

## Case report

# Severe Neurotoxic Envenoming and Cardiac Complications after the Bite of a 'Sind Krait' (*Bungarus cf. sindanus*) in Maharashtra, India

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**Abstract:** We report a case of severe envenoming with unusual complications and two anecdotal cases of fatalities following proven 17-scale-row 'Sind krait' (*Bungarus cf. sindanus*) bites on people sleeping in temporary huts at construction sites in Pune District, Maharashtra, India. A 25-yr-old male developed progressive neuromuscular paralysis, abdominal pain and autonomic disturbances complicated by four prolonged episodes of pulseless ventricular tachycardia requiring defibrillation, and followed by pulmonary edema secondary to impaired left ventricular systolic function and hyperfusion. There was no response to antivenom; mechanical ventilation was required for six days. Only one other case of fatal envenoming likely caused by this species had been reported previously in India. The distribution of *B. sindanus* sensu lato from eastern Afghanistan to India overlaps with that of the superficially very similar common krait (*Bungarus caeruleus*). Thus, *B. cf. sindanus* envenoming may be common but routinely overlooked or misdiagnosed.

**Key words:** envenoming, snake, *Bungarus cf. sindanus*, neurotoxic, antivenom, Maharashtra, India

## INTRODUCTION

Envenoming as a result of snake bites is a globally neglected disease and a major public health problem in South Asia [1–4]. While antivenoms manufactured by Indian companies have been available for 60 years, production has traditionally focused on only four species of venomous snakes regarded as medically significant: the common krait (*Bungarus caeruleus*), the spectacled cobra (*Naja naja*), Russell's viper (*Daboia russelii*), and the saw-scaled viper (*Echis carinatus*). Among these, *B. caeruleus* is well known for inflicting bites on sleeping people inside their homes and causing long-lasting severe neuromuscular paralysis with high mortality in the absence of significant local envenoming [1, 5].

*Bungarus caeruleus* has a wide distribution in South Asia but shares most of its range with other, superficially similar krait species regarding which reports of envenoming are rare or lacking [1, 6, 7]. One of these, the Sind krait (*Bungarus sindanus* sensu stricto) was first described more

than a century ago as a deadly snake much feared by locals in the Sind Desert [8], but was later regarded by taxonomists as a subspecies, synonym, or rare mutation of *B. caeruleus* and forgotten. Although the identity of *B. sindanus* as a distinct species of krait was reconfirmed and its distinctive morphological feature of having 17 dorsal scale rows (rather than 15 as in *B. caeruleus*) revalidated more than a quarter century ago [9], we know of no published reports of envenoming by this species except a fatal case that was very likely caused by this species in Indore, India, in 1908 [10]. Here, we report the clinical details of a case of severe envenoming and anecdotal data on two fatalities following proven *B. cf. sindanus* bites, identifying this species as an additional cause of fatal snake bite in India.

## CASE REPORT

A 25-yr-old previously healthy male was bitten by a snake on the right forearm in the middle of the night while sleeping in a hut at a construction site in Pimple Saudagar,

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Kalewadi, Chinchwad, Pune District, Maharashtra State, India, on 3 June 2005. He killed the snake and shortly after the bite experienced breathlessness, abdominal pain and sweating. He was admitted to a primary hospital and given 30 ml of polyvalent antivenom (of Indian production, manufacturer unknown, raised against the venoms of *B. caeruleus*, *N. naja*, *D. russelii*, and *E. carinatus*) by i.v. route 1.5 hr after the bite, preceded by unspecified steroids, and then referred to Lokmanya Hospital.

On admission 3 hr after the bite he was drowsy, obeying verbal commands but having difficulty opening his eyes, speaking, swallowing, and walking. Two fang marks were visible over the right elbow without any local swelling or inflammation. The patient appeared tachypnoeic and diaphoretic (pulse 120/min, respiration 36/min, blood pressure 140/80 mm Hg), had bilateral ptosis, dilated pupils (4 mm) not reacting to light, fasciculations, neck muscle weakness, and reduced limb power of grade 3/5 (able to move limbs but not against gravity, unable to lift hands). ECG on admission showed sinus tachycardia with 1 mm ST depression and T inversion in anterior chest leads. Laboratory investigations on admission revealed hypokalaemia ( $K^+$  3.0 mmol/l) and leucocyte counts ( $9000/cm^3$ ) in the upper normal range. The diagnosis of krait (*Bungarus*) bite envenoming was made based on the clinical syndrome of snake bite with neurotoxicity in the absence of local envenoming [5, 11] and was later confirmed in the ward by the inspection of genus-specific external features [12] of the dead snake brought by the patient's relatives.

The patient was given i.v. dexamethasone (100 mg), pheniramine maleate (45.5 mg) and s.c. adrenaline (0.2 ml, 1:1000) followed 3 hr 40 min after the bite by 100 ml of polyvalent antivenom (ASVS-Asia, Bharat Serums and Vaccines Ltd., Mumbai, India; batch no. 304) diluted with 500 ml of normal i.v. saline infusion. Atropine (0.6 mg i.v.) was also given 3 hr 40 min after the bite followed 10 min later by neostigmine (0.2 mg i.v.). Three additional doses of atropine and neostigmine were given in 15 min intervals. There was no response to the antivenom and anticholinesterase treatment as evaluated based on the progression of neurological signs of muscle paralysis. Ptosis worsened, there was progressive muscle weakness, deteriorating sensorium, and increased respiratory distress. The patient became unresponsive and was intubated and mechanically ventilated 5 hr after the bite. Under controlled ventilatory support, arterial blood gas values of the patient remained stable within normal ranges. Laboratory investigations 9 hr after the bite showed normal results except for slightly elevated levels of creatine kinase (CK-MB 34 U/L, CK-NAC 181 U/L; not assayed previously) in the absence of intramuscular injections. Additional i.v. doses of polyvalent an-

tivenom (20 ml in 100 ml saline over 1 hr) were given 2-hourly starting 9.5 hr after the bite up to a total of 390 ml (including antivenom received at the primary hospital) without signs of adverse reactions.

The patient continued to be unresponsive with tachycardia, sweating, lacrimation, hypertension and mydriasis. Fifteen hours after the bite he had four prolonged episodes of pulseless ventricular tachycardia requiring defibrillation. The ECG revealed 2 mm ST depression with T wave inversion in all leads. 2D-echocardiography showed generalized myocardial damage with impaired systolic function (approximate ejection fraction 40%). The patient had to be shocked three times (200 J, 320 J and 320J); 300 mg amiodarone was given as an i.v. bolus injection over 2 min after which a fourth shock (320 J) was required before reversion to sinus rhythm. Intravenous amiodarone infusion (900 mg in 500 ml of 5% dextrose) was continued over a period of 24 hr. Post-defibrillation (21 hr after the bite), creatine kinase (CK-NAC 9470 U/L, CK-MB 173 U/L) and lactate dehydrogenase (603 U/L) levels were elevated.

Immediately following this episode the patient was in hypotension (systolic blood pressure of 70–90 mm Hg) for 8 hr and developed pulmonary edema. His blood pressure was maintained with dopamine and dobutamine (5  $\mu$ g/kg/min i.v. each) which was tapered off without a fall in blood pressure, and he was ventilated with a high fraction of inspired oxygen and positive end-expiratory pressure over the next 48 hr. Pulmonary edema was diagnosed by excessive frothy secretions from the endotracheal tube, sudden increase in peak inspiratory pressure on ventilator settings, and fall in  $pO_2$ , and was confirmed by chest X-ray. It resolved with i.v. furosemide (40 mg initially followed by 20 mg 8-hourly); ventilation, X-ray resolution required 10 hr. Serial ECG recordings showed persisting ST depression and T wave inversion.

Over the following days the patient's muscle power gradually improved, the ptosis slowly subsided, and he became capable of communicating by writing on paper. He could be weaned off the ventilator and extubated on the 6th day of admission. The patient absconded from hospital on the 8th day with persisting mydriasis and proximal muscle weakness of the lower limbs. The snake that had caused the envenoming (Fig. 1D) was preserved and deposited in the herpetological collection of the Bombay Natural History Society (catalogue number BNHS 3401). Detailed morphological study revealed that it was an adult female 17-scale-row krait that keyed out to *B. cf. sindanus* (see below) and measured 885 mm in total length.

According to the taxonomic revision of Khan [13], *B. sindanus* comprises three subspecies, i.e., *B. sindanus razai* from rocky deserts of north-western Pakistan, *B. sindanus*

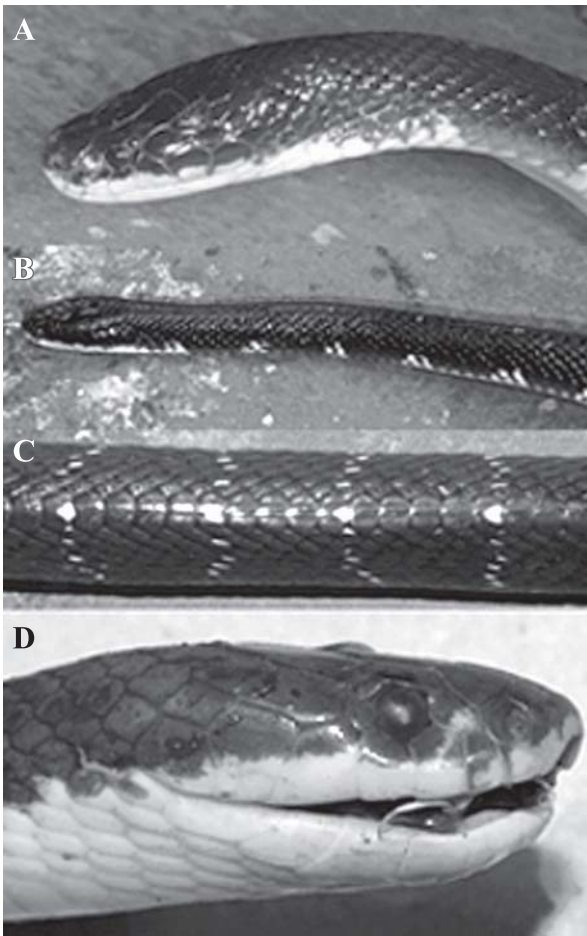


Fig. 1. **A–C**, Live adult ‘Sind kraits’ (*Bungarus cf. sindanus*) from Pune District, Maharashtra, India. **A**, Lateral view of the head and neck. **B**, Dorsolateral view of the head and anterior body. **C**, Dorsal view of the midbody showing the greatly enlarged mid-dorsal scales seen in all krait species except *Bungarus lividus*. Photos by Ashok Captain, specimens courtesy of Anil Kumar Khaire. **D**, Adult *Bungarus cf. sindanus* (885 mm total length) that caused the bite in case 1; lateral view of the head (specimen preserved in the herpetological collection of the Bombay Natural History Society; BNHS 3401). Photo by Ashok Captain. *Bungarus sindanus* sensu lato differs from its co-distributed congener *Bungarus caeruleus* (the common krait) in having 17 (vs. 15) rows of dorsal scales across the body.

*sindanus* from sandy deserts of Sind and Rajasthan, and *B. sindanus walli* from the Gangetic floodplains of South Asia. Following Khan’s [9, 13] concept, populations from western India east of Rajasthan belong to *B. s. walli* and they have consequently been assigned this name in the relevant literature [e.g., 12]. Molecular genetic studies in progress, however, suggest that at least some 17-scale-row kraits from Maharashtra are closely related to typical *B. s.*



Fig. 2. Persisting mydriasis following envenoming from the bite of a ‘Sind krait’ (*Bungarus cf. sindanus*) from Pune District, Maharashtra, India (case 1, bitten by specimen BNHS 3401), photographed two days after the bite. Fixed dilated pupils in paralyzed krait bite patients must not be misinterpreted as indicating brain death. Photo by Lalitha V. Pillai.

*sindanus* from the Sind Desert of Pakistan and highly distinct from *B. s. walli* (Kuch *et al.*, unpublished data). As we do not wish to exacerbate the taxonomic confusion that already exists, we refrain from assigning these snakes to any subspecific rank pending the completion of further molecular and morphological investigations. Instead, we provisionally refer to them as *Bungarus cf. sindanus*.

Previous to this case, an adult *B. cf. sindanus* was caught in 2002 by Pimpri Chinchwad Municipal Corporation (PCMC) Zoo staff at a construction site in Rahatni near Pimpri City (Pune District, Maharashtra State, India), where the snake had bitten a woman and her father in a temporary hut. The woman was brought to Yashwantrao Chavan M. H. Hospital where she died soon after arrival. Her father was drunk when he was bitten and not taken to hospital until he complained of stomach pain. In view of the death of his daughter, the family decided to bring him to a different hospital in Pune (Sassoon Hospital), but he also died.

Several additional *B. cf. sindanus* have been removed from different localities in Pune District by PCMC Zoo staff in response to nuisance reports during the late rainy season (August and September) in recent years. These snakes were all caught in or near houses (e.g., under construction materials) in seasonally wet areas that are very dry and sparsely vegetated during the rest of the year. In captivity, the behaviour of these snakes differed greatly from that of local *B. caeruleus*: While the latter preferred snakes as prey, the *B. cf. sindanus* refused snakes and instead envenomed and swallowed adult Swiss mice. Also, whereas the *B.*

*caeruleus* were usually timid by day and active at night, the *B. cf. sindanus* responded rapidly to movements even during the day and were quick to strike if disturbed. Similar behavioural differences were also observed between representatives of these two species from Pakistan.

## DISCUSSION

In the absence of diagnostic tests, most physicians in South Asia have to rely on the circumstances of the bite and the clinical features of envenoming to infer the species of the biting snake [1, 2, 11]. In Sri Lanka, a characteristic epidemiologic and clinical pattern has been reported for proven *B. caeruleus* bites [5]. Although the clinical picture of severe neuromuscular paralysis and autonomic disturbances appears to be similar for both species, the present case of *B. cf. sindanus* envenoming underscores the suggestion that certain krait venom components have previously overlooked functions (or side-effects, in addition to clinically most relevant effects like neurotoxicity) that may confront clinicians with additional unusual and challenging situations in already critically ill patients. Such surprising clinical observations have recently been reported for the Malayan krait (*Bungarus candidus*) in Thailand and southern Vietnam (hyponatremia, alterations in blood pressure, persistent mydriasis, rhabdomyolysis with fatal acute renal failure [14, 15]), for the greater black krait (*Bungarus niger*) in Bangladesh (rhabdomyolysis with fatal hyperkalemia [6]), and for many-banded kraits (*Bungarus cf. multicinctus*) in northern Vietnam (generalized myalgia, persistent mydriasis, fatal hyponatremia [16, 17]). A case of pulmonary edema following a krait bite with a similar clinical picture to ours was reported in India [18] but without evidence regarding the identity of the snake (stated to be *B. caeruleus*) or information on the volume of i.v. fluids given to the patient prior to the manifestation of this complication.

While the post-defibrillation creatine kinase values probably largely reflect this intervention, we interpret the values and CK-NAC/CK-MB ratio assayed 6 hr before the pulseless ventricular tachycardia (9 hr after the bite) as an indication of myocardial damage that already existed approximately around the time of admission (~3 hr after the bite). These pre-defibrillation creatine kinase values and the initial ECG of the patient are compatible with various scenarios including myocardial infarction or myocarditis. In view of the age of the patient, later ECG recordings with persisting ST depression and T wave inversion and the generalized rather than focal myocardial damage revealed by 2D-echocardiography, we consider toxic myocarditis due to components of the snake venom to be the likely cause.

This evidence for early myocardial damage in a young

bite victim with no previous history of heart disease suggests the possibility that *B. sindanus* venom may contain myotoxic and/or cardiotoxic factors. Krait venoms in general are known to be rich sources of different classes of toxins with membrane-modifying properties [2]. There has been experimental evidence of krait venom myotoxicity [6, 19], and clinical cases of severe venom-induced generalized rhabdomyolysis and renal failure following krait bites were recently reported [6, 14]. Thus, it is possible that envenoming by different krait species may cause a variable degree of muscle damage that is unnoticed in most cases because of the predominant syndrome of severe neuromuscular paralysis and the relative rarity with which creatine kinase assays are performed in such patients.

The subsequent complications of ventricular tachycardia and pulmonary edema in our patient, on the other hand, are probably best explained by hyperfusion in the presence of toxic myocardial damage and resulting left heart insufficiency. Likewise, we interpret the prolonged hypotensive episode after defibrillation as a side-effect of the rapid i.v. bolus and infusion of amiodarone rather than myocardial damage, and the significant increase of lactate dehydrogenase shortly after amiodarone as a result of the hepatotoxic potential of this drug [20] rather than a feature of envenoming.

The observed lack of response to treatment with the acetylcholinesterase inhibitor neostigmine is in broad agreement with clinical experiences from the treatment of envenoming by various krait species including those in South Asia [e.g., 5–7, 11, 21]. The observation that such anticholinesterase drugs are usually ineffective in reversing paralysis caused by krait venoms is well explained by the mechanism of action of their most lethal components, beta-bungarotoxins, which cause acute denervation of muscle fibres by destruction of motor nerve terminals [22, 23]. However, there have been cases of severe envenoming by *Bungarus* species where patients apparently benefited from anticholinesterase treatment [e.g., 11, 24]. Such differences may be explained by variability in venom composition, in particular by variable proportions of presynaptically acting beta-bungarotoxins and postsynaptically acting nicotinic acetylcholine receptor antagonists (e.g., alpha-bungarotoxins) in *Bungarus* venoms. Quantitative variability of this kind can be substantial even among kraits of the same species and locality (Kuch et al., unpublished data). Thus, a single test dose of anticholinesterase is recommended [11], preferably using a short-acting drug (edrophonium chloride) if available.

In conclusion, the present cases of envenoming inflicted on people sleeping in temporary huts at construction sites in Maharashtra State identify *B. cf. sindanus* as an ad-

ditional cause of fatal snake bite in India. They further contribute to the mounting evidence that more snake species than previously believed contribute to morbidity and mortality in South Asia [1, 2, 6, 7] and point to the role of environmental changes like increased urbanization in human-snake encounters. As the geographic distribution of *B. sindanus* sensu lato from eastern Afghanistan to India broadly overlaps with that of the superficially very similar *B. caeruleus* [12, 25], we suggest that envenoming by *B. cf. sindanus* may be common at least regionally but is routinely misdiagnosed, although these species can be reliably distinguished from each other by the number of dorsal scale rows on the body (15 in *B. caeruleus* vs. 17 in *B. sindanus* sensu lato [9, 12, 25]). Unusual findings like fasciculations and apparent cardiotoxicity suggest the possibility of clinically relevant differences between their venoms. Thus, further studies on the epidemiology, ecology, and toxinology of these medically highly important but nevertheless poorly known snake species are indicated.

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#### CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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