CLINICAL FEATURES OF 60 CONSECUTIVE ICU-TREATED PATIENTS ENVENOMED BY *BUNGARUS MULTICINCTUS*

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Abstract. In northern Vietnam, *Bungarus multicinctus* is the only krait of medical importance. We report 60 consecutive patients admitted to an ICU in Hanoi during 2000-2003 because of envenoming by *B. multicinctus*. Their mean age was 33 years (range 12-67), 77% were male. The majority were agricultural workers, 69% of the snakebites occurred during the night. The mean length of time until the first symptom developed was 3 hours (range 0.5-24 hours). The only sign at the site of the bite was fang marks, which were noted in 90%. The most common neuromuscular symptoms were ptosis and mydriasis (93%), ophthalmoplegia (82%), jaw weakness (90%), pharyngeal pain (83%), palatal palsy (90%), neck muscle paralysis (85%), limb paralysis (85%), and paralysis of the respiratory muscles (87%). No antivenom was available. Fifty-two patients (87%) needed mechanical ventilation for a mean of 8 days. The most surprising laboratory finding was a high rate of significant hyponatremia (42%). The mean duration of the ICU stay was 12 days and the hospital mortality was 7%. According to the Poisoning Severity Score criteria, 54 patients (90%) were classified as severe or lethal envenoming.

INTRODUCTION

Bites by venomous snakes are a worldwide problem, especially in tropical regions (Cheng and Currie, 2004). In Vietnam, two snake families have poisonous members, the Elapidea and the Viperidea. The elapid snakes include, among others, the kraits represented by 12 species worldwide within the single genus *Bungarus*. The kraits are generally unagressive nocturnal animals that frequently enter rural houses. Their venom can cause severe neuromuscular blockade but do not give rise to swelling or necrosis at the site of the bite (Warrel, 1995). Envenoming by several krait species is known to cause respiratory failure and fatality (Sawai *et al*, 1992; Hung, 2004). Alpha-bungarotoxin is a postsynaptically active toxin which binds to the acetylcholine receptors and prevents binding of acetylcholine. The result is a non-depolarising type of neuromuscular blockage. Moreover, the venom also contains β and γ-gungarotoxins which act presynaptically and depress the release of acetylcholine from the nerve endings. The presence of the latter toxins explains why treatment with cholinesterase inhibitors has not been very efficient (Chan *et al*, 1995; Rowan, 2001). The clinical characteristics arising from bites from *Bungarus multicinctus* (many-banded krait, Chinese krait) have rarely been described (Chan *et al*, 1995; Pe *et al*, 1997).

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B. multicinctus are found in many Asian countries, including southern China, Taiwan, Hong Kong, and northern parts of Lao PDR, Myanmar, and Vietnam (Warrel, 1995). Along the back of this snake is a series of black to bluish-black saddle-shaped markings separated by 30-50 white bands (Fig 1). The maximum length is 1.84 meters (Chan *et al*, 1995). In northern Vietnam *B. multicinctus* is the only krait species of medical significance in humans. We report a study of consecutive patients admitted to the National Poison Control Center (PCC) at Bach Mai Hospital in Hanoi during the period 2000-2003 because of envenomation by *B. multicinctus*.

MATERIALS AND METHODS

In this retrospective study the medical records of all patients treated in the intensive care unit (ICU) of the PCC for envenoming by *B. multicinctus* during the 4-year period 2000-2003 were carefully reviewed. In a majority of cases, the type of snake was determined either at the hospital by investigation of a snake specimen brought to the PCC or by the patient in connection with the bite. In some cases the snake was never seen, however, the diagnosis was then established by the circumstances of the bite together with the presence of typical clinical features. A predetermined study protocol was developed. Pertinent data of each case were recorded, including demographics, the time and circumstances of the bite, the body parts bitten, symptoms and signs, laboratory findings, any complications, length of time spent in the ICU, and the outcome. The severity of each case was defined using a 5-grade (0-4) Poisoning Severity Score (PSS) (Persson *et al*, 1998). Treatment measures documented in the medical records, such as mechanical ventilation, were also noted.

Table 1
The occupational distribution of the study population (*N*=60).

Occupation	*n* (%)
Agricultural worker	34 (57)
Student	16 (27)
Service occupations	5 (8)
Other (one patient raised snakes for trade)	5 (8)

Table 2
Site of the snake attack (*N*=60).

Site	*n* (%)
Home	21 (35)
Rice field	20 (33)
Village road	11 (18)
Ponds	5 (8)
Other	3 (5)

RESULTS

A total of 60 consecutive cases admitted to the ICU during the study period for the treatment of envenoming by *B. multicinctus* were collected. Forty-six patients were male (77%) and 14 were female. Their mean age was 33.3 ± 13.5 years, ranging from 12 to 67 years. The most common occupational categories among the patients were agricultural workers and students (Table 1).

Most commonly the attack took place either at home or in the rice field (Table 2). The majority of the snakebites occurred at night (Fig 2). The snake was recognized by 38 patients (63%). The body parts most commonly bitten were the hands and feet (Table 3).

Immediately after being bitten, the patients often carried out different kinds of first aid measures, such as the use of traditional

Table 3
The part of the body bitten (*N*=60).

Body part bitten	*n* (%)
Hand	32 (53)
Foot	16 (27)
Leg	4 (7)
Trunk	3 (5)
Arm	2 (3)
Unknown	3 (5)

Table 4
The first symptom developed after envenomation (*N*=60).

Symptoms	*n* (%)
Pharyngeal pain	13 (22)
Ptosis	12 (20)
General myalgia	9 (15)
Dyspnea	8 (13)
Dysphagia	6 (10)
Difficulty in opening the mouth	3 (5)
General weakness	3 (5)
Blurred vision	2 (3)
Limb paralysis	1 (2)
Abdominal pain	1 (2)
Missing information	2 (3)

medicine (42%), squeezing (32%), application of a tourniquet (28%), incision (20%), or cleaning (3%). The mean time until the first symptom developed was 3.0 ± 3.6 hours, ranging from 0.5 to 24 hours. Most commonly the first manifestations were pharyngeal pain, ptosis, general myalgia, dyspnea, and dysphagia (Table 4). According to the PSS criteria, 54 patients (90%) were classified as having severe or lethal envenomation (PSS grades 3-4), and only 3 patients (5%) displayed mild symptoms (PSS grade 1).

The clinical manifestations of the snakebite were rather specific. Not one single patient had any local symptoms such as swelling or necrosis. Fang marks were noted in 54 cases. The neuromuscular symptoms and signs most commonly observed during the ICU stay were ptosis, mydriasis, ophthalmoplegia, jaw weakness, pharyngeal pain, palatal palsy, general myalgia, neck muscle paralysis, paralysis of the extremities (most pronounced proximally), absent or diminished tendon reflexes, paralysis of the respiratory muscles, urinary retention, and decreased bowel movements (Table 5).

Table 5
Neuromuscular symptoms and signs commonly recorded during the ICU stay (*N*=60).

Neuromuscular symptoms and signs	*n* (%)
Ptosis	56 (93)
Mydriasis	56 (93)
Proximal limb palsy	51 (85)
Distal limb palsy	46 (77)
Absent or diminished deep tendon reflexes	47 (78)
Ophthalmoplegia	49 (82)
Jaw paralysis	54 (90)
Palatal paralysis	54 (90)
Pharyngeal pain	50 (83)
Neck muscle paralysis	51 (85)
Diaphragmatic palsy	49 (82)
Intercostal muscle palsy	52 (87)
Dyspnea	52 (87)
General myalgia	41 (68)
Urine retention	40 (67)
Absent or decreased bowel movements	27 (45)

Respiratory failure was either a result of respiratory muscle paralysis and/or palatal paralysis leading to accumulation of secretions. The cardiovascular signs most often documented were tachycardia (defined as a heart rate faster than 100 beats per minute during >6 hours during the first two days) and hypertension (above 140/90 mmHg during >6 hours during the first two days). Conjunctivitis as a result of dry eyes

Fig 1–*Bungarus multicinctus.*

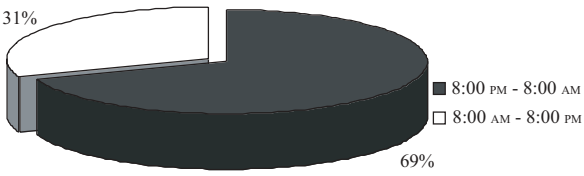

Fig 2–The time of day of the attack.

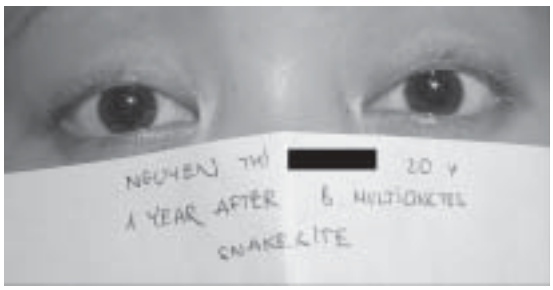

Fig 3–Persistent mydriasis one year after envenomation.

was also commonly noted. Among the laboratory results, the most surprising finding was a high rate of significant hyponatremia (serum sodium level less than 130 mmol/l) (Table 6). When it occurred, this occurred Day 2 or 3 after the snakebite.

The most commonly recorded complication was ventilator-associated pneumonia

Table 6
Extra-neuromuscular symptoms and signs commonly recorded during the ICU stay (*N*=60).

Symptoms and signs	*n* (%)
Tachycardia	50 (83)
Hypertension	26 (43)
Conjunctivitis	41 (68)
Corneitis	1 (2)
Hyponatremia	25 (42)

Table 7
The ICU management of the 60 envenomed patients.

Treatment given	*n* (%)
Endotracheal intubation	52 (87)
Tracheotomy	2 (3)
Mechanical ventilation	52 (87)
Antibiotic therapy	40 (67)
Sodium replacement	40 (67)
Ophthalmologic therapy (vitamin A, antibiotics)	48 (80)

due to long-term mechanical ventilation; this was observed in 37 patients (62%). Other important complications documented were infection of the urinary tract (23 cases) and ileus (2 cases). No antivenom was available during the study period. Supportive care, especially mechanical ventilation, was therefore the main treatment given. Fifty-two of the patients in the study population had to be endotracheally intubated for this purpose. The duration of artificial ventilation averaged 8.2 ± 7.3 days, ranging from 1 to 29 days. A majority of the patients were also treated with antibiotics and sodium replacement as well as local ophthalmologic therapy (Table 7).

The mean duration of the ICU stay in the study population was 12 ± 9 days, rang-

ing from 1 to 36 days. The hospital mortality rate was 7%; all 4 patients died in the ICU. Two died on admission to the ICU, another because of a malfunction of a ventilator, and the fourth died due to severe hyponatremia-induced brain damage. In addition, two patients suffered long-term sequelae. One had an anoxic brain injury and another became dependent on a tracheostomy cannula.

DISCUSSION

This study involves the largest number of patients severely envenomed by *B. multicinctus* reported in the literature so far. A few case series and epidemiologic studies have previously been reported, from the Southeast Asian region (Chan *et al*, 1995; Pe *et al*, 1997), Taiwan (Hung, 2004), and the south of China (Sawai *et al*, 1992). The major findings in this study were the high proportion needing mechanical ventilation and the high rate of acute hyponatremia. The study population was highly selective as all patients were admitted to an ICU. The 54 severe cases from the area surrounding Hanoi during the 4-year period show the grave prognosis if untreated.

In accordance with other case series, the bite by *B. multicinctus* was found to occur commonly in rural areas, where the habitats of snakes overlap those of humans (Chan *et al*, 1995; Hung, 2004). Agricultural workers clearly predominated among the victims. As with other krait species, such as *B. caeruleus* and *B. candidus* (Warrel *et al*, 1983; Kularatne, 2002), the attacks of *B. multicinctus* usually occur at night (Chan *et al*, 1995; Pe *et al*, 1997). The most common locations of the attacks in our study, the patients' homes and the rice field, are similar to those reported in other case series (Pe *et al*, 1997; Hung, 2004).

In previously reported *B. multicinctus* envenoming, the first neurological symptoms developed within a few hours after the bite (Chan *et al*, 1995; Pe *et al*, 1997), and in envenoming by other krait species, they appeared within 12 hours (Warrel *et al*, 1983; Seneviratne, 2002). In the present study the first symptoms developed within a wide time-range of 0.5 to 24 hours. This should be considered regarding the duration of observation required in these patients.

The neuromuscular symptoms and signs recorded in this study were in conformity with those described in previous case series of envenoming by *B. multicinctus* (Chan *et al*, 1995; Pe *et al*, 1997), as well as by some other kraits (Kanchanapongkul, 2002; Kularatne, 2002; Seneviratne and Dissanayake, 2002). Ptosis and ophthalmoplegia were frequently observed and often led to dry eyes and conjunctivitis, or even corneitis in one case. These events are important to recognize and require particular nursing care. Mydriasis was also recorded in the majority of patients. The dilatation of the pupils was often maximal and was extremely persistent in some cases (Fig 3). The commonly documented palatal paralysis with inability to swallow was one of the reasons for respiratory failure in the early phase of the ICU course, but was also a cause of extubation failure in some cases in the late phase. This should be carefully considered, concomitantly with respiratory muscle palsy in the respiratory management of these cases. The most severely affected patients developed generalized muscle paralysis and became completely unresponsive. This situation, combined with apnea and dilated pupils, may easily be misdiagnosed as brain death. Electroencephalography and nerve conduction studies therefore may be indicated in situations of uncertainty.

The envenomed patients in the study often experienced general myalgia (Table 5). Some patients still had pain and numbness several months after discharge, requiring analgesic therapy. This phenomenon re-

sembles the case of peripheral sensory neuropathy after a krait bite reported from Sri Lanka (Seneviratne and Dissanayake, 2002).

Tachycardia and hypertension were noted in many patients. These findings have been reported previously after snakebite by *B. multicinctus* (Chan *et al*, 1995) and also by another krait species, namely *B. candidus*. It has been suggested that these clinical features may be due to a decreased parasympathetic tone and may be treated with beta adrenergic blockers (Laothong and Sitprija, 2001).

The important finding of a rapidly developing significant hyponatremia in nearly half of the present study population was surprising. This electrolyte disturbance has not been reported previously after envenoming by *B. multicinctus*. We do not know the exact mechanism of the disturbance, but the sodium content of the urine was found to be elevated in a majority of the cases. Hyponatremia has been reported following bites by the American coral snake. The mechanism underlying the electrolyte disturbance after that snakebite was reported to be a natriuretic peptide in the venom (Ho *et al*, 1997). We strongly recommend that serum electrolyte levels be followed up in every patient envenomed by *B. multicinctus*, and that sodium be replaced immediately if necessary.

Fifty-two patients or 87% of the study population needed mechanical ventilation. This finding emphasizes the seriousness of snakebite from this particular species. The duration of the artificial ventilation in our study was longer than that in a study from India describing severe neuroparalytic pulmonary status after different snake envenomations (Aggarwal *et al*, 2001). The recorded hospital mortality rate of 7% in our study, despite ICU treatment, also underlines the danger of envenoming by *B. multicinctus*.

In conclusion, this study provides important information on envenoming by *B. multicinctus*. The new finding of a high rate of significant hyponatremia makes screening and prompt sodium replacement imperative, and the severe clinical features recorded indicate an urgent need for a specific antivenom.

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