Short Communication

# Neurological Consequences of Snakebite: What One Should Know

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**ABSTRACT**

Central nervous system manifestations due to venomous neurotoxic snakebite have varied presentations, followed by survival or fatality. Early recognition, timely intubation and ventilator support, along with antisnake venom and supportive measures, are all crucial for a favourable outcome.

**Key Words:** Venomous snakebite; Neurotoxic snakebite; Antisnake venom; ASV

## INTRODUCTION

Neuroparalytic snakebite is one of the common life-threatening medical emergencies encountered in Indian hospitals, particularly in rural and farm areas, especially after the onset of monsoon. Snakebite is a familiar occupational hazard of farmers, rubber, coffee and other plantation workers, fishermen, and those who handle snakes, resulting in thousands of deaths each year, and innumerable cases of chronic physical handicap. India has the highest number of deaths (35,000–50,000 people dying per year) due to snakebites.[1] The neurological consequences of snakebite are predominantly the result of inhibition of neuromuscular transmission. Symptoms and signs vary according to the species of snake responsible for the bite and the amount of venom injected.[1]

## DISCUSSION

Various neurological manifestations and complications are related to venom affecting the coagulation cascade, the neuromuscular transmission, or both. Venom of vipers contain metalloproteinases, serine proteases, and C-type lentins having anticoagulant or procoagulant activity, and either agonists or antagonists of platelet aggregation, which may lead to ischaemic or haemorrhagic strokes. Phospholipase $A_2$, beta-bungarotoxin and three-finger proteins (common in elapids) are potent neurotoxins affecting the neuromuscular transmission at either presynaptic or post-synaptic levels, which inhibit peripheral nerve impulses causing muscle weakness. Presynaptic beta-neurotoxins inhibit the release of acetylcholine, and post-synaptic alpha-neurotoxins cause a reversible blockage of acetylcholine receptors. Most snake venoms have multisystem effects on their victims.[2]

Neurotoxic envenomations have the potential to cause a broad spectrum of presentations. The common neurological manifestations are alteration in the level of consciousness, paraesthesiae, abnormalities of taste and smell, ptosis, heavy eyelids, external ophthalmoplegia, paralysis of facial muscles and other muscles innervated by the cranial nerves, aphonia, palatal weakness, difficulty in swallowing secretions, neck muscle weakness, limb weakness, respiratory failure, generalised flaccid paralysis, and delayed sensory neuropathy. Most of the neurological symptoms are noticed usually within 6 hrs after the bite.[1,3]

Other less common manifestaions includes ischaemic stroke, haemorrhagic stroke (meningism from subarachnoid haemorrhage, lateralizing signs and/or coma from cerebral haemorrhage), posterior circulation stroke, locked-in syndrome, cerebellar ataxia, diffuse encephalopathy, or widespread cerebral hypoxia and associated focal neurological deficits, bilateral optic neuritis, delayed peripheral neuropathy, cortical blindness, anterograde memory loss and acute disseminated encephalomyelitis.[1,4-13]

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Possible mechanism of ischaemic stroke in snakebite patients include disseminated intravascular coagulation, endothelial damage, toxin-induced vasculitis resulting in thrombosis and hypotension due to hypovolaemia leading to watershed infarct.[5,14] Blindness in snakebite can be due to retinal cell damage causing bilateral optic neuritis or cortical blindness. The major causes of cortical blindness are asphyxia, hypoxia or ischaemia. Direct effect of the venom or hypersensitivity reaction to antisnake venom (ASV) or extensive haemorrhage and capillary damage can cause retinal or optic nerve damage.[10,15]

Locked-in syndrome is a severe form of neuromuscular junction blockade characterized by quadriparesis and anarthria in conscious patients. Communication is possible only by means of eye movements and blinking.[6] Brain death secondary to prolonged hypoxia may occur, but adequate ventilation can improve the neurological functions.[16] Features of delayed neurotoxicity including cerebellar ataxia and ADEM (acute disseminated encephalomyelitis) can occur due to demyelination, or structural damage to nerve endings or nerve fibres, which could be responsible for such manifestations.[7,13] The immunopathogenesis of demyelination following snakebite may be related to molecular mimicry between one of the components of snake venom and myelin, and subsequent generation of pathogenic auto-antibodies causing myelin damage, or it may also develop as a consequence of a serum sickness-like reaction to the administration of antivenin.[11]

Guillain Barre syndrome (GBS) following snakebite is very unusual, but has been observed by a few authors.[9,17] Electrodiagnostic studies were suggestive of motor and sensory neuropathy, primarily demyelination with secondary axonal degeneration. Features of GBS can be attributed to the snakebite or the administration of tetanus toxoid or antisnake venom.[9,17]

Neurological symptoms commonly develop from 30 min to 2 hrs after the bite.[3] In cases of neurotoxic envenomation with respiratory failure and neuromuscular paralysis, early administration of antisnake venom, anticholinestrase therapy and cardio-respiratory support remain the mainstay of treatment.[18]

Role of mechanical ventilation is to prevent death, expedite recovery, and to prevent hypoxic injury to brain. Timely intubation should be given to those who are unable to protect their airway with signs of bulbar paralysis (reduced gag reflex, reduced cough reflex, inability to swallow, and speak leading to collection of secretions and drooling of saliva). Ventilatory support should be started in those patients with loss of consciousness, marked respiratory distress due to aspiration, or respiratory muscle paralysis leading to respiratory failure, low oxygen saturation and haemodynamically unstable patients (patients with hypotension and shock on arrival).[19] Timely institution of antisnake venom and ventilatory support are associated with excellent outcomes.[20,21]

## CONCLUSION

We conclude that the CNS manifestations of snakebite are varied and the possibility of snakebite should always be entertained by physicians in patients with unexplained neuroparalytic syndrome even in the absence of history of snakebite, in endemic areas. Management should be started early and before the occurrence of irreversible hypoxic insult to brain.

Central nervous system (CNS) manifestations of snakebite are varied. The target of neurotoxin is primarily at the neuromuscular junction, which may be pre-synaptic or post-synaptic. CNS complications are due to direct toxic effect of venom leading to cerebral bleed due to haemotoxins, or may be secondary to hypoxic ischaemic injury as a consequence of massive bleed leading to haemodynamic instability. Neurotoxic envenomation can cause respiratory muscle paralysis leading to hypoxia and hypoxic encephalopathy. The hypoxic effect on brain is likely to be related to prolonged respiratory paralysis and cardiac arrest that may occur following neurotoxic envenomation.

Demyelination may be due to direct effect of toxin or iatrogenic (antisnake venom administration). The signs of brain death may be misleading when the patient is under the effect of neurotoxic envenomation. Therefore, mechanical ventilation should be continued despite features suggestive of brain stem dysfunction, locked in syndrome or apparent death, as it may sometimes take more than a few days before the response becomes apparent.

Early hospital referral is necessary for better management to reduce fatalities. Timely intubation is crucial to prevent death or hypoxic injury to brain, and therefore it is important that all neurotoxic snakebite patients be promptly intubated at the right time before it is too late.

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