

Dramatic neuromuscular paralysis following occult snakebites: An awareness for the primary care physician

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ABSTRACT

Neurotoxic snakebites are a common emergency in tropical countries and account for significant morbidity and mortality worldwide. Manifestations vary from mild ptosis and ophthalmoplegia to severe flaccid paralysis with ventilatory failure. At times, the neuromuscular paralysis may be severe enough for patients to be misdiagnosed as a locked-in syndrome or brain dead. Occult snakebites, wherein patients are unaware of the bite and fang marks are absent, have been reported in kraits, an endemic neurotoxic snake belonging to the Elapidae family. We report a series of three cases in which young males presented with dramatic neuromuscular paralysis and were likely suffering from elapid snake bites. Each of these patients presented an intriguing clinical challenge and had different in-hospital outcomes. Primary care physicians in the emergency department are usually the first respondents to such patients. Owing to a lack of snake bite history and unavailability of specific diagnostic tests, severe envenomation presents a challenge for physicians, unless they are aware of it and a high level of suspicion is maintained.

Keywords: Brain death mimics, krait envenomation, occult snakebite

Introduction

Neurotoxic snakebites, a common emergency in tropical countries, may manifest from mild ptosis and ophthalmoplegia to severe flaccid paralysis and respiratory failure. More severe neuromuscular paralysis has also been reported, labeled variously as locked-in syndrome,^[1,2] early morning neuroparalytic syndrome,^[3,4] or “brain dead” presentation.^[5,6] Although a majority of these cases are diagnosed by a history of snakebite or the presence of visible fang marks, occult snakebites, wherein patients are unaware of the bite and fang marks are absent, are an underreported entity leading to a lack of knowledge about

its existence. This has been described in kraits – an endemic neurotoxic snake belonging to the Elapidae family.^[7] They are believed to be nocturnal and possess small teeth. As a result, the victim is often unaware of the bite, and fang marks are invisible.

As primary care physicians are usually the first respondents to such patients, it is essential that they are aware of this entity to prevent misdiagnosis and delayed treatment. Owing to a lack of snakebite history and unavailability of specific diagnostic tests, this diagnosis presents a challenge for practicing physicians, unless they maintain a high degree of suspicion. Here, we report three cases of young males with dramatic neuromuscular paralysis likely suffering from occult krait bites, emphasizing the need for early recognition of this entity and prompt treatment with anti-snake venom (ASV). Awareness and good clinical judgment avoid unnecessary investigations and lead to excellent outcomes.

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Case Reports

Case 1

An 18-year-old male, with no premorbid conditions, had a sudden awakening from sleep at 1 am followed by abdominal pain, vomiting, tingling sensation in both lower limbs, and unresponsiveness within the next 1 h. He was transferred to a hospital where he was given preliminary treatment, intubated, and then referred to our emergency department with a provisional diagnosis of stroke. We were informed that he had slept on a low-lying cot the previous night. Despite repeated questioning, his relatives denied the possibility of snakebite or substance intoxication.

On arrival to our hospital, his Glasgow Coma Scale (GCS) was E1VTM1, his pulse rate was 90 beats per min, blood pressure 130/86 mm Hg, and SpO₂ 67% with no respiratory effort. Both his pupils were dilated and non-reactive to light, he was quadriplegic and had absent deep tendon and superficial reflexes with no movement on verbal commands and pain stimulus. Corneal as well as doll's eye reflex was absent, and he was presumed to be brain dead. Despite a thorough clinical examination, no fang marks were found. A differential diagnosis of unknown poisoning, pyogenic meningoencephalitis, Guillain Barré Syndrome and its variants, Miller Fisher-Bickerstaff overlap syndrome, posterior circulation stroke, subarachnoid hemorrhage, and cortical venous thrombosis was considered. Computed tomography (CT) brain and CT Angiogram and Venogram of head and neck vessels were done to look for the possibility of stroke, subarachnoid hemorrhage, and cortical venous thrombosis, but were within normal limits. He was transferred to the ICU and treatment was initiated with broad-spectrum antibiotics, proton-pump inhibitors, intravenous methylprednisolone pulse therapy, and mechanical ventilation.

Initial investigations revealed a raised total leukocyte count (TLC) of 18,900 cells/mm³, whereas his electrolytes and renal and liver function tests were within normal limits. Lumbar puncture was done considering an encephalitic process, but the cerebrospinal fluid (CSF) study was unremarkable. A toxicology screen was also performed which was negative. On the 4th day of ICU stay, he had flickering of fingers, and he developed spontaneous eye-opening. In view of inconclusive diagnostic tests, occult snakebite was considered as the likely diagnosis, and empirical polyvalent antsnake venom (ASV; Haffkine Institute, Mumbai) and intravenous neostigmine, a peripheral acetylcholinesterase inhibitor, was started on day 6. Considering GBS and Miller Fisher-Bickerstaff overlap syndrome, a repeat CSF study was done on day 8 but it failed to show albuminocytological dissociation, and Ganglioside IgM and IgG panel was negative.

He became responsive to verbal commands by day 9 of admission. Distal muscle power in all limbs improved gradually to Grade 4 by day 14, whereas proximal muscle power improved to Grade 3. Subsequently, he developed Ventilator-Associated Pneumonia (VAP), which was conservatively treated. He was weaned off ventilation on day 21 of admission.

Magnetic Resonance Imaging (MRI) Brain was within normal limits. By the end of week 4, he was discharged with a power of Grade 4 in both upper limbs and lower limbs, mid-dilated and sluggishly reactive pupils [Figure 1]. Nerve Conduction Study done after recovery revealed decreased compound muscle action potential (CMAP) amplitudes in peroneal, tibial, and ulnar nerves suggestive of critical illness neuropathy. At 1-month follow-up, he had regained Grade 5 power in all limbs, had normal deep tendon reflexes, and pupils were 2.5 mm in size and reactive to light [Figure 2].

Case 2

A 23-year-old male presented to the emergency department with acute breathlessness followed by loss of consciousness. He was sleeping on his bed the previous night, after which he woke up at around 3:00 am complaining of abdominal pain and breathlessness which was rapidly progressive. His GCS was E1V1M1, with absent deep tendon reflexes, atonia, and minimal respiratory effort. He was shifted to the ICU, intubated, and mechanically ventilated. There were no fang marks, and his relatives denied any history of snakebite. Initial investigations including CT Brain and CSF study were within normal limits. A diagnosis of occult snakebite was presumed, and 30 vials of ASV were administered on day 1, along with neostigmine, broad-spectrum antibiotics, and other supportive treatment. He developed spontaneous eye-opening on day 2 of ICU admission, with complete recovery of muscle power and reflexes in all limbs by day 4. He was weaned off ventilation, antibiotics were stepped down, and he was discharged in stable condition on day 7. At 1 month follow-up, the patient was asymptomatic and had no residual weakness or disability.

Case 3

A 20-year-old male who had slept on the ground at night was brought to our hospital in an unconscious state. He had experienced abdominal pain and multiple episodes of vomiting an hour before losing consciousness. At presentation, his GCS was E2V1M1 with a pulse rate of 124 beats per min and blood



Figure 1: Patient 1 at the time of discharge



Figure 2: Patient 1 at 1-month follow up

pressure of 98/66 mm Hg. He had no respiratory effort, and his SpO₂ was 60%. Again, fang marks were absent. He was immediately intubated and mechanically ventilated. He had flaccid paralysis of all muscles with areflexia.

Arterial blood gas (ABG) analysis revealed severe respiratory acidosis with a pCO₂ of 95 mm Hg which was corrected by mechanical ventilation. Other investigations were within normal limits. He was treated with 20 vials of antsnake venom (ASV) and neostigmine and responded dramatically within 8 h with the recovery of Grade 3 power in all limbs, spontaneous eye-opening, and ability to follow verbal commands. However, on day 2 of admission, he developed complications of tube block and severe respiratory acidosis to which he succumbed despite resuscitative measures.

Discussion

It is estimated that 5.4 million people are bitten by snakes every year.^[8] Furthermore, almost half of these bites occur in India, and out of these nearly 60,000 people die every annually.^[9] Given the burden of this disease; it is imperative that physicians are aware of its varying presentations. The two most important families of venomous snakes are Elapidae and Viperidae. Elapids commonly found in South-East Asia are kraits, cobras, coral snakes, and sea snakes. They have shorter and more erect fangs, compared to the Viperidae group, and envenomation from many, but not all frequently leads to flaccid paralysis.

Krait bites are sometimes painless and occur during the night. Often, a history of snakebite and visible fang marks are absent.^[10] Patients usually experience symptoms like abdominal pain, nausea, vomiting, and malaise. This is followed by ptosis, external ophthalmoplegia, distal muscle weakness, and lastly diaphragmatic and respiratory muscle involvement. Respiratory failure is the most common cause of death. Autonomic dysfunction leads to internal ophthalmoplegia thus mimicking brain death.^[11] Most snake neurotoxins, however, do not cross the blood-brain barrier,^[12] and act at the neuromuscular

junction either presynaptically, postsynaptically, or both. The bungarotoxin (Krait toxin) is a Phospholipase A2 neurotoxin and acts on the presynaptic junction.

In the first case, our initial suspicion revolved predominantly around the possibility of (GBS), drug intoxication, and stroke. As the bedside Nerve Conduction Study was not available at our hospital, we had to rely on CSF studies and Ganglioside antibody panel to exclude GBS. A negative toxicology screen and a normal CT brain prompted us to look for other alternatives.

As we could not reach a conclusive diagnosis despite all available investigations and the similarity of our patient's presentation to an occult Krait bite, we empirically treated him with ASV and an anticholinesterase. However, due to delayed initiation of antivenom, it remains unclear whether he responded to ASV or had a spontaneous recovery. Polyvalent antsnake venom available in India is effective against *Naja naja* (Cobra), *Bungarus caeruleus* (Krait), *Daboia russelii* (Russell's viper), and *Echis carinatus* (Saw-scaled viper) and is produced by more than seven pharmaceutical laboratories.^[13]

Subsequently, two patients presented to our emergency department with symptoms having a striking similarity to the first case. In both these patients, we had an early suspicion of snakebite and initiated therapy with ASV and anticholinesterase promptly. Both patients showed a remarkable response to therapy and, despite the unfortunate outcome in the third case, based on the recovery in power and improvement in consciousness level, we can attribute his presentation to an occult snakebite mimicking brain death.

It has been reported that the inability of primary care physicians to recognize systemic signs of envenomation is an important cause of mortality in snakebites.^[14] Although such dramatic neuromuscular paralysis has been reported previously, it is an altogether infrequent presentation and maybe frequently misdiagnosed as brain death by treating primary care physicians and neurologists, as they are unaware of this entity. This may lead to premature withdrawal of supportive care and disastrous outcomes. Before evaluating a patient for brain death, the patient should have an established neurologic diagnosis that can lead to the complete and irreversible loss of all brain function.^[15] As blood flow studies and bedside electroencephalogram (EEG) facility are not available at our center, they could not be performed at presentation for these patients to confirm or exclude brain death at the outset. This would be ideal in a more equipped center.

In summary, the above cases highlight the important role of primary care physicians in recognizing occult dramatic neurotoxic snakebites and subsequent severe neuromuscular paralysis as an important treatable medical emergency. In patients presenting with unexplained neuromuscular paralysis, especially with onset early in the morning, it is important to consider an elapid snakebite even without evidence of fang marks or a history

of snakebite. Early and appropriate treatment usually leads to complete recovery and excellent outcomes.

Declaration of patient consent

Written informed consent has been obtained from patients/next of kin for this publication.

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Conflicts of interest

There are no conflicts of interest.

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