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Early Morning Bulbar Weakness, Why and When to Suspect Snake Bite

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Abstract: ***Snakebite is a neglected tropical disease which is of global importance. The severity of respiratory muscle paralysis and the time to recover depends upon the dose of the venom injected, the severity of the venom, the species of the snake, the time of presentation to the hospital, and the time and dose of administration of anti - snake venom (ASV). The reasons for this delayed neuromuscular recovery still remain a stumper. We have highlighted such a case of a young adult who had delayed neuromuscular recovery and prolonged ventilatory support following a neurotoxic snakebite.***

Keywords: Snake bite; Ptosis

1. Introduction

Globally snake envenoming is a major cause of morbidity and mortality in the rural tropics [1]. Neurotoxicity causing paralysis is one of the major clinical syndromes of snake envenomation and it occurs mainly with the elapids (Australasian elapids, American coral snakes, Asian kraits and some cobra species) [2, 3]. Envenoming may result in prolonged hospital stay if ventilatory support is available or significant mortality where such medical resources are not available. Despite the magnitude of the health impact of neurotoxic snake envenomation, it continues to be associated with several unresolved issues of clinical importance [2]. Envenoming due to krait (Genus: Bungarus) bites is common and is also a serious health issue in South and South - East Asia. Common krait (Bungaruscaeruleus) is distributed throughout South Asia, and is responsible for large numbers of cases of severe neurotoxic envenoming each year[4]. The common krait, is nocturnal, terrestrial snake that enters human dwellings in search of prey such as rats, mice, and lizards during the course of hunting activity[5]. It usually resides in the vicinity of human habitation, near the mud, small hut, dwelling wattle and daub, hunts nocturnally, and isquick to bite people sleeping on the floor, often without waking their victims since venom is painless and associated with minimal local changes. [6] It results in a descending flaccid paralysis progressing to life threatening respiratory paralysis unless mechanical ventilation is available. [7 - 9] Krait venom contains β - bungarotoxins, which are presynaptic neurotoxins with phospholipase A2 activity and considered to be the major cause of paralysis [10]. The pre - synaptic action is irreversible and is the reason that once paralysis develops it is not reversed with antivenom. [11]Cobra bites tend to occur during daytime and early darkness while walking outside, and improper or careless handling while rescuing the cobra. Cobra bites results in tender local swelling, blistering and necrosis. Victims may experience severe pain at bite site having fang marks, with rapid progression of swelling. Skin around the bite site is ecchymosed. Subsequent formation of tense blebs and massive damage of skin and subcutaneous tissue occurs due to myocytolysis. [12]Cobra venom is rich in postsynaptic neurotoxins called alpha - bungarotoxin and cobratoxin, which bind, especially to postsynaptic acetylcholine receptors, preventing the interaction between Achand receptors on postsynaptic membrane, resulting in neuromuscular blockade. Cardiotoxin content of cobra venom has direct action on cardiac and smooth muscles causing circulatory failure, cardiac arrhythmias, various heart blocks, and cardiac arrest. Cobra venom has smaller molecular size hence it is rapidly absorbed intocirculation. Cobra unlike the krait deposits its venom deeply. This in combination with hyaluronidase allows spread of the venom rapidly and symptoms to arise abruptly. Absorption is further accelerated by running due to fear and the liberated catecholamines can kill the victim within8 min [13]. Paralysis is heralded byptosis followed by ophthalmoplegia. Blurring of vision and loss of accommodation are earliest sign of neurological envenomation. Paralysis of facial, neck, tongue and palatal muscles follow. Respiratory failure, precipitated by upper airway obstruction and paralysis of intercostals and diaphragm, is the usual cause of death. [6]Here, we report a case of a 15 - year - old boy who presented with features of neurotoxic snake bite, had a long duration of hospital stay and prolonged ventilatory support, and had a delayed neuromuscular recovery.

2. Case Report

A 15 year old male, was brought to the emergency department by his family around 7.00 am. He had a history of abdominal pain around 2.00 am, while he was sleeping on the floor followed by acute onset of breathlessness since 3.00 am. The patient subsequently developed dropping of eyelids. He was brought to hospital after receiving first aid at nearby primary health center. At the time of admission, patient was irritable, dyspneic, partially obeys oral commands, a febrile, tachycardiac (118beats/min), tachypneic (30breath/ minute), normotensive (120/ 80mmHg), hypoxemic Spo2 - 80% on room air, 94%with 15LO2 with severe respiratory acidosis (Ph 7.08, PCo2 80 mmHg) and had no fang marks, no external markers and injuries. Respiratory system revealed bilateralextensive wheeze. Cardiovascular examination showed noabnormality. Neurological examination revealed bilateral ptosis with bilateral external ophthalmoplegia with pupils sluggishly

reactive to light and bilateral plantar mute. In the view of his worsening respiratory failure due to poor respiratory efforts, he was intubated and started on mechanical ventilation. His base line blood investigations were normal. His whole blood 20minute clotting time (WBCT) did not reveal any coagulation abnormalities. In view of H/o sleeping in the floor and H/o seeing snakes multiple times in his home, he was given an initial dose of 10 vials of polyvalent ASV (each vial neutralizing 0.6 mg of cobra (Najanaja) venom, 0.45 mg of common krait (Bungaruscaeruleus) venom, 0.6 mg of Russell's viper (Viperarusselli) venom, and 0.45 mg of saw - scaled viper (Echiscarinatus) as an intravenous infusion in normal saline over 45 minutes, and since there was no improvement in his neurological status, a further 10 vials of polyvalent ASV were given over another 45 minutes in a similar fashion.

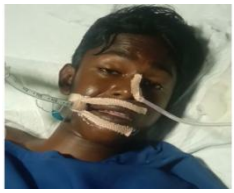

Figure 1

On day 2 of hospital admission, as the patient was continued to be on ventilator support, patient underwent MRI brain imaging to rule out intracranial pathology which was normal. Bplood investigations showed no electrolyte abnormality and RFT, AntiAchRantibody, Anti Musk Ab were normal. As there were no meningeal signs, CSF analysis was not done. The possibility of OPC was considered in the view of respiratory paralysis. It was ruled out by his serum cholinesterase was 7252U/L. (normal range 4500 to 11000 U/L). On day 3 (figure - 2), he started to show minimal response to painful stimuli. Multiple attempts for Ventilatory support was unsuccessful in view of his persistent muscle weakness. On day 4 he started to show good response to oral commands, moved all four limbs, but bilateral ptosis with ophthalmoplegiadid not improve. On day 5, ptosis improved and slightly he was able to move the eye ball in all directions (figure - 2).

Figure 2

On day 6 (figure - 3), ptosis completely recovered and EOM was full and patient was able to hold his neck and weaning process was started.

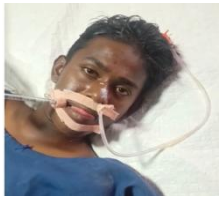

Figure - 3

On day 7 of admission, he was finally weaned off the ventilation and was maintaining adequate saturation on room air. Patient was shifted out from ICU on day 7 and was treated in the ward. On day 8 he had difficulty in lifting left hand, x ray showed no shoulder dislocation. NCS (FIGURE - 4) showed axonotmesis of left axillary and musculocutanous nerve. Physiotherapy was given. On day 12 patient was discharged and advised for regular follow up.

3. Discussion

The common venomous snakes in India belong to the cobra species and krait species, which are members of the Elapidae family [14]. The envenomation by these snakes results in neurotoxicity. Neurotoxicity can result in acute neuromuscular paralysis of all muscles, including respiratory muscles and bulbar muscles, and direct toxicity to the nerves. The variations in the clinical presentations of patients with neurotoxic envenomation may be due to the variations in the constituent toxins of the venom across seasons, geographical areas, and genetic difference within the species. In patients who have a prolonged course of manifestations due to snakebite, may attribute to various possible reasons, such as the dose of the venom injected, the dose of the ASV administered, the makeup of the snake venom injectedand the delay in presentation to the hospital. [15]

The venom of Elapidae contains neurotoxins that is classified into alpha and beta bungarotoxins. Alpha bungaro toxins secreted by cobra act postsynaptically, whereas beta toxins secreted by krait species act presynaptically. [16]Beta bungarotoxins contain predominantly phospholipase A2, which can lead to the depletion of synaptic vesicles from the motor nerve terminals of the skeletal muscle which is followed by the destruction of the motor nerve terminal and the degeneration of the intramuscular axonal cytoskeleton by disrupting the phospholipids present in the cell membranes. [17]Presynaptic neurotoxins results in irreversible nerve injury, hence the neurotoxicity is expected not to respond to antivenom once it has developed. Despite the patient received early antivenom and antivenom rapidly clearing free venom in blood, the paralysis got worsened and required prolonged mechanical ventilation for several days. Antivenom cannot reverse neuromuscular injury and recovery occurs through the natural nerve terminal repair [18, 19] This demonstrate that Indian polyvalent antivenom is efficacious (binds venom) but is not effective for common kraitbecause of the irreversibility of the pre - synaptic neurotoxicity. [20] Antivenom was able to clear circulating free venom, so given early enough antivenom may still be beneficial in preventing progression of neuromuscular dysfunction. It has been demonstrated in studies of Papuan taipan bites where early anti venom (<6h post - bite) has reduced the number of patients requiring intubation. [21]

4. Conclusion

The delayed recovery of neurotoxicity features is attributed to direct injury to nerve terminals and the poor response to ASV treatment and anticholinesterase drugs is attributed to presynaptic damage. Although some patients may mimic other neurological conditions such as Myasthenia Crisis,

GuillianBarre Syndrome it is necessary to remember the possibility of snake envenomation in such patients, especially when there is no clear history available. Differential diagnosis of krait snake envenomation is considered in a patient with early morning bulbar weakness, even if no clear bite history available and as bites are painless due to abscene of local reaction and thin delicate fangs. Hence occult snake bite envenomation must be suspected if patient had abdominal pain with no fang mark, sleeping on the floor and with previous history of seeing snakes in their home. The acute abdomen like picture in Krait bite envenomation has been attributed to submucosal erosion by postpartum studies whether it is a part of bleeding manifestation or due to autonomic neuropathy is a question to be addressed. Monovalent ASV and better anticholinergic drugs with more targeted action and nerve growth factor were needed for better outcome.

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