Severe neurotoxic envenomation following cobra bite in Northern Nigeria: A report of three cases

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Abstract

Cobra is a common snake throughout Africa and Asia, however, there are few literatures reporting neurotoxic cobra bite from Sub-Saharan Africa (SSA), including Northern Nigeria. Here, we report 3 cases that were bitten by cobra in the savannah region of Nigeria. All the 3 cases presented with features of severe neurotoxic envenomation: generalized hypotonia, ptosis, and features of autonomic dysfunction, which include excessive salivation and sweating. One of the 3 victims progressed to develop respiratory paralysis that resulted in death. The other 2 cases survived after receiving polyvalent anti-snake venom.

Introduction

Snake Bite Envenoming (SBE) is a major underappreciated medical and public health problem causing significant mortality and morbidity among rural dwellers throughout the tropics.[1] There are more than 3,000 species of snakes in the world, but in Africa, only a few of these are known to cause mortality, and these mainly belong to four families, *Viperidae* (vipers and adders), *Elapidae* (cobras and mambas), *Colubridae* (boomslang), and *Hydrophiidae* (sea snakes found in Coastal East and South Africa). Neurotoxic cobra is widely distributed in Africa, its venom contains several lethal neurotoxins. Clinical presentation is with progressive descending paralysis, starting with ptosis (drooping eyelids), external ophthalmoplegia (causing diplopia), and paralysis of the facial muscles, jaw, tongue, neck flexors (causing the "broken neck" sign).

Here, we report 3 cases of severe cobra related neurotoxic envenomation.[2]

Case reports

Case 1

A 28-year-old cleric who was rushed to the accident and emergency unit of an urban tertiary hospital on account of snakebite injury involving the left forearm of about 10 hours duration. This was reported to have occurred in the evening while the man was in his generator room trying to put on the electric generator. He subsequently developed pain at the site of the bite with swelling of the forearm. There was history of persistent vomiting and hyper-salivation. However, there was no history of bleeding from the site of bite, no hematemesis, hematuria or bleeding from any orifice. He later became confused with altered level of consciousness. No history of seizure or headache, no trauma to the head. Had associated history of breathlessness but no cough, no palpitation and no orthopnea or paroxysmal nocturnal dyspnea. Review of the other systems not contributory. Not a known hypertensive or diabetic with no history of alcohol ingestion or cigarette smoking. He is married with children.

On examination, we found a young man, with no evidence of pallor, cyanosis, jaundice, dehydration or edema state. He had normal cardiovascular examination findings. Was confused with a Glasgow Coma Score of 11/15. He was unable to hold his neck upright (Figure 1), with bilateral ptosis. Pupils were 3mm, equal and reactive to light. Tone was normal in all the limbs, power difficult to ascertain due to the impaired level of consciousness. Normal reflexes globally. Chest and abdominal examination findings were normal; 20 mins whole blood clotting test was normal.

An assessment of snakebite with neurotoxicity was made. Serum electrolyte, urea and creatinine were essentially normal. Had a packed cell volume of 36%. Received 20mls (2 vials) of intravenous polyvalent Anti-snake venom (EchiTab-plus). He was transferred to Intensive Care Unit (ICU) for close monitoring, though he was not intubated. Improved with resolution of symptoms and signs. Importantly, ptosis resolved, and patient became fully conscious. Was discharged home on the fifth day of admission.

Case 2

42-year-old snake charmer presented to General Hospital Kaltungo (GHK) with 7-hour history of snake bite on dorsum of left hand while displaying. The victim was bitten on 15/5/17 around 10:00am. Snake was brought alive in a plastic bucket and was identified as cobra (Naja melanoleuca). There was history of dysphagia, continuous tonic-clonic spasm, excessive salivation, vomiting, profuse sweating, difficulty in breathing, and was unable to talk.

On examination, there was mild swelling at the site of bite, was restless, with bilateral ptosis (Figure 2), pupils were dilated; 20 mins whole blood clotting test was normal. Received IV fluids and paracetamol, neither Anti-Snake Venom (ASV) no tensilon was available at the time of presentation. Died of respiratory paralysis around 3:00am on16/5/17.

Case 3

17 years old cattle herder presented to GHK with an hour history of snake bite on dorsum of left foot that happened while walking at home. The snake was killed, and the head brought to the hospital, which was identified as cobra (*Naja melanoleuca*). Had minimal bleeding and sharp pains at the site of bite. There was history of paraethesia on the affected limb, dysphagia, excessive salivation, sweating, difficulty in

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breathing and was unable to talk.

On examination the victim was weak, with bilateral ptosis (Figure 3), pupils were dilated. First Aid given includes attaching black stone to the site of bite, oral and topical traditional medication. 20 mins whole blood clotting test was normal.

Received 3 ampoules of Anti-snake venom ASV (Echitab plus), Intravenous Fluid, paracetamol and promethazine. He survived and recovered fully, was discharged on 17/6/17. Duration of hospital stay was seven days.

Discussion

Cobra neurotoxicity is typically associated with Ptosis, generalized hypotonia, and features of autonomic dysregulation. These features were observed in the 3 cases highlighted above. 20 mins whole blood clotting test was normal in all the 3 cases and coagulopathy did not develop.

The venoms of cobras and most other elapid species contain neurotoxins that induce a descending flaccid neuromuscular paralysis, which can include life-threatening blockade of bulbar and respiratory muscles. Two main types of neurotoxins are found in snake venoms: α-neurotoxins and β-neurotoxins. α-Neurotoxins belong to the threefinger toxin family and exert their action post-synaptically at neuromuscular junctions.[3] They bind with high affinity to the cholinergic receptors at the motor end plate, thereby inhibiting the binding of acetylcholine and provoking flaccid paralysis.[3] In contrast, β-neurotoxins are typically phospholipase A2 (PLA2s) that act at the presynaptic nerve terminal of neuromuscular junctions.[4] Upon binding to their targets, neurotoxic PLA2s induce enzymatic hydrolysis of phospholipids at the nerve terminal plasma membrane, which causes neurotoxicity.[5]

Case 1, the victim presented with typical features of neurotoxicity *i.e.* ptosis, confusion and inability to control the neck (broken neck sign) Figure 1. The incidence occurred in a semi-urban settlement in Northern Nigeria. Cobras are known to breed near human dwellings which implies that cases of snakebite envenomation can occur in both urban and semi-urban areas as reported in case 1.

The snake responsible for the bite was brought to the hospital alive by a snake charmer and close examination of the snake showed features consistent with *Naja sanegalensis*. These snakes are found in the savannah region of Africa, belong to the class of elapids/non-spitting cobras and are known to cause neurotoxic envenomation.[2]

The victim received 2 vials (20mls) of anti-snake venom (EchiTab-plus, a polyvalent anti-snake venom developed for managing envenomation caused by 3 most common Nigerian snakes: Echis ocelatus, Bitis ariantes, and Naja spp[6].). Symptoms and signs of neurotoxicity resolved completely within 48 hours. The victim was admitted to ICU though he had no intubation/artificial respiration. At presentation in the tertiary health center, there was stock-out of Anti-snake venom. The managing team was however able to get 2 vials of anti-snake venom (EchiTab plus) which was primarily bought for laboratory experiment.

Respiratory paralysis occurred in the 2nd case and is thought to occur due to venom neurotoxin acting post-synaptically at neuromuscular junction.[7,8] They bind with high affinity to the cholinergic receptor at the motor end plate in muscle fibres, thereby inhibiting the binding of acetylcholine and provoking flaccid paralysis.[7,8]

The 2 cases that survived proved that antivenom is of great value even when signs of neurotoxicity were established. The antivenom used was effective even though it was not developed to neutralize neurotoxic cobra envenomation. This could be explained by para-specificity, where antivenom neutralize the venom of few related species of snakes, in this instance Naja spp.

Scarcity of potent and effective anti-snake venom has been reported in SSA and affordability is a challenge for patients and health systems. Antivenom is the main intervention against snakebite envenomation but is relatively scarce, unaffordable and the situation has been compounded further by the cessation of production of effective antivenoms by major producers, and marketing of inappropriate products.[9,10,11]

Anti-snake venom minimizes the risk of death following neurotoxic envenomation.[10] None of the victims received anticholinesterase, an important intervention in the management of neurotoxic envenomation as it is not available in most parts of sub-Saharan Africa.

Dependence on antivenom imports places African countries at supply risk, since supply is solely from external sources.[11] It is important for African countries to prioritize local antivenom production through public-private partnership. Care and treatment of snakebite envenoming should be included in national health insurance schemes for rural populations to improve access and affordability of treatment.

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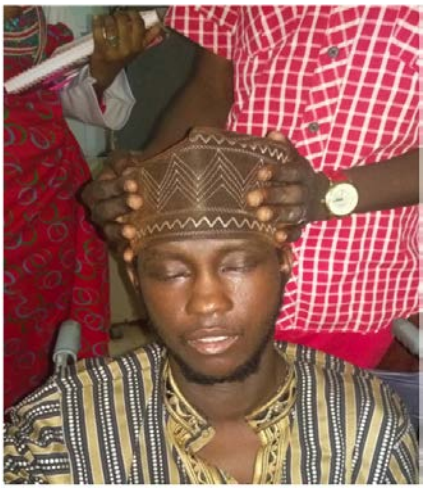

Figure 1. Neurotoxicity following cobra bite, showing bilateral ptosis and "broken neck sign": victim requires support to keep the neck erect.

Figure 2. Neurotoxicity following cobra bite, showing bilateral ptosis, external ophthalmoplegia and facial paralysis.

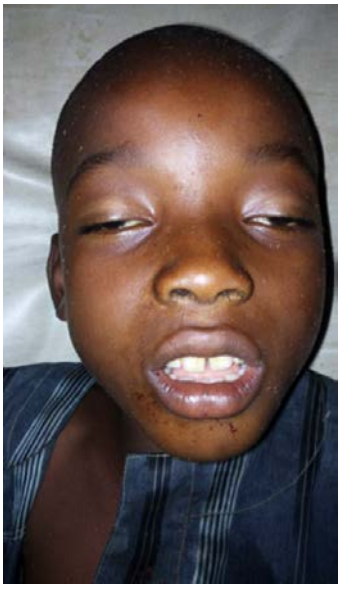

Figure 3. Neurotoxicity following cobra bite, showing bilateral ptosis.

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