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Clinical case report based study

Severe hypertension in elapid envenomation

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ABSTRACT

Snakebite is not an uncommon medical emergency in India; however, symptoms of autonomic dysfunction in snakebite are rare. The elapid snake envenomation is a frequent occurrence in India, and the krait bite is prevalent in the south Indian region. Here, we present three cases of snakebite with severe hypertension and requiring intravenous nitroglycerin (NTG). As the level of blood pressure (BP) decreased significantly following antisnake venom (ASV) injection in all three cases, it is likely that snake venom-induced dysautonomia might have contributed to severe hypertension in such patients. Clinical and therapeutic challenges of these cases are highlighted, so that practitioners coping with medical emergencies in resource-limited situations can consider snake (krait) bite in the differential diagnosis, and also manage effectively according to corroborative clinical evidences.

1. Introduction

Snake envenomation is a common medical emergency in India with an estimated mortality rate of 35,000–50,000 people per annum.[1] Indeed, elapid snake envenomation has been recorded as a frequent occurrence in India, in which the common (or 'Indian') krait species (*Bungarus caeruleus*) is also included. The classic symptoms observed in krait bite (which is often described as painless) are early morning symptoms such as abdominal pain or cramps,[2] together with progressive muscular paralysis which often commences with ptosis.

Here, we present three cases of elapid envenomation with severe hypertension requiring intravenous antihypertensives. Interestingly, snake (krait) bite was unknown to all three individuals, but was brought out after an elaborate history and conducting a detailed physical examination. These cases are presented to create an awareness of such issues amongst those practicing under resource-limited environs wherein snakebites are prevalent.

2. Case reports

2.1. Case 1

A 26-year-old male farmer was referred to the emergency room in the early morning from a peripheral hospital for high blood pressure (BP). He complained of giddiness, abdominal pain, and vomiting. His past medical or family history was not contributory. He was a nonsmoker, nonalcoholic, and not taking any form of medication. He had never been diagnosed to have hypertension, diabetes, or kidney diseases, and was using neither traditional herbal medication nor illicit drugs. He also denied having febrile episodes or any particular fear, anxiety, or emotional distress. On admission, his supine brachial BP was 240/180 mmHg with a strong peripheral pulse, and there was no significant difference in the measurements between the arms. The physical examination including fundus revealed no abnormalities. Laboratory tests including complete blood count, serum electrolytes (with an expected low potassium level), hepatic and renal function tests, coagulation profile, toxicology screen, urinary catecholamines, and renin/aldosterone were unremarkable. An electrocardiogram showed normal sinus rhythm without any evidence of left ventricular hypertrophy. The urinalysis showed no proteinuria. Chest radiograph, ultrasound of the abdomen, and a head-computed tomography scan were found to be noncontributory toward hypertension. Meanwhile, 90 min after admission, he developed ptosis and external ophthalmoplegia, and complained of difficulty in breathing, swallowing, and speaking. He became cyanotic and his level of sensorium started declining. He was electively intubated and mechanically ventilated. Even with adequate sedation, there was a fluctuation in heart rate and the BP remained persistently high (range: 220–240 mmHg systolic and 160–180 mmHg diastolic). Though intravenous nitroglycerin (NTG) infusion was commenced to control hypertension, BP levels remained the same

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as those measured preinfusion. The rapidly progressive ptosis, diplopia, dysphasia, dysarthria, dyspnea, and weakness raised a suspicion of neuroparalytic symptoms observable following snakebite. Further, careful examination of the patient's skin revealed a fang mark of snakebite in the lateral aspect of the left leg with evidence of regional lymphadenopathy (he did not give a history of any possible snakebite). On benefit of doubt, the injection of polyvalent antisnake venom (ASV, 10 vials) was instigated. Through the next 6 h, his neurological status and hypertension gradually improved, and then NTG infusion was tapered and terminated. He was extubated after 36 h of mechanical ventilation, and then discharged after five days of hospital stay (his BP during the hospital stay period was within normal limits). During the follow-up, he was found to be perfectly healthy with normal BP values.

2.2. Case 2

A 24-year-old married woman was admitted to the Emergency Department (ED) of our hospital with a sudden episode of nausea, vomiting, and abdominal pain, and became acutely unwell whilst at work early in the morning. Her periods were normal and pregnancy test was negative. There was no past medical history, and she was not on any regular medication. On examination, she was of normal body weight, and afebrile with stable vitals. Her BP was 210/150 mmHg with no postural changes and without significant differences in these values between the arms. The physical examination and investigations (as outlined in case 1) were within normal limits. One hour after admission, the patient developed dysphagia and difficulty in breathing, following which she became delirious and experienced apnea. She was immediately put on ventilatory support. She had bilateral ptosis with reactive pupils. A thorough history of the dwelling and sleeping habits of her family revealed crucial evidence. Being farmers, they resided close to the fields and frequently slept on the floor. Further careful examination of the patient's skin revealed a fang mark characteristic of snakebite in the dorsum of her right foot, with evidence of regional lymphadenopathy. Based on clinical findings and corroborative evidences, 10 vials of polyvalent ASV in 100 mL of 0.9% saline were administered to her. During the following 6 h, she displayed marked neurological improvement and her BP values diminished. She was weaned off the ventilator 36 h later and was discharged from the hospital on day 4. During the follow-up, she was perfectly healthy with normal BP levels.

2.3. Case 3

A 35-year-old male presented to the ED with abnormal sensations all over his body when he got up from sleep early in the morning. He also had nausea, abdominal pain, and giddiness; he had no other significant past medical history. On examination, his BP was 200/140 mmHg with a normal general and systemic examination. The pertinent laboratory parameters and imaging tests (detailed in case 1) revealed no abnormalities. He was kept under observation for further evaluation and NTG infusion was commenced. He subsequently developed acute paralysis with respiratory failure 2 h after arrival at the hospital. He was intubated and then put on continuous mechanical ventilation. At this point, he had partial ptosis, dilated pupils, complete external ophthalmoplegia, and flaccid quadriparesis, with a flexor plantar response. A fang mark characteristic of snakebite was seen in the lateral aspect of the right leg and he was started on a standard dose of injection ASV. After 2 h of ASV infusion, he began to show spontaneous respiratory effort and required mechanical ventilation for a further 12 h. His BP became normal within 3 h of commencement of ASV. His neurological manifestations resolved over the next two days, and he was discharged after four days from his day of admission. Follow-up visits were uneventful.

In all the three cases, the snake was identified as a krait. It is well known that kraits are active and agile at night, and during the rainy season, they frequently seek refuge in dry places, such as those inside a house or dwelling place. Additionally, if humans are bitten by this snake during their sleep, they are seldom aware of it, as their experience of the bite generally resembles that from an ant or a mosquito, a phenomenon giving rise to a false level of reassurance to the victim.

3. Discussion

Elapid envenomation predominantly gives rise to neurotoxicity, a consequence of neuromuscular blockade, which manifests as paralysis of the bulbar, ocular, limb, and respiratory muscles, leading to respiratory failure.[3] The elapid venom contains both presynaptic and postsynaptic neurotoxins; however, krait venom exerts a predominant action in presynaptic neurons.[3] Predominantly, presynaptic neurotoxins present in the venom of the *Bungarus* species are highly potent and suppress the capacity of neuron endings to release biochemical transmitters. Transmitter release is primarily blocked subsequent to envenomation with such bungarotoxins (giving rise to a brief paralysis), a process followed by a period of substantial overexcitation (including cramps, spasms, and tremors), which, in turn, leads to further paralysis.

Hypertension in our cases was probably ascribable to snake venom, as the secondary causes of hypertension were ruled out. Moreover, BP levels normalized following ASV therapy, and the recoveries from neuromuscular paralysis observed indicate that krait venom might have contributed toward hypertensive episodes in such cases. Autonomic dysfunction following snakebite may induce various symptoms such as abdominal pain, vomiting, sweating, and mild-to-moderate hypertension or hypotension, and cardiac arrhythmia. In a previous study, it was observed that more than 50% of the patients with krait bite had elevated BP.[4] However, severe hypertension subsequent to snake envenomation and requiring intravenous NTG is under-reported.[5] The pathogenesis for autonomic dysfunction in snakebite is unclear. However, it may be attributable to the presynaptic alpha-2 adrenoreceptor inhibition by elapid neurotoxin, thereby blocking inhibition of the neutrally mediated release of norepinephrine. Hence, this process gives rise to sympathetic overactivity and decreased parasympathetic stimulation.[4,6] A patient who was bitten by a Malayan krait experienced sweating, tachycardia, dilated pupils, and hypertension arising from parasympathetic abnormalities.[7]

In a case of a *Vipera berus bosniensis* bite in Hungary, a high BP of 200/120 mmHg was recorded, with the victim responding promptly to the administration of an angiotensin-converting enzyme (ACE) inhibitor. Hence, the authors of this case report suggested that the venom of certain of the *Vipera* population may contain cardiotoxins, which have the potential to act at or via autonomic synapses[8]; moreover, snake venom releases catecholamines which influence BP.[9] Hypertension without neurotoxic symptoms was observed in patients with Western Russell's viper envenomation,[10] and neurotoxic signs without hypertension were observed in an episode of the Eastern Russell's viper envenomation. It therefore appears that different toxins are responsible for cardiovascular and neurological symptoms.[9] Further attributable causes for hypertension are pain, distress, or hypoxia. However, severe hypertension in such cases is extremely rare. Additionally, the normalization of BP with improvements in autonomic function increases the possibility of a relationship between the venom and hypertension.

A limitation of this report is nonconfirmation of snakebite by immunoassay methods in view of technical limitations and the unavailability of facilities to perform such screening tests.

4. Conclusions

In conclusion, physicians should consider the possibility of severe hypertension in neurotoxic snake envenomation which may be ascribable to autonomic storm. Such patients may require intravenous NTG for the control of hypertension, together with other conventional management protocols for snakebite. The drug of choice for the management of severe hypertension in such cases is NTG. Preferably, beta-blockers should be avoided in such situations where there is an excess of catecholamines, as these agents can precipitate severe alpha-agonist effects via the blockage of beta-receptor effects.

Conflicts of interest

All authors have none to declare.

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