Case Report

A case series of Samar cobra, *Naja samarensis* Peters, 1861 (Elapidae) envenomation

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[1] **Abbreviations:** GCS, Glasgow Coma Scale; PCAV, Purified Cobra Antivenom; PEA, pulseless electrical activities; RITM, Research Institute of Tropical Medicine; SαNTX, short-chain alpha-neurotoxins

Abstract

The Samar cobra, *Naja samarensis* Peters, 1861 is one of the World Health Organization's category I venomous snakes in the Philippines. Although *N. samarensis* is known to inhabit Eastern Visayas, unlike *N. philippinensis* in Luzon, no clinical case reports have yet been published in the international literature. No immuno-diagnostic assays have been developed for venomous snakes in the Philippines, even for research purposes. Therefore, identification of the causative snake in hospitals is challenging. *In vivo* assay using mice, pre-clinical tests of locally-produced antivenom raised against *N. philippinensis* venom, ["Purified Cobra Antivenom (PCAV)"], has shown cross neutralisation of *N. samarensis* venom. Here, we present five snakebite envenomation cases where causative snakes were confirmed in photos as *N. samarensis* by an expert local herpetologist. Patients' symptoms and signs varied, from mild to extensive local cytotoxic and systemic neurotoxic envenomation. In one case, venom had been spat into the eye. Out of five patients, two underwent surgical debridement of necrotic tissue at the bite site. One paediatric patient was intubated because of cardiopulmonary arrest. Except for the spitting cobra case, four cases were successfully treated with PCAV and supportive management. These are the first clinical case reports of confirmed *N. samarensis* envenomation.

Keywords: *Naja samarensis***,** snakebite, neurotoxic, cytotoxic, antivenom, Elapidae

1. Introduction

The Samar cobra, *Naja samarensis* Peters, 1861 (Figure 1) is one of the World Health Organization's category I venomous snakes in the Philippines, together with *N. philippinensis*, the Northern Philippine cobra.[1] *N. philippinensis* is found in the Luzon region, while *N. samarensis* inhabits mainly the Visayas-Mindanao region of the southern Philippines.[2] Although the actual number of snakebites in the Philippines has not been reported, a recent study with decision analytic model showed that estimated 13,377 (95% credibility interval, CI: 11,452–15,772) annual snakebites in the Philippines with 550 (95%CI: 274–1099) deaths.[3] Several species-specific studies on *N. philippinensis* have been reported previously.[4,5,6,7,8] Although possible cases of *N. samarensis* envenomation have been described locally in the Philippines,[9,10] there are no published reports both in local and international literature that identified the causative snake definitively as *N. samarensis* and described the clinical course of envenoming in detail.

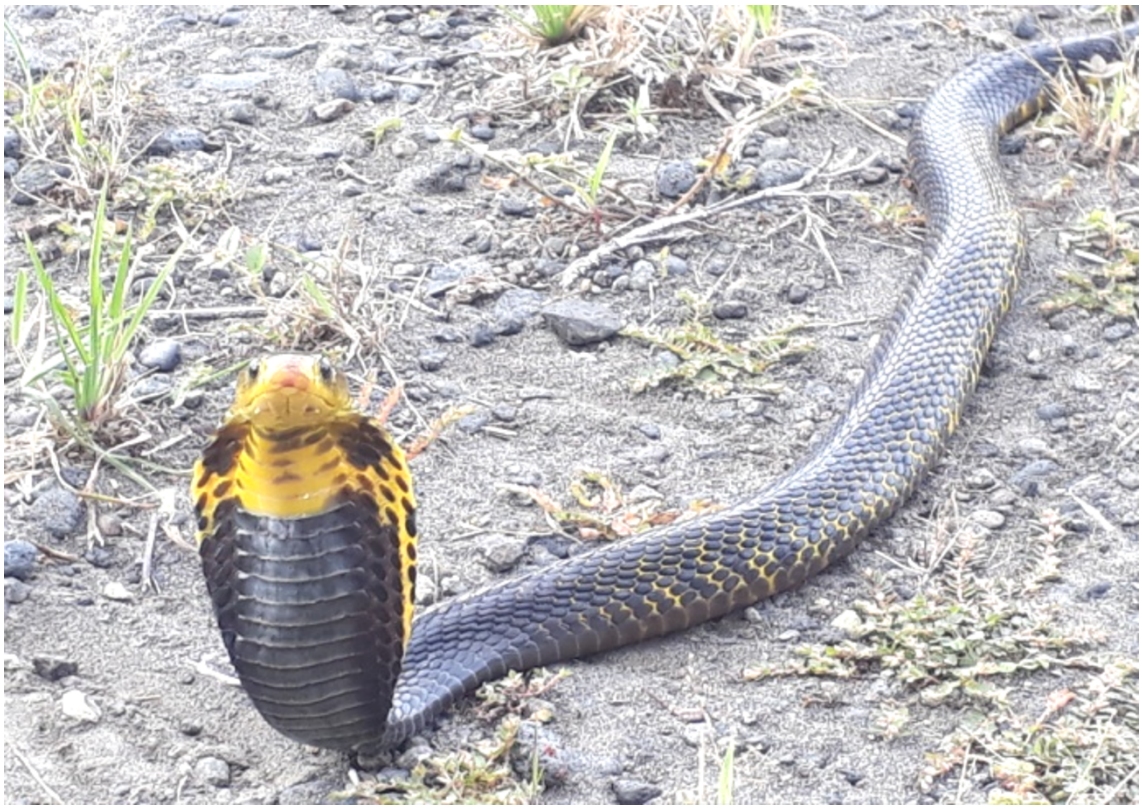

Figure 1.

Samar cobra (*Naja samarensis*) *in situ,* Santa Fe, Leyte. © MJ Sarmiento, 2019

The only antivenom currently produced in the Philippines for snakebite treatment is monovalent Purified Cobra Antivenom (PCAV), raised against *N. philippinensis* venom by the Research Institute of Tropical Medicine (RITM).[11] A pre-clinical *in vivo* assay using mice showed that PCAV cross neutralised *N. samarensis* venom, but it was pointed out that at least two times or more doses might be needed for neutralisation of this venom.[12] In the Eastern Visayas region, PCAV has been used empirically for neurotoxic snakebite envenomation but has not been formally validated.

No immuno-diagnostic assays have been developed to identify venomous snakes in the Philippines, even for research purposes. Therefore, identification of the causative snake in hospitals is challenging. However, recent development and widely using of mobile phones with photographic functions have made it ppossible to capture the causative snake in photo-images on site and allowed their identification. Here, we report five cases of photographically confirmed snakebites by *N. samarensis* seen at the Eastern Visayas Medical Center, the only tertiary care hospital in the Eastern Visayas region (covering the islands of Samar, Leyte, and Biliran) from March 2020 to December 2021. These are the first reports of confirmed *N. samarensis* envenomation.

2. Case descriptions

2.1. Case 1

A 64-year-old woman with a history of hypertension and diabetes mellitus visited the emergency department in March 2020, after a snake spat venom into her left eye. While cleaning her garage at her house in Abuyog, Tabigue, Leyte, around noon, a black and yellow snake (Figure 2A) emerged from a bag of stored rice and suddenly spat liquid into her left eye. She felt pain and noticed redness of the eye. She

was referred from the district hospital without any specific treatment. On admission (2.5 hours after the spitting), there was no conjunctival injection or visual abnormality in the left eye, despite mild pain. No neurological or other systemic symptoms and signs were observed. After the affected eye was irrigated, she was monitoring for 6 hours, and eventually discharged with analgesics. After returning home, her symptoms improved with no complications observed over the subsequent two years.

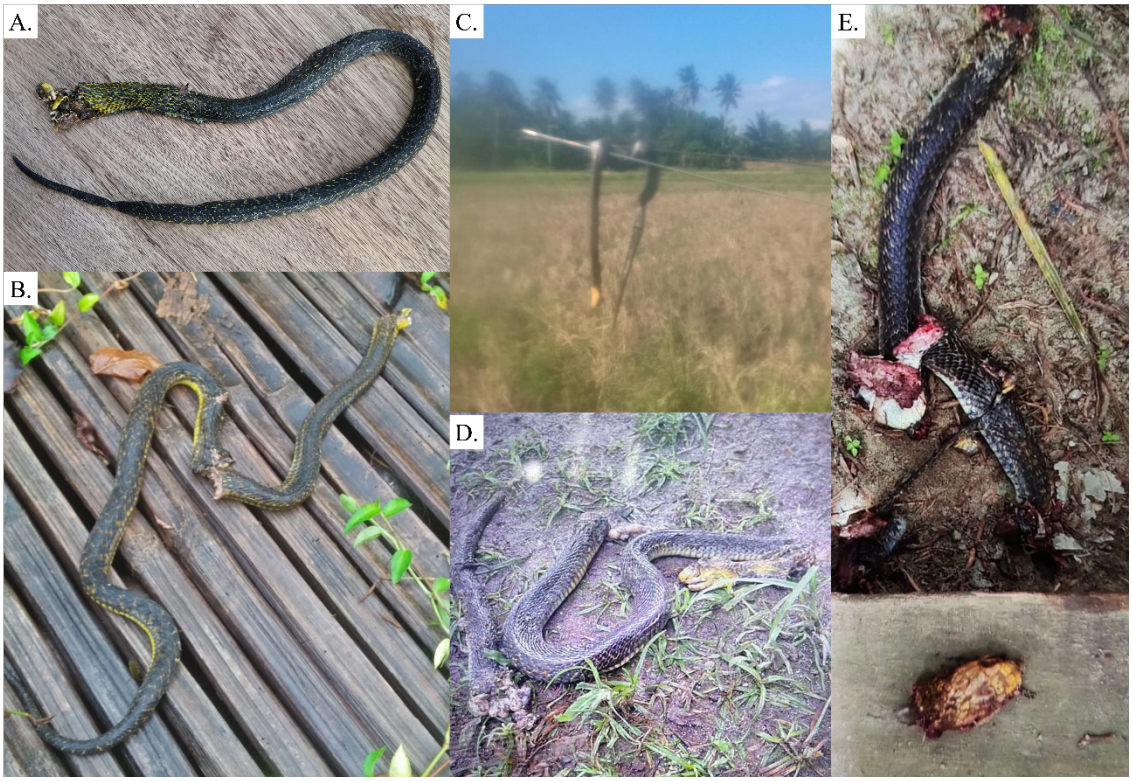

Figure 2.

Photograph of the causative snakes, *Naja samarensis*

(A) Case 1 *Naja samarensis* with its head crushed.

(B) Case 2 *Naja samarensis* with its head crushed and its body cut.

(C) Case 3 Living *Naja samarensis* in the rice field, with its yellow head and predominantly black coloured body.

(D) Case 4 Killed *Naja samarensis*, with its body cut in three parts.

(E) Case 5 Killed *Naja samarensis*, and its severed head .

2.2. Case 2

A 79-year-old woman with no past medical history was brought to the emergency department after a snakebite. Around 17:00 of May 2020, she was bitten on the middle finger of her left hand by a black and yellow snake (Figure 2B) outside her house in Pansud, Lapaz, Leyte, while getting kerosene. A neighbour applied a tourniquet around her forearm, and she was also brought to a traditional healer who recited a ritual prayer. No special treatment was given at the rural health unit, before she was transported to the medical centre. On admission 3.5 hours after the bite, her blood pressure was 180/100 mmHg, her level of consciousness was reduced [Glasgow Coma Scale (GCS) 9 (E3V1M5)], and bilateral ptosis was observed. Normal oxygen saturation was maintained on ambient air with no dyspneic episodes. Two fang punctures were observed on the left third proximal interphalangeal joint with swelling, tenderness, and bruising (Figure 3). Swelling extended to the wrist. Based on the photo of the snake and the neurological signs, a diagnosis of envenomation by *N. samarensis* was made, and two ampoules (1600 mouse units) of PCAV were administered intravenously over one hour. No tracheal intubation or ventilator management was required. On the second day of hospitalization, the patient became fully conscious. Surgical debridement was performed due to progressive local necrosis. The patient was discharged on the fifth day of hospitalization after continued observation of her neurological condition and local findings. Uppon follow-up, approximately four weeks later, the wound already re-epithelialized.

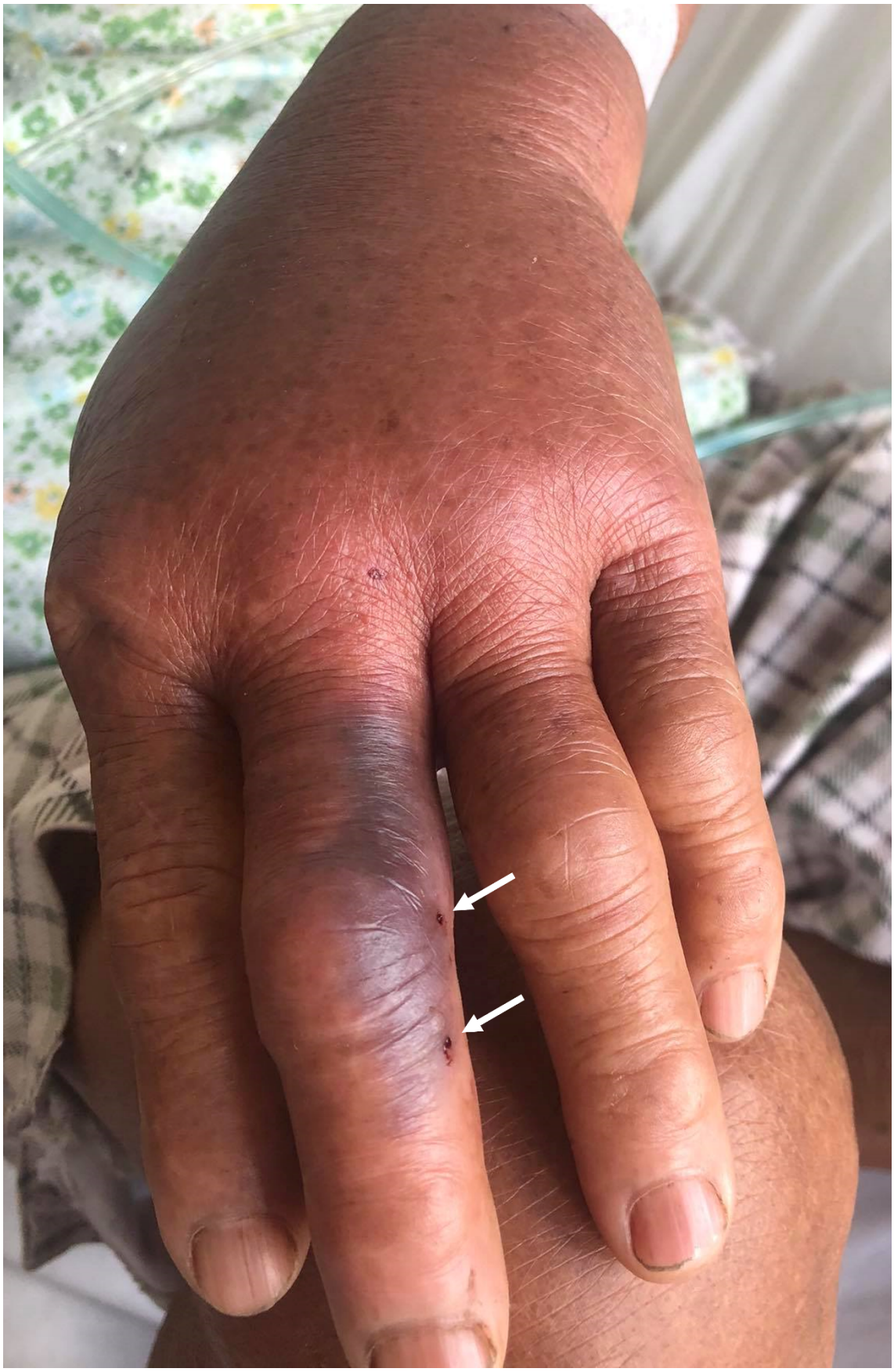

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Figure 3.

3.8 hours after the bite, the third finger had fang marks (white arrows) on the proximal interphalangeal joint. The phalanx was swollen and tender, with bruising. The swelling extended to the wrist.

2.3. Case 3

A 34-year-old farmer without underlying disease visited the emergency department after a snakebite on his left forearm. Around 11:00 of April 2021, while irrigating a paddy field in Libas, Burauen, Leyte, he accidentally inserted his hand into a hole, and suddenly felt pain in his left forearm. He saw a black and yellow snake (Figure 2C). A tourniquet was applied by his family, and he visited the local district hospital. He was referred to the emergency department with no specific treatment despite feeling numbness in the bitten arm. At presentation, 3 hours after the bite, he was hemodynamically stable. The bite site showed a single fang mark and mild swelling on the left distal forearm. He was conscious but had bilateral ptosis and weakness of the left upper and lower extremities. *N. samarensis* envenomation was diagnosed, and two ampules (1600 mouse units) of PCAV were administered intravenously over one hour. The ptosis was rapidly improved, leftt-side hemiparalysis improved gradually, and he became able to walk. In the absence of any further symptoms, he was discharged after six days in hospital.

2.4. Case 4

A 5-year-old previously-healthy boy was brought to the emergency department after a snakebite on his right middle finger. In May 2021, at around 10:00, he was bitten by a black and yellow snake (Figure 2D) while inserting his hand into a hole in his house which was under construction in Canhidoc, Palo, Leyte. He was seen at a nearby hospital and was transferred eventually to the emergency department via ambulance after starting a fluid infusion. On admission 2.5 hours after the bite, his vital sign showed reduced level of consciousness [GCS 8 (E2V2M4)], bradypnea (respiratory rate of 8/min), and bradycardia (50 bpm) with

impalpable pulse. Normal body temperature of 36.0°C and slightly elevated blood glucose (244 mg/dL) were noted. Diagnosed as pulseless electrical activities (PEA), chest compressions started followed by intubation, administration of adrenaline and mechanical ventilation; fortunately then, he had return of spontaneous circulation. The bite site had fang marks on the middle phalanx of the right middle finger, with mild swelling of the surrounding area. He also had bilateral ptosis and flaccid paralysis. Two ampules of PCAV (1600 mouse units) were administered intravenously over one hour. Spontaneous breathing and limb movements were observed approximately 10 minutes after PCAV infusion was started. Additional four ampules of PCAV (3200 mouse units) were administered over the next four hours. Five hours after starting PCAV, the patient became active and self-extubated. Over the next day, he was fully conscious, and neurological symptoms did not reappear. Local signs around fang marks had not been worsen nor spread, and the patient was discharged after six days in hospital with no adverse effects of PCAV observed.

2.5. Case 5

A 56-year-old male farmer with a history of hypertension was bitten by a snake on his right upper arm. He had been bitten twice in the past by nonvenomous snakes. In December 2021, at around 8:00, he was bitten by a black and yellow snake (Figure 2E) on his right upper arm while trying to carry wood in a pig pen in his yard in Mac, Sogod, Southern Leyte. He went to a traditional healer in the area where he was offered a prayer. The bitten site began to swell, hence he went directly to the emergency department. On the 6th hour post-bite, he had a high blood pressure, tachycardia, and tachypnoea but was well-oxygenated breathing ambient air. He was fully conscious, but with bilateral ptosis. There was a 2.0 x 1.5 cm bite wound with bruising and surrounding swelling, and tenderness on the distal extensor surface of the right upper arm (Figure 4A). *N. samarensis* envenomation was diagnosed, two ampules of PCAV (1600 mouse units) were administered intravenously over one hour, and the ptosis quickly improved. The patient underwent surgical debridement on the third day of hospitalization because of progressive necrosis of the wound (Figure 4B).

He was discharged on the 10th day of hospitalization but was lost to follow-up because of financial constraints. According to the patient, the wound re-epithelialized around four months later with scaring.

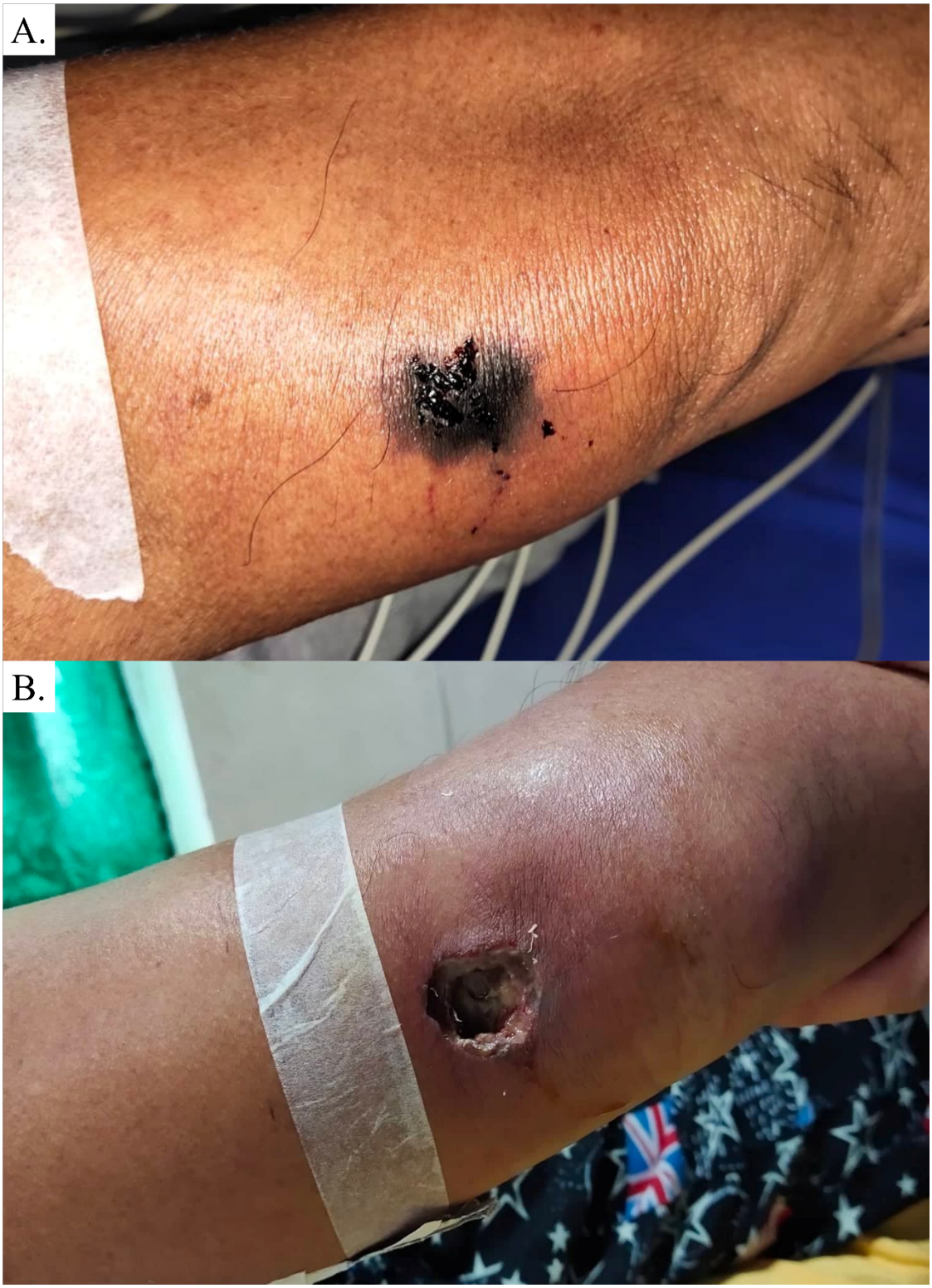

Figure 4.

(A) Bitten site on the distal right upper arm with a 2.0 cm x 1.5cm bruise 6 hours after the bite. Local swelling, tenderness, and mild bleeding were observed.

(B) Bitten lesion post-debridement for progressive skin necrosis on day 3.

2.6. Snake identification

In all cases, the patient or family member brought a photograph of the snake responsible. An expert local herpetologist confirmed *N. samarensis* in all cases, based on distinctive morphology (i) colour above dark brown to black, usually with a trace of a light lateral line[13] (Figure 2B) and (ii) throat and first few ventrals yellowish followed by a distinct broad black band (Figure 2C), which gradually fades to light gray[13] (Figure 2E).

2.7. Summary of the cases

Table 1 shows the patient characteristics of the five cases reported. Patients ranged from a child to the elderly, and all had good outcomes, although some had severe acute neurological symptoms. The case of spitting venom into the eye was not severe and had no neurologic complications. All the bitten patients showed neurological symptoms; one required intubation and mechanical ventilation. Administration of PCAV in doses of 2-6 ampoules resulted to a rapid improvement in neurological symptoms. Local swelling and redness were observed in all the bite cases, but there was no development of compartment syndrome. However, local necrosis progressed in two cases, requiring surgical debridement. There was no evidence of hematologic, cardiovascular, muscular, or renal toxicity. All patients were discharged from the hospital without sequelae.

3. Discussion

This is the first description of the clinical course of Samar cobra, *N. samarensis*, envenomation in which the snakes responsible were identified photographically. The Samar cobra (*N. samarensis*), also known as Peter's or Visayas cobra, is endemic to the Philippines. It has been recorded in Bohol, Camiguin Sur, Dinagat, Leyte, Samar, Mindanao, Basilan, Agusan del Norte, Bukidnon, Davao del Sur, Lanao, Misamis Occidental, South Cotabato, Zamboanga City, and Siquijor.[2,14,15,16] Its body is dark brownish-black with yellow skin between the scales and yellow or pale sides of the head and neck, throat, and edge of the hood.[17] They occupy a wide range of habitats, from tropical moist forests to rice paddies, pineapple plantations, coconut forests, and rural villages. The International Union for Conservation of Nature and Natural Resources Red List of Threatened Species in 2007 rates the species as a "Least concern,"[18] but future habitat loss is predicted due to recent climate change.[19] In the present report, two of the five victims were bitten by snakes while farming in the fields, and the other three were bitten or spat at by snakes in their houses. There is no clear distinction between wet and dry seasons in the Leyte region, but four cases were seen in the drier season (March to May).

As with envenomation by other neurotoxic cobras, ptosis was observed in all bite cases; and, as with *N. philippinensis*, the signs of envenomation were predominantly neurotoxic. In one paediatric case, cardiac arrest resulted from respiratory arrest caused by respiratory muscle paralysis, confirming the dangers of envenomation in the absence of appropriate prehospital care. In the previous study, patient age younger than 12 years was one of the factors associated with severe systemic snakebite envenomation.[20] In addition, *N. samarensis* appears to cause more severe local envenomation than *N. philippinensis*. Two of the cases required surgical debridement due to progressive local necrosis. It has been reported that in cases of *N. philippinensis* envenomation, local findings are often unremarkable.[21] Recent venom analysis of *N. samarensis* has detected cytotoxic three finger toxins in addition to dominant short-chain alpha-neurotoxins (SαNTX),[22] which could explain the present findings. Even among the four bite cases, local envenoming

ranged from inconspicuous to necrosis. Larger case series is needed to indicate its clinical importance.

PCAV appeared effective in reversing neurotoxic signs of *N. samarensis* envenomation. For *N. philippinensis*, 5-10 ampoules of PCAV are usually recommended initially, depending on the severity of neurological symptoms, according to the protocol by RITM. In the present small case series, however, two ampoules for moderate neurological symptoms and a total of six ampules even for respiratory paralysis appeared effective. Hospitals have a limited supply of PCAV, and so small doses are administered. The findings suggest that guidelines for *N. philippinensis* may not necessarily apply to *N. samarensis* envenomation. The difference between the lower neutralising activity of PCAV against *N. samarensis* venom in mice[12] and what is observed in this clinical practice needs to be verified by additional studies, such as examining the neutralizing activity of PCAV against serum venom antigen levels in patients with signs of envenomation. The rapid improvement in neurological signs suggests that the observed neurotoxicity resulting from *N. samarensis* neurotoxicity is due to postsynaptic acetylcholine receptor inhibition. The use of anti-acetylcholinesterase may be as effective, as in the case of *N. philippinensis* envenoming. Neostigmine has been recommended as a first-aid or adjunctive treatment for envenoming by other species whose neurotoxicity is predominantly post-synaptic, such as cobras and Oceanian death adders (*Acanthophis*).[5,6,23,24,25,26]

It took 2-6 hours from bite to consultation, and two cases were seen by traditional healers. In some cases, tourniquets, which are not recommended, were applied before they reached hospital. Improved prehospital care is essential to improve the survival of snakebite victims.[27,28] In future, it will be necessary to identify communities with a high number of cases and conduct community-based educational activities to promote appropriate first-aid. Improving logistics, such as means of transport and distribution of antivenom, is also a long-term challenge. Killing of the snake responsible is not recommended and should be discouraged, both to prevent the risk of additional snakebites and to conserve these ecologically-important animals. In our series, except for case 3, the snakes were photographed after being killed by

patients or family members. Since attempting to capture the snake alive is even more dangerous, it will be necessary to instruct people to take photographs safely, to allow identification of the causative snake, and to leave the area as soon as possible to ensure their safety. Alternatively, immunodiagnosis should be developed for the Philippines, for clinical and research purposes.

4. Conclusion

We report five cases of *N.samarensis* envenomation. Small doses of PCAV were effective in treating neurological symptoms. Further studies are needed, including the effects of PCAV against local envenomation. Raising awareness in the community, about prehospital behaviour and management is important.

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Data Availability Statement:

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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353 **Table 1. Socio-demographic and clinical characteristics of five patients with *Naja samarensis***

354 **envenomation.**

	Case 1	Case 2	Case 3	Case 4	Case 5
Age (years)	64	79	34	5	56
Sex	Female	Female	Male	Male	Male
Occupations	Housewife	Retired	Farmer	Student	Farmer
Address (City or Rural)	Rural	Rural	Rural	Rural	Rural
Underlying diseases	HT, DM	None	None	None	HT
Number of previous snakebites	0	0	0	0	2
Month of bite	March	May	April	May	December
Time of bite	12:00	17:00	11:00	10:00	8:00
Place of bite	House (garage)	House	Rice field	House (under construction)	Yard
Activity at time of bite	Cleaning	Opening the door	Farming	Playing	Farming
Traditional healers	None	Praying	None	None	Praying
The hospital before visit	District	Rural Health Unit	District	Public	None
Treatment before visit	None	Tourniquets	None	Wash, infusion	None
Ambulance use	Yes	Yes	Yes	Yes	No

Duration between bite and visit (hours)	2.4	3.8	3.5	2.5	5.8
Vital signs on admission	Tachycardia	Hypertension	Normal	Bradypnea, hypotension, bradycardia	Tachypnoea, hypertension, tachycardia
Glasgow Coma Scale (GCS)	15	9	15	8	15
Affected part of the body	Eye	Finger	Forearm	Finger	Upper arm
Local signs	Pain, redness	Pain, swelling, redness, necrosis	Pain, swelling, redness	Pain, swelling, redness	Pain, swelling, redness, bleeding, necrosis
Compartment syndrome	-	-	-	-	-
Neurological signs	-	Ptosis	Ptosis, numbness, paralysis	Ptosis, paralysis	Ptosis
Respiratory failure	-	-	-	+	-
PCAV (ampules)	0	2	6	2	2
Other medicines	Analgesics	TT, ATS, analgesics, antibiotics	TT, ATS, analgesics, antibiotics, PPI	TT, ATS, analgesics, antibiotics	TT, ATS, analgesics, antibiotics
Surgical procedures	None	Debridement on Day 2	None	None	Debridement on Day 3
ICU admission	-	-	-	+	-

Ventilator hours	0	0	0	4.5	0
Hospital hours	6	112	125	119	219
Complications	None	None	None	None	None
Outcomes	Survived	Survived	Survived	Survived	Survived

HT, hypertension; DM, diabetes mellitus; PCAV, Purified Cobra Antivenom; TT, tetanus toxoid; ATS, anti-tetanus serum; PPI, proton-pomp inhibitor; ICU, intensive care unit

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