cases with neurotoxic symptoms	Cases with necrosis	Ratio of neurotoxicity to local tissue necrosis
Malayan cobra (*Naja naja leucodira* and *Naja naja kaouthia**)[4]	13% (6/47)	43% (20/47)	1:3.6
Philippine cobra (*Naja philippinensis*)[6]	97% (38/39)	8% (3/39)	12.6:1
Thai cobra (*Naja kaouthia*)[14]	31% (14/45) prospective study; 13% (5/40) retrospective study	91% (41/45) prospective study; 65% (26/40) retrospective study	1:3.5 (overall)
Chinese cobra (*Naja atra*) in Taiwan[11]	15% (4/27)	30% (8/27)	1:2
Chinese cobra (*Naja atra*) in Hong Kong (*present study*)	20% (3/15)†	40% (6/15)	1:2

* New names: *Naja sumatrana* and *Naja kaouthia*
† Only three patients presented with progressive paresthesia over the injured limbs and there was no neurotoxic paralysis with systemic muscle weakness

neurotoxicity after bites by *N atra* was not encountered. Antivenom therapy and respiratory support are the mainstay for treating neuromuscular paralysis.[20] In addition, neostigmine has been successfully used to overcome neuromuscular blockade after Asiatic cobra bites.[19]

Cardiotoxicity

The cardiotoxic effect (systolic cardiac arrest) due to cobra venom was discovered following experiments entailing perfusing the hearts of the frogs and toads with the whole cobra venom and venom-derived fractions. The action of cardiotoxins on the heart was subsequently found to depend on the properties of an intact cell membrane and this explains their diverse local and systemic actions.[21] Reid[4] reported significant ECG changes (ST segment depression and T wave changes) in a patient after a cobra bite. Sinus node dysfunction manifesting as a marked atrioventricular junctional escape rhythm and left bundle branch block after a cobra bite has also been reported.[22] Cardiovascular instability is more prone to occur in patients with hypoxia and acidosis secondary to respiratory paralysis. The absence of respiratory paralysis may have contributed to the cardiovascular stability of our cases.

Haemolysis

Animal studies have demonstrated that the venom from *N atra* has significant haemolytic activity,[23] including a synergistic effect of the cardiotoxin with phospholipidase A_2.[23,24] An in-vitro study revealed that the cardiotoxin from *N atra* venom caused disintegration of the membrane structure of human erythrocytes, which potentiates the hydrolysis of phospholipids in the membrane by the phospholipase A_2.[25] Reid[4] reported three cases of haemolysis, with a 30 to 40 g/L decrease of Hb level, in 47 patients bitten by *Naja sumatrana* and *Naja kaouthia*. In our study, patients 12 and 18 developed features of haemolysis with decreases in Hb concentration (by 25 and 7 g/L, respectively), and increases of both bilirubin and LDH levels.

Coagulopathy

Venoms from African cobra species cause impairment of haemostasis. In-vitro study of venoms from *Naja melanoleuca* and *Naja nigricollis* showed an anticoagulant effect due to digestion of the fibrinogen and an inhibitory effect on platelet aggregation.[26] Warell et al[27] reported spontaneous haemorrhage in three patients after *N nigricollis* bites, one of whom died of subarachnoid haemorrhage. In several large studies on Asiatic cobra bites, no significant coagulopathy was reported.[4,14,28] Patient 12 in our series developed disseminated intravascular coagulopathy secondary to wound infection; his international normalised ratio increased to 1.4 on day 9 after the injury. Therefore, the coagulopathy could have been a complication of the wound, rather than the direct effect of cobra venom.

Local tissue necrosis

Cobra venoms cause extensive local tissue destruction, mainly due to the effect of cytotoxins and myotoxic phospholipase A_2, while the local effects from viper bites are mainly due to haemorrhagic metalloproteinases, which are also responsible for the haemorrhagic syndrome after such envenomation.[29] Metalloproteinase has not been identified in the *N atra* venom.[16] Animal studies show that tissue damage occurs as early as 5 minutes after intradermal injection of *N nigricollis*.[30] Histopathological study on *N atra* bite wounds in humans revealed focal necrosis within the epidermis with thrombosis and fibrinoid deposits in the superficial and deep dermal vessels, as well as features of leukocytoclastic vasculitis.[31] The extensive local tissue damage from cobra venom is believed to result from the direct cytotoxic effects, with ischaemia secondary to vascular change of the dermal vessels and subsequent bacterial infection. Extensive areas of dark discolouration over the wounds in our patients probably indicate local tissue ischaemia that could be an early sign of irreversible tissue damage.

In contrast to viper bites that cause deep tissue damage, local tissue damage due to cobra bites is generally superficial and limited to the skin and subcutaneous tissue.[28] Our series demonstrated that Chinese cobra envenomation caused necrosis involving skin and subcutaneous tissue, with sparing of the muscle layer. The depth and extension of tissue involvement probably depend on the depth to which venom is injected. The cobra has short fangs so that the venom is injected in the subcutaneous layer and rarely causes extensive muscle damage.

Ocular injury (cobra venom ophthalmia)

The spitting behaviour of cobra is a defensive mechanism. Ocular injury from spitting of venom by *N atra* had been reported in Taiwan.[10] The spitting ability is related to fang modification, by which constriction of the discharge orifice enables the spitting behaviour.[32] Permanent blindness can result from delayed management of ocular injuries caused by cobra venom. Ocular exposure of venom from *N nigricollis* causes corneal ulcers, diffuse superficial keratitis, and globe perforation.[33] Prompt irrigation with copious amount of water should be started at the scene as soon as possible. Any benefit for ocular injuries from cobra venom following local antivenom therapy currently remains unproven. One patient received diluted antivenom over the injured eye due

to persistent pain; her symptoms improved with the treatment. All three of our patients recovered without any serious ocular complications.

Bacterial infection

A study from Hong Kong showed the presence of multiple pathogenic bacteria in the oral cavity of *N atra*, including *Morganella morganii* and *Enterococcus faecalis*, which play an important role in the wound complications from cobra bites.[34] Notably, *Enterococcus* and *Acinetobacter* species were commonly found in the wounds of our patients (Table 3).

Antivenom therapy for local tissue damage

According to clinical experience from overseas, antivenom is not effective in the management of local complications of cobra bites; notably local tissue damage is not believed to be reversed by such treatment.[35] In their study on the use of a single bolus of antivenom in patients with Thai cobra (*N kaouthia* and *Naja siamensis*) bites causing respiratory failure, Pochanugool et al[20] showed no positive correlation between the severity of necrosis and the quantity of antivenom administered. However, local complications were not the targeted outcome in their study, and important factors affecting the response to antivenom (initial condition of the wound, bite-to-needle time) were not mentioned. Warrell et al[27] reported 14 cases of *N nigricollis* bites in which eight patients developed necrosis around the bite site despite receiving antivenom in doses of up to 80 mL. However, all the patients presented to the respective hospitals after a delay; their bite-to-admission time ranged from 6 to 24 hours. Delayed administration could be the major cause of antivenom ineffectiveness in preventing local tissue necrosis.

An animal study showed that tissue necrosis developed within 1 hour of intracutaneous *N atra* venom injection.[36] Early intravenous administration of antivenom (within 30 minutes) was shown to reduce the area of damage from cobra venom in mice.[37] A pharmacokinetic study of the cytotoxin from *N atra* venom in rabbits demonstrated that it had a strong local tissue–binding affinity, evident as incomplete systemic absorption after intramuscular injection of the cytotoxin.[38] The early administration of an adequate dose of antivenom may theoretically minimise the extent of local tissue damage by neutralising the cobra venom in the local tissues and control the destructive effects of the cytotoxin. In our patients, an apparently favourable trend on local (skin) clinical outcomes was demonstrated in patients who had received adequate doses of antivenom early. The effective dose of antivenom for the prevention of tissue necrosis was not clearly defined in our series of patients, but a minimum of two vials was used in patients with favourable clinical outcomes. Late dosing of antivenom (after more than 24 hours) did not prevent skin necrosis. In patients who underwent extensive surgery, a high venom load combined with delayed and/or inadequate antivenom dosing (patients 11, 12, and 13) may well have hindered tissue salvage. Moreover, patient co-morbidity may also affect such outcomes. Thus, patient 14 had diabetes mellitus and subsequently developed extensive skin necrosis despite early administration of antivenom. Medical illnesses that impair the peripheral circulation could well affect the distribution of antivenom in the affected area as well as the innate ability of compromised tissues to recover.

In our series, although extensive skin necrosis only occurred in the lower limbs, the relationship between the injured parts of body and clinical outcome was not clearly defined, as other factors, including the presenting skin condition and the timing and dosing of antivenom, appeared important. We look forward to a further study focusing on early use of antivenom after cobra bites, to evaluate possible improvement at the site of injury, minimisation of tissue necrosis, and avoidance of destructive surgical interventions. This strategy appears justified, as none of our patients developed anaphylaxis or delayed serum sickness even after very large doses (up to 21 vials), and according to other local experience with snake antivenom, allergic reactions are uncommon.[39]

Although early signs of skin necrosis—skin discolouration and blister formation—developed in the first 3 days after envenomation in most of the patients, delayed necrosis also seemed to occur (patient 11). Follow-up assessment is needed after 1 week, even if the progression of swelling appears well-controlled following initial antivenom therapy.

Limitations

The sample size of our series of cobra bites was small, which precluded the use of precise statistical evaluation. The highly variable venom loads could also confound the prediction of clinical outcomes from cobra bites, and cause difficulty in evaluating the response to antivenom therapy in individual patients.

Conclusion

Envenoming by *N atra* in Hong Kong may cause serious local complications. Our study showed a trend towards better local outcomes associated with early antivenom use (within 12 hours). Further study is needed to confirm or refute this possibility. If confirmed, it is also necessary to determine the optimal dose and effective timing of such therapy following cobra bites, with a view to minimising the development of local tissue necrosis and prevent the need for surgical interventions.

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