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Case Report

Acute neuromuscular paralysis, rhabdomyolysis and long lasting neurological deficits in Ceylon krait (*Bungarus ceylonicus*) bites: Two authentic cases from a serpentarium in Sri Lanka

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ABSTRACT

The Ceylon krait (*Bungarus ceylonicus*) is a highly venomous elapid snake endemic to Sri Lanka. Its bites are rare and only seven reports are found in the literature. Therefore, the clinical manifestations and natural history of envenoming of Ceylon krait are not well studied yet. Neuroparalysis is the main clinical manifestation of their bites. We report two cases of proven Ceylon krait bites of two young snake keepers working in a serpentarium. They developed acute neuroparalysis, abdominal pain and a period of amnesia. The first patient developed myalgia and increased level of serum creatine kinase suggestive of rhabdomyolysis. One was treated with Indian polyvalent antivenom and both recovered with some long-lasting clinical disabilities namely impairment of sensation of the bitten arm and persistent refraction errors in the eyes in the first patient. The second patient had persistent marked nystagmus.

1. Introduction

The Ceylon krait, *Bungarus ceylonicus* (Gunther, 1864), is endemic to Sri Lanka, highly venomous and mainly confined to the wet zone of the island. It is a relative of banded kraits having a distinct colouration of alternating white and black bands crossing both dorsal and ventral sides of the body. This snake is different to the common krait (*Bungarus caeruleus*, Schneider, 1801) which inhabits the dry zone of Sri Lanka causing frequent bites (De Silva, 1992; Kularatne, 2002). Ceylon krait bites, on the other hand, are uncommon and publications of authentic bites are few in number in the literature (Green, 1908; De Silva, 1979, 1987 De Silva et al., 1993; De Silva and Perera, 1987; Namal Rathnayaka et al., 2017Dalugama and Gawarammana, 2017). There is no antivenom raised against its venom and the current Indian antivenom used in Sri Lanka is ineffective against it. To address this issue the University of Peradeniya has established a serpentarium for the purpose of developing an antivenom specific to the Sri Lankan species of highly venomous snakes, with the approval of the Department of Wildlife Conservation of Sri Lanka. The snakes in the serpentarium are cared for by an experienced senior world-renowned herpetologist and two young keepers. The proposed polyvalent antivenom is being produced against the venoms of the cobra (*Naja naja*), Russell's viper (*Daboia russelii*), saw scaled viper (*Echis carinatus*), hump-nosed pit viper (*Hypnale spp.*) and the common krait (*Bungarus caeruleus*). The Ceylon krait is not included in the antivenom development for the time being as collecting Ceylon kraits is extremely difficult; it is a rare wild snake and human encounter is uncommon. However, two live Ceylon kraits mistakenly identified as common kraits when collected were found in the serpentarium. These two Ceylon kraits are slender and small in size (Figs. 2 and 3). Ceylon kraits have the potential to grow bigger, as reported by de Silva and Perera, 1987, who recorded a male Ceylon krait measuring 1349 mm in length from Hakgala in the central hills of Sri Lanka. The two snakes in the serpentarium were fed and cared for by two young keepers. Probably due to careless handling of these snakes, both were bitten by them on two separate occasions about a year apart. These two young men had significant envenoming and

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Fig. 1. Neuroparalytic features of case 1 patient.

were treated in the University hospital a few kilometres away. It is commonly understood that the authenticity of most Ceylon krait bites is questionable due to its nocturnal behaviour, un-witnessed night bites and rare occurrence. As a result, the clinical manifestations and natural history of envenoming by the Ceylon krait have not been well studied and documented. As it is an endemic species, there is no international literature as well. This report attempts to overcome this deficit by closely monitoring these two patients during their hospital stay and subsequent follow up. After recovery from envenoming they were followed up for long term effects.

2. Case reports

2.1. Case 1 (clinical details and follow up of 7 months)

A 22-year-old snake keeper with three years experience of working in a serpentarium decided to clean the box where a Ceylon krait was kept in captivity as his routine work at 0830 h on 12th July 2018. He opened the cover of the transparent plastic box and replaced the water in the container. At that time, he observed that the occupant Ceylon krait crept behind the log inside the cage and he did not pay much attention to its movements. Without disturbing the snake he attempted to close the cover of the cage, but the snake got entrapped between the cover and the brim of the box. Noticing what happened, he lifted the cover, but in a flash the snake bit his left index finger and retracted back into the box. He closed the cover and saw the snake gliding back under the log. There was a drop of blood on his finger along with pain. Within minutes, his finger felt benumbed and pain ascended gradually along the medial side of the left upper arm up to the axilla where he developed painful lymph nodes. He also felt a vague discomfort in the left side of the face. In half an hour, he re-examined the box and found that the snake was alive. At 0930 h, he was admitted to the Teaching Hospital, Peradeniya where clinical examination on admission was unremarkable except his subjective symptoms of pain and numbness.

Two hours after the snakebite at 1000 h, he developed lower abdominal pain and discomfort. At about 1200 noon he found difficulty in speaking and also drooping of the eyelids (Fig. 1).

At about 1300 h, he was admitted to the Intensive Care Unit (ICU) for observation. At that time single fibre electromyography (EMG), nerve conduction studies and repetitive nerve stimulation tests were done. Stimulated single fibre EMG studies of orbicularis oculi muscle after stimulating facial nerve using monopolar needle electrode showed normal jitter with abnormal fibres less than the upper limit of normality. Facial nerve conduction showed normal latency and amplitude of compound motor action potentials recorded from frontalis, nasalis and orbicularis oris muscles. Repetitive nerve stimulation of the facial nerve showed no decremental response recorded from the orbicularis oculi muscle.

At about 1400 h, he felt discomfort in the throat and difficulty in swallowing. He had to spit out saliva as he was unable to swallow. The abdominal pain persisted and he had generalized muscle pains. As symptoms such as difficulty in walking and drooping of the eye lids persisted, he was confined to bed and an indwelling urinary catheter was inserted for monitoring urine output. Later, he could not remember the catheterization. He maintained respiration without assisted ventilation, but needed 40% oxygen via a venturi mask to maintain oxygen saturation. His radial pulse rate was 92 beats per min, regular and blood pressure was 130/90 mmHg. His parents visited him at 1700 h of the same day, but he could not recall their visit when questioned later after full recovery. His mind became cloudy and could not remember anything that happened more than 24 hours from that afternoon.

The next morning at 0900 h, 24 h after the bite, he was rousable, recognized people, but looked drowsy. He complained of muscle pains and was unable to open his eyes fully due to near complete ptosis. He had full external opthalmoplegia and facial muscle weakness. He was unable to open the mouth and just made little movements of the tongue. He was unable to move the lower limbs at all but was able to make little movements of the fingers of hands. He was unable to lift his head up from the pillow. He had all his sensory modalities intact. The respiratory rate was 30 breaths per min and peripheral oxygen saturation (SpO_2) was 95%. His pupils were 4mm in size and reacted to light. He had tender muscles on palpation and passed normal amounts of urine through the indwelling urinary catheter. The urine was of alight brownish colour.

The next 24 h was uneventful and at 0800 h on 14th July, he showed marked improvement of neuromuscular functions. He was able to open his eyes and had only mild ptosis. Pupil size was 3mm and reacted to light. External opthalmoplegia was minimal and the mouth opening was full. He was able to do palatal movements and gag reflex was present. He lifted his head up and was able to sit up and moved all four limbs (power grade 4). He had muscle tenderness and passed dark brown coloured urine. He was hungry and oral sips of water commenced. On the same day in the afternoon, he started taking soup and water. The next morning he had normal muscle power and did not have muscle tenderness. As he had rising serum creatine kinase (CK), he was kept under observation and released from the hospital on the 16th (4 days after the bite). Despite recovery, the bitten finger remained benumbed. Sensory testing showed impaired pain and touch sensation of the finger that extended in an approximately 2 cm wide strip along the posterior forearm up to the elbow. He was re-examined one month later and found to have impaired sensation in the same distribution. Recovery of this sensory disability took about three months. Additionally, he experienced visual problems from the 18th after going to his parent's residence. From time to time he developed lateral deviation of both eyes resulting in double vision where he saw the road dividing into two. Resolution occurred when the eyes were kept shut for a while. This phenomenon lasted for 10 days and he developed refraction errors in the eyes that required spectacles for correction. However, he resumed his previous job of snake handling three weeks after the incident. He was strongly advised to handle snakes with care and caution.

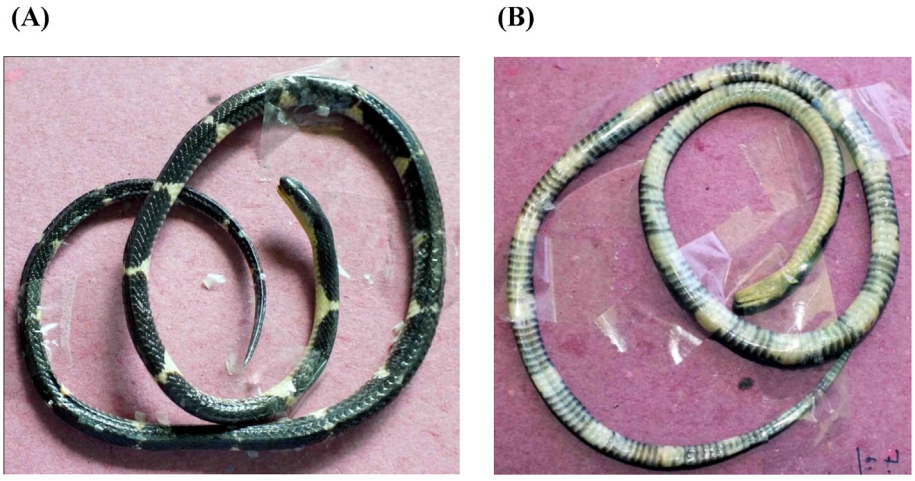

Fig. 2. Preserved specimen responsible for bite in case 1 patient-Ceylon krait, a female snake from Peradeniya (7°16′N 80°36′E) (A) dorsal view - Note that the vertebral scales are polygonal and larger than the costal scales, which is the characteristic feature of kraits (*B.ceylonicus* and *B. caeruleus*), distinguishing them from other similar non-venomous snakes. (B) ventral view- Note that the alternating white and black bands cross both dorsal and ventral sides of the body.

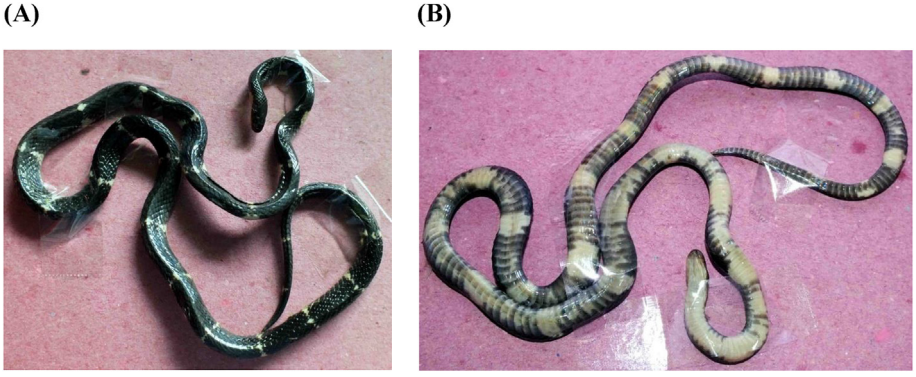

Fig. 3. Ceylon krait, a female snake from Peradeniya (7°16′N 80°36′E)-the snake responsible for bite in case 2 patient (A) dorsal view (B) ventral view.

Table 1
Laboratory findings of case 1 patient.

Investigation	Reference range	Day from the snakebite			
		1	2	3	4
WBC (x10^3/μL)	4–11	8	11	9	
Neutrophils (x10^3/μL)	2–7	6 (76%)	9 (86%)	7 (79%)	
Lymphocytes (x10^3/μL)	0.8–4	1 (11%)	0.8 (7%)	1 (11%)	
Platelets (x10^3/μL)	150–450	223	256	225	
RBC (x10^6/μL)	4–6	5.9	6	5.4	
Hb (g/dL)	11–16	16.4	16.9	15.1	
PCV (%)	37–54	50	51	46	
MCV (fL)	80–100	86	85	85	
PT (sec.)	10–15	12/12			10.4/12
INR	1–1.4	1			0.86
Na^+ (mmol/L)	135–145	135	135	133	133
K^+(mmol/L)	3.5–4.5	4.2	3.6	3.6	3.8
Blood urea (mmol/L)		3.4		2.6	3.6
Creatinine (μmol/L)	60–115	70		68	60
SGOT (AST) [U/l]	0–35	24			36
SGPT (ALT) [U/l]	0–45	15			14
Albumin (g/L)	36–48		47		
CRP (mg/L)	< 6			7	
CPK (U/L)	26–174		448	1360	1454
Corrected Calcium (mmol/L)	2.1–2.55		2.59		
Urinary myoglobin	None			Negative	
pH	7.35–7.4				7.412
Pco_2 (mmHg)	35–40				36
Po_2 (mmHg)	100				94
Lactate (mmol/L)	1–1.5				0.7
HCO_3^-(mmol/L)	24				23.5

During the hospital stay, the patient did not develop coagulopathy and all clotting tests including 20 min whole blood clotting test were normal. As there was no specific antivenom for Ceylon krait bite, he was not given the available polyvalent Indian antivenom and it was decided to give only supportive treatment. Dark discolouration of urine persisted only for three days. A urine sample was tested for myoglobin in a private laboratory and it was negative. He had rising creatine kinase which got normalized later (Table 1).

On the same day of the bite, at noon, the senior herpetologist opened the cage of the offending Ceylon krait and found the snake dead. He examined the dead snake and found no injuries and its fangs were intact. The patient strongly denied killing the snake. The death of the snake remains a mystery and the specimen was preserved. The preserved snake is a small Ceylon krait, a female with snout to vent length of 490 mm and tail length of 65 mm (Fig. 2).

Five months after the incident, he was reassessed and it was found that he needs spectacles to correct the refractive errors. Cranial nerve examination was normal including optic fundi. He had normal sensation in the limbs. He underwent brainstem evoked potential testing that did not detect any delay suggestive of permanent brainstem dysfunction. He continues to wear spectacles.

2.2. Case 2

(follow up of 18 months and permanent neurological deficits and epidemiology).

The acute clinical picture and management of this patient have already been published (Dalugama and Gawarammana, 2017) and this report highlights only missing epidemiological data of the previous publication and details of the close follow up of the patient during the ensuing 18 months while he was working in the same serpentarium of

the University of Peradeniya. The patient was 26-years old when he was bitten by a relatively bigger Ceylon krait in captivity in August 2017 in the same serpentarium as in the first case. The bite happened due to careless handling of the snake in the serpentarium where he worked as a keeper of snakes. The snake bit the finger web of 2nd and 3rd fingers of right hand at about 1400 h. Initially, he ignored the bite, but developed abdominal pain a few hours later and got admitted to the hospital at about 1900 h. He had developed moderate neuromuscular paralysis that reversed in three days with preserved respiratory capacity. He had been treated with Indian polyvalent antivenom which has no cover for Ceylon krait. He had loss of memory for about 18 hours during the peak muscle paralysis period where he could not recall details after full recovery. After full recovery of muscle power, he had found difficulty in reading and focusing the eyes. Examination revealed marked nystagmus in both eyes in all directions, but mostly in horizontal movements. During the first three months, nystagmus was more marked and he had to tilt his head to overcome the visual difficulty when doing his job in the serpentarium. But with time, the severity of nystagmus reduced and was manageable enough to enable him to do his work. Even at the 18th month of follow up, nystagmus was persisting. He underwent visual and brain stem evoked potential investigation after 18 months and these were found to be normal. His visual acuity was normal. The offending Ceylon krait died later and the specimen was preserved. It is a female snake of snout to vent length of 674 mm and tail length of 75 mm (Fig. 3).

3. Discussion

In our patients, the bites were provocative due to careless handling of the snakes leading to significant envenoming. Both patients developed moderately severe neuromuscular paralysis, lasting about 48 hours, manageable without assisted ventilation. Onset of bulbar muscle weakness commenced about 5 hours following the bite. The first patient felt pain in the bitten finger with numbness of the arm and painful lymph nodes in the axilla. There was no local swelling. Further, he had muscle pain and passed dark brown urine with rising serum CK levels suggestive of rhabdomyolysis. Both patients reported development of abdominal pain a few hours after the bite. Interestingly, both patients could not recall events after the neuromuscular paralysis and were amnesic for close to 24 hours. Once acute envenoming was over, they had novel developments hither-to unknown. The first patients had persistent sensory impairment of the bitten arm for months and developed short lived visual phenomena and persistent refraction errors of the eyes. The second patient developed marked nystagmus which became less severe but persisting for more than 2 years to date. Their visual evoked potentials and visual acuity are normal. The first patient was not given Indian polyvalent antivenom knowing that it was effective only for common krait (*B. caeruleus*). However, the 2nd patient had been given the same antivenom with neither benefit nor reaction.

The two offending Ceylon kraits were females, 550 mm and 750 mm in total length. In comparison, the incriminated Ceylon krait of the fatal case published in 1993 was a male of 1050 mm in length (De Silva et al., 1993) and Namal Rathnayaka et al., 2017 reported an envenomed patient who had been bitten by a Ceylon krait of total length 405 mm (Namal Rathnayaka et al., 2017). Another report published in 1979 records the length of a Ceylon krait as 1153 mm from the central hills of Sri Lanka (De Silva, 1979). The Ceylon krait is regarded as an inoffensive snake and bites only under extreme provocation. When alarmed, it coils itself, hiding the head (De Silva, 1979). It may be that this behaviour of the snake that made our two victims to develop over confidence when handling them in the serpentarium resulting in the bites. In the local Sinhala language Ceylon krait is called "*Mudukarawala*" referring to the bands mimicking rings. This morphological feature makes it more similar to banded kraits of South East Asia particularly with *B. fasciatus* which also has circumferential black bands (Tun-Pe et al., 1997) and the Malayan krait (*B. candidus*) which has thick dorsal bands (Warrell et al., 1983).

Acute neuromuscular paralysis is the main manifestation in virtually all species of krait bite. However, depending on the species other manifestations have been reported. In a series of 42 patients with bites by the Malayan krait (*Bungarus candidus*) from Southern Viet Nam, other than neuromuscular paralysis, some patients had developed hypersalivation, hypertension, shock, hyponatreamia, high serum creatinine kinase suggestive of rhabdomyolysis and persistent mydriasis (Trinh et al., 2010). The first author has managed a 32 year-old military serviceman from Sri Lanka who developed severe respiratory failure after a bite by an unknown snake while sleeping in the jungle at night. He developed locked-in syndrome due to severe neuromuscular paralysis with rhabdomyolysis and had persistent mydriasis for years. This clinical picture is somewhat similar to *Bungarus candidus* envenoming (Kularatne unpublished report). However, Sri Lanka has only the Ceylon krait and the common krait, and of them the common krait (*B.caeruleus*) is known to cause severe neuromuscular paralysis and in some cases hypokalaemia, autonomic disturbances, anterograde memory loss and deep coma (Kularatne, 2002). Envenoming by the greater black krait (*Bungarus niger*), distributed in India, Nepal, Bhutan, Bangladesh and Burma causes neuro-myotoxic manifestations leading to severe rhabdomyolysis and even acute renal failure (Fais et al., 2010). In the back drop of the above knowledge, we found Ceylon krait envenoming causing diverse manifestations such as local pain, benumbed bitten area, lymphadenopathy, abdominal pain, memory loss, rhabdomyolysis during the acute stage and late residual clinical manifestations such as refractive errors and nystagmus. However, hyponatreamia and persistent mydriasis were absent in our patients. These clinical manifestations suggest that the Ceylon krait is more closely related to other South East Asian *Bungarus* species than its local counterpart the common krait (*B. caeruleus*). Furthermore, this assumption will be interesting in use of antivenom in Ceylon krait envenoming where Indian polyvalent antivenin which include *B. caeruleus* in its spectrum has no benefit as we observed in our case. Further, antivenom reactions are detrimental as reported in the fatal Ceylon krait bite in 1983 (De Silva et al., 1993). It will be intriguing to see whether antivenoms raised against South East Asian *Bungarus* species are effective in Ceylon krait envenoming.

The observed effects of envenoming by these Ceylon krait bites arouse curiosity to explain the pathophysiology of krait venom. It is proven beyond doubt that phospholipase A_2 is the main enzyme in the venom toxins that causes neuromuscular paralysis by binding to presynaptic nerve endings (Silva et al., 2016). Single fibre nerve conduction studies have shown this peripheral effect of venom toxins (Silva et al., 2016). Phospholipase A_2 can cause myolysis as well. However, further explanations and research are needed to explain the other diverse manifestations of krait venom. Even though some authorities may not agree, we have to revisit the pathophysiology of krait venom to see whether venom toxins have central cerebral effects, both acute and chronic.

These two cases highlight gradual development of neuromuscular paralysis in Ceylon krait envenoming and reversal in 48 hours. But in common krait bite, the onset of severe paralysis and its duration are highly variable (Kularatne, 2002). As Ceylon krait bites are rare, we have no idea about the full spectrum of envenoming as well as its relationship to the size of the snake. There are anecdotal accounts of fatal Ceylon krait bites in central Sri Lanka. In these two authentic cases, the severity of envenoming was moderate not requiring assisted ventilation. It is good to have an open mind as Ceylon krait bites could be fatal and are best managed at a setting with all facilities.

Consent

Written consent for publication of these case histories and photographs was obtained from the patients.

Authors' contributions

SAMK and AK involved in patients' management. ADS got the morphological features of snakes. VW involved in doing evoked potentials. RMMKNR involved in literature search. SAMK, ADS and RMMKNR drafted the first manuscript and wrote the case histories. All authors read and approved the final manuscript.

Declaration of competing interest

The authors declare that they have no competing interests.

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