1	Case	Report

2	A	case series of Samar cobra, <i>Naja samarensis</i> 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 alphaneurotoxins

33 Abstract

34 The Samar cobra, Naja samarensis Peters, 1861 is one of the World Health Organization's category I 35 venomous snakes in the Philippines. Although N. samarensis is known to inhabit Eastern Visayas, unlike 36 *N. philippinensis* in Luzon, no clinical case reports have yet been published in the international literature. 37 No immuno-diagnostic assays have been developed for venomous snakes in the Philippines, even for 38 research purposes. Therefore, identification of the causative snake in hospitals is challenging. In vivo assay 39 using mice, pre-clinical tests of locally-produced antivenom raised against N. philippinensis venom, 40 ["Purified Cobra Antivenom (PCAV)"], has shown cross neutralisation of N. samarensis venom. Here, we 41 present five snakebite envenomation cases where causative snakes were confirmed in photos as N. 42 samarensis by an expert local herpetologist. Patients' symptoms and signs varied, from mild to extensive 43 local cytotoxic and systemic neurotoxic envenomation. In one case, venom had been spat into the eye. Out 44 of five patients, two underwent surgical debridement of necrotic tissue at the bite site. One paediatric patient 45 was intubated because of cardiopulmonary arrest. Except for the spitting cobra case, four cases were 46 successfully treated with PCAV and supportive management. These are the first clinical case reports of 47 confirmed N. samarensis envenomation.

49	Keywords: Naja	samarensis, snakebite,	neurotoxic, cytotoxic,	antivenom, Elapidae
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53 Introduction 1.

54 The Samar cobra, Naja samarensis Peters, 1861 (Figure 1) is one of the World Health Organization's 55 category I venomous snakes in the Philippines, together with N. philippinensis, the Northern Philippine 56 cobra.¹ N. philippinensis is found in the Luzon region, while N. samarensis inhabits mainly the Visayas-57 Mindanao region of the southern Philippines.² Although the actual number of snakebites in the Philippines 58 has not been reported, a recent study with decision analytic model showed that estimated 13,377 (95% 59 credibility interval, CI: 11,452–15,772) annual snakebites in the Philippines with 550 (95%CI: 274–1099) 60 deaths.³ Several species-specific studies on N. philippinensis have been reported previously.^{4,5,6,7,8} Although 61 possible cases of N. samarensis envenomation have been described locally in the Philippines,^{9,10} there are 62 no published reports both in local and international literature that identified the causative snake definitively 63 as N. samarensis and described the clinical course of envenoming in detail.



67 Figure 1.

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

69

70 The only antivenom currently produced in the Philippines for snakebite treatment is monovalent 71 Purified Cobra Antivenom (PCAV), raised against N. philippinensis venom by the Research Institute of 72 Tropical Medicine (RITM).¹¹ A pre-clinical in vivo assay using mice showed that PCAV cross neutralised 73 N. samarensis venom, but it was pointed out that at least two times or more doses might be needed for 74 neutralisation of this venom.¹² In the Eastern Visayas region, PCAV has been used empirically for 75 neurotoxic snakebite envenomation but has not been formally validated. 76 No immuno-diagnostic assays have been developed to identify venomous snakes in the 77 Philippines, even for research purposes. Therefore, identification of the causative snake in hospitals is 78 challenging. However, recent development and widely using of mobile phones with photographic functions 79 have made it ppossible to capture the causative snake in photo-images on site and allowed their 80 identification. Here, we report five cases of photographically confirmed snakebites by N. samarensis seen 81 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.

84

85 2. Case descriptions

86 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 91 was referred from the district hospital without any specific treatment. On admission (2.5 hours after the 92 spitting), there was no conjunctival injection or visual abnormality in the left eye, despite mild pain. No 93 neurological or other systemic symptoms and signs were observed. After the affected eye was irrigated, she 94 was monitoring for 6 hours, and eventually discharged with analgesics. After returning home, her symptoms 95 improved with no complications observed over the subsequent two years.



- 98
- 99 **Figure 2.**
- 100 Photograph of the causative snakes, *Naja samarensis*
- 101 (A) Case 1 Naja samarensis with its head crushed.
- 102 (B) Case 2 Naja samarensis with its head crushed and its body cut.
- 103 (C) Case 3 Living Naja samarensis in the rice field, with its yellow head and predominantly black
- 104 coloured body.

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

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

107

108 **2.2.** Case 2

109 A 79-year-old woman with no past medical history was brought to the emergency department after a 110 snakebite. Around 17:00 of May 2020, she was bitten on the middle finger of her left hand by a black and 111 yellow snake (Figure 2B) outside her house in Pansud, Lapaz, Leyte, while getting kerosene. A neighbour 112 applied a tourniquet around her forearm, and she was also brought to a traditional healer who recited a ritual 113 prayer. No special treatment was given at the rural health unit, before she was transported to the medical 114 centre. On admission 3.5 hours after the bite, her blood pressure was 180/100 mmHg, her level of 115 consciousness was reduced [Glasgow Coma Scale (GCS) 9 (E3V1M5)], and bilateral ptosis was observed. 116 Normal oxygen saturation was maintained on ambient air with no dyspneic episodes. Two fang punctures 117 were observed on the left third proximal interphalangeal joint with swelling, tenderness, and bruising 118 (Figure 3). Swelling extended to the wrist. Based on the photo of the snake and the neurological signs, a 119 diagnosis of envenomation by N. samarensis was made, and two ampoules (1600 mouse units) of PCAV 120 were administered intravenously over one hour. No tracheal intubation or ventilator management was 121 required. On the second day of hospitalization, the patient became fully conscious. Surgical debridement 122 was performed due to progressive local necrosis. The patient was discharged on the fifth day of 123 hospitalization after continued observation of her neurological condition and local findings. Uppon follow-124 up, approximately four weeks later, the wound already re-epithelialized.



127 **Figure 3**.

128 3.8 hours after the bite, the third finger had fang marks (white arrows) on the proximal interphalangeal joint.

129 The phalanx was swollen and tender, with bruising. The swelling extended to the wrist.

130

131 **2.3. Case 3**

132 A 34-year-old farmer without underlying disease visited the emergency department after a snakebite on his 133 left forearm. Around 11:00 of April 2021, while irrigating a paddy field in Libas, Burauen, Leyte, he 134 accidentally inserted his hand into a hole, and suddenly felt pain in his left forearm. He saw a black and 135 yellow snake (Figure 2C). A tourniquet was applied by his family, and he visited the local district hospital. 136 He was referred to the emergency department with no specific treatment despite feeling numbress in the 137 bitten arm. At presentation, 3 hours after the bite, he was hemodynamically stable. The bite site showed a 138 single fang mark and mild swelling on the left distal forearm. He was conscious but had bilateral ptosis and 139 weakness of the left upper and lower extremities. N. samarensis envenomation was diagnosed, and two 140 ampules (1600 mouse units) of PCAV were administered intravenously over one hour. The ptosis was 141 rapidly improved, leftt-side hemiparalysis improved gradually, and he became able to walk. In the absence 142 of any further symptoms, he was discharged after six days in hospital.

143

144 **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 151 impalpable pulse. Normal body temperature of 36.0°C and slightly elevated blood glucose (244 mg/dL) 152 were noted. Diagnosed as pulseless electrical activities (PEA), chest compressions started followed by 153 intubation, administration of adrenaline and mechanical ventilation; fortunately then, he had return of 154 spontaneous circulation. The bite site had fang marks on the middle phalanx of the right middle finger, with 155 mild swelling of the surrounding area. He also had bilateral ptosis and flaccid paralysis. Two ampules of 156 PCAV (1600 mouse units) were administered intravenously over one hour. Spontaneous breathing and limb 157 movements were observed approximately 10 minutes after PCAV infusion was started. Additional four 158 ampules of PCAV (3200 mouse units) were administered over the next four hours. Five hours after starting 159 PCAV, the patient became active and self-extubated. Over the next day, he was fully conscious, and 160 neurological symptoms did not reappear. Local signs around fang marks had not been worsen nor spread, 161 and the patient was discharged after six days in hospital with no adverse effects of PCAV observed.

162

163 **2.5.** Case 5

164 A 56-year-old male farmer with a history of hypertension was bitten by a snake on his right upper arm. He 165 had been bitten twice in the past by nonvenomous snakes. In December 2021, at around 8:00, he was bitten 166 by a black and yellow snake (Figure 2E) on his right upper arm while trying to carry wood in a pig pen in 167 his yard in Mac, Sogod, Southern Leyte. He went to a traditional healer in the area where he was offered a 168 prayer. The bitten site began to swell, hence he went directly to the emergency department. On the 6th hour 169 post-bite, he had a high blood pressure, tachycardia, and tachypnoea but was well-oxygenated breathing 170 ambient air. He was fully conscious, but with bilateral ptosis. There was a 2.0 x 1.5 cm bite wound with 171 bruising and surrounding swelling, and tenderness on the distal extensor surface of the right upper arm 172 (Figure 4A). N. samarensis envenomation was diagnosed, two ampules of PCAV (1600 mouse units) were 173 administered intravenously over one hour, and the ptosis quickly improved. The patient underwent surgical 174 debridement on the third day of hospitalization because of progressive necrosis of the wound (Figure 4B).

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



178

179 **Figure 4**.

180 (A) Bitten site on the distal right upper arm with a 2.0 cm x 1.5cm bruise 6 hours after the bite. Local

- 181 swelling, tenderness, and mild bleeding were observed.
- 182 (B) Bitten lesion post-debridement for progressive skin necrosis on day 3.

183

184 **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 line¹³ (Figure 2B) and (ii) throat and first few ventrals yellowish followed by a distinct broad black band (Figure 2C), which gradually fades to light gray¹³ (Figure 2E).

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191 **2.7. Summary of the cases**

192 Table 1 shows the patient characteristics of the five cases reported. Patients ranged from a child to the 193 elderly, and all had good outcomes, although some had severe acute neurological symptoms. The case of 194 spitting venom into the eye was not severe and had no neurologic complications. All the bitten patients 195 showed neurological symptoms; one required intubation and mechanical ventilation. Administration of 196 PCAV in doses of 2-6 ampoules resulted to a rapid improvement in neurological symptoms. Local swelling 197 and redness were observed in all the bite cases, but there was no development of compartment syndrome. 198 However, local necrosis progressed in two cases, requiring surgical debridement. There was no evidence of 199 hematologic, cardiovascular, muscular, or renal toxicity. All patients were discharged from the hospital 200 without sequelae.

202 **3.** Discussion

203 This is the first description of the clinical course of Samar cobra, N. samarensis, envenomation in which 204the snakes responsible were identified photographically. The Samar cobra (N. samarensis), also known as 205 Peter's or Visayas cobra, is endemic to the Philippines. It has been recorded in Bohol, Camiguin Sur, 206 Dinagat, Leyte, Samar, Mindanao, Basilan, Agusan del Norte, Bukidnon, Davao del Sur, Lanao, Misamis 207 Occidental, South Cotabato, Zamboanga City, and Siquijor.^{2,14,15,16} Its body is dark brownish-black with 208 vellow skin between the scales and yellow or pale sides of the head and neck, throat, and edge of the hood.¹⁷ 209 They occupy a wide range of habitats, from tropical moist forests to rice paddies, pineapple plantations, 210 coconut forests, and rural villages. The International Union for Conservation of Nature and Natural 211 Resources Red List of Threatened Species in 2007 rates the species as a "Least concern,"¹⁸ but future 212 habitat loss is predicted due to recent climate change.¹⁹ In the present report, two of the five victims were 213 bitten by snakes while farming in the fields, and the other three were bitten or spat at by snakes in their 214 houses. There is no clear distinction between wet and dry seasons in the Leyte region, but four cases were 215 seen in the drier season (March to May).

216 As with envenomation by other neurotoxic cobras, ptosis was observed in all bite cases; and, as 217 with N. philippinensis, the signs of envenomation were predominantly neurotoxic. In one paediatric case, 218 cardiac arrest resulted from respiratory arrest caused by respiratory muscle paralysis, confirming the 219 dangers of envenomation in the absence of appropriate prehospital care. In the previous study, patient age 220 younger than 12 years was one of the factors associated with severe systemic snakebite envenomation.²⁰ In 221 addition, N. samarensis appears to cause more severe local envenomation than N. philippinensis. Two of 222 the cases required surgical debridement due to progressive local necrosis. It has been reported that in cases 223 of N. philippinensis envenomation, local findings are often unremarkable.²¹ Recent venom analysis of N. 224samarensis has detected cytotoxic three finger toxins in addition to dominant short-chain alpha-neurotoxins 225 (SaNTX),²² which could explain the present findings. Even among the four bite cases, local envenoming 226 ranged from inconspicuous to necrosis. Larger case series is needed to indicate its clinical importance.

227 PCAV appeared effective in reversing neurotoxic signs of N. samarensis envenomation. For N. 228 philippinensis, 5-10 ampoules of PCAV are usually recommended initially, depending on the severity of 229 neurological symptoms, according to the protocol by RITM. In the present small case series, however, two 230 ampoules for moderate neurological symptoms and a total of six ampules even for respiratory paralysis 231 appeared effective. Hospitals have a limited supply of PCAV, and so small doses are administered. The 232 findings suggest that guidelines for N. philippinensis may not necessarily apply to N. samarensis 233 envenomation. The difference between the lower neutralising activity of PCAV against N. samarensis 234 venom in mice¹² and what is observed in this clinical practice needs to be verified by additional studies, 235 such as examining the neutralizing activity of PCAV against serum venom antigen levels in patients with 236 signs of envenomation. The rapid improvement in neurological signs suggests that the observed 237 neurotoxicity resulting from N. samarensis neurotoxicity is due to postsynaptic acetylcholine receptor 238 inhibition. The use of anti-acetylcholinesterase may be as effective, as in the case of N. philippinensis 239 envenoming. Neostigmine has been recommended as a first-aid or adjunctive treatment for envenoming by 240 other species whose neurotoxicity is predominantly post-synaptic, such as cobras and Oceanian death 241 adders (Acanthophis).5,6,23,24,25,26

242 It took 2-6 hours from bite to consultation, and two cases were seen by traditional healers. In 243 some cases, tourniquets, which are not recommended, were applied before they reached hospital. Improved 244 prehospital care is essential to improve the survival of snakebite victims.^{27,28} In future, it will be necessary 245 to identify communities with a high number of cases and conduct community-based educational activities 246 to promote appropriate first-aid. Improving logistics, such as means of transport and distribution of 247 antivenom, is also a long-term challenge. Killing of the snake responsible is not recommended and should 248be discouraged, both to prevent the risk of additional snakebites and to conserve these ecologically-249 important animals. In our series, except for case 3, the snakes were photographed after being killed by

250	patients or family members. Since attempting to capture the snake alive is even more dangerous, it will be
251	necessary to instruct people to take photographs safely, to allow identification of the causative snake, and
252	to leave the area as soon as possible to ensure their safety. Alternatively, immunodiagnosis should be
253	developed for the Philippines, for clinical and research purposes.
254	
255	4. Conclusion
256	We report five cases of N.samarensis envenomation. Small doses of PCAV were effective in treating
257	neurological symptoms. Further studies are needed, including the effects of PCAV against local
258	envenomation. Raising awareness in the community, about prehospital behaviour and management is
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268	All data generated or analysed during this study are included in this article. Further enquiries can be directed
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- 352

	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

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

354 envenomation.

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;