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SNAKEBITE POISONING - LEUKOENCEHALOPATHY: A CASE REPORT

Anaesthesiology

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ABSTRACT

Snake bite has been considered to be a fatal rather than harmful to life with regards to severe adversities in the form of mortality and morbidity in tropical and subtropical countries like India. Aftermath of neurological deficits have been very well postulated following vasculotoxic snake bite which trigger intracranial hemorrhage or subarachnoid bleed commencing due to consumption coagulopathy. In addition to this ischemic strokes and acute disseminated encephalomyelitis have also been detected in some instances. One case of snake bite is hereby reported leading to leukoencephalopathy. Impact of neurotoxins may trigger within minutes extending upto a few hours following inoculation of venom thus causing fatigue, drowsiness, weakness and trauma concerning to blockage of synaptic transmission at either presynaptic or postsynaptic levels. Occasionally, cerebral infarction may not be due to snake bite and may be owing to underlying medical illness.

KEYWORDS

INTRODUCTION

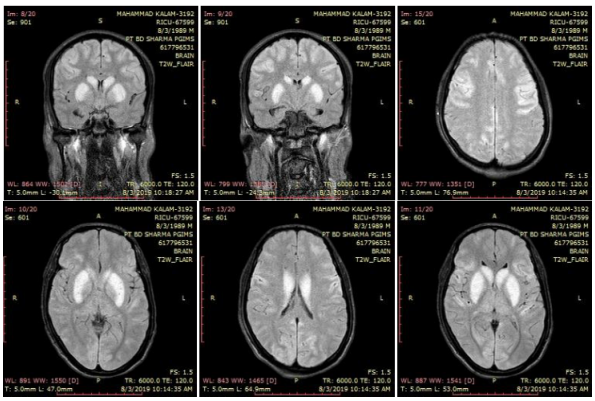
Snake bites are very common in India especially in the rainy season (June-September). Depending on their fang marks poisonous snakes are classified into five families. In India only three families of snakes namely Viperidae (Vipers), Elapidae (Cobra and Krait) and Hydrophidae (Sea snakes) are commonly found. Elapidae (King cobra) one of the leading cause of fatal snake bite in India. Venom components may have cytotoxic, hypotensive, neurotoxic, and anticoagulant or procoagulant effects, which account for the local and systemic clinical manifestations of snake bites.[1] Relevant snake venom toxins include metalloproteinases (factor X activators), serine proteases (prothrombin activators), snake venom C-type lectins, and three-finger toxins (anticoagulant or procoagulant activity).[2]

Neurological manifestations are the most feared complications of venomous snake bites, because they add significant morbidity and mortality to the victims.[3] These are not caused by direct toxic effects of the venom within the central nervous system, because venom proteins do not cross the blood-brain barrier. Instead, they are most often related to blockage of the neuromuscular transmission, causing paralysis,[4] and abnormalities in the coagulation cascade (or other more complex pathogenetic mechanisms), producing cerebrovascular events.[5] Stroke occurring in the setting of a venomous snake bite may be hemorrhagic or ischemic. Although the pathogenesis of intracranial hemorrhages after venomous snake bites is well understood, the pathogenesis of ischemic strokes is still in dispute. Different mechanisms, including toxin-induced hypercoagulability, systemic hypotension, thrombotic microangiopathy, and immune-mediated vasculitis, have been proposed to explain the occurrence of cerebral infarctions in snake bite victims.[3,5,6] Alternatively, venom-induced endothelial damage may be the cause of ischemic strokes in these patients.[7] Ischaemic infarction involving different arterial territories,[8-10] including brain stem infarction[11] and acute disseminated encephalomyelitis (ADEM)[12] following viper envenomation have been described. Asymmetric leucoencephalopathic changes after viper bite are a rare phenomenon and data in this regard is sparse. This case is the case of leukoencephalopathy in a venomous snake victim to be reported, and it provides more insights into the pathogenesis of venomous snake bite-induced cerebral ischemia.

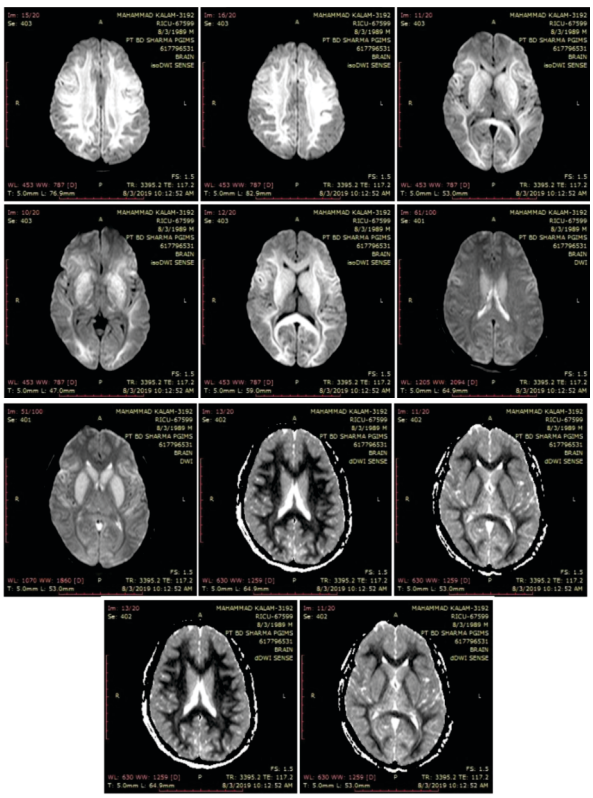
CASE REPORT

A 30 year old, previously healthy male came to emergency department with history of snake bite on left foot while working in the factory during daytime. At the time of presentation patient was in altered sensorium with Glasgow Coma Scale (GCS) score of 7 (E1M4V2) and fang marks were noticed over the left foot with swelling of foot. Patient was afebrile with a pulse rate of 120 beats/min regular, noninvasive blood pressure (NIBP) was 100/60 mm Hg in right arm supine position, SpO_2 89% on room air and the respiratory rate was 20 breaths/min. Pupils were bilateral (B/L) constricted and sluggishly reactive to light. Deep tendon reflexes were diminished and the plantar response was flexor bilaterally. On auscultation of chest there was B/L reduced air entry. Other systems examinations were within normal limits and patient was passing adequate urine. Patient was immediately intubated using endotracheal tube of size 8 mm internal diameter and was ventilated with AMBU bag with O_2 at flow of 3 L/min. Ten vials of polyvalent Anti Snake Venom (ASV) were started after sensitivity testing. Tetanus toxoid was given and patient was shifted to intensive care unit. On receiving patient in intensive care unit NIBP was 110/70 mmHg in right arm supine position, pulse rate was130 beats/min, SpO_2 was 98% on oxygen. Patient was sedated with Midazolam infusion at 2mg/hr and put on ventilatory support on SIMV mode of ventilation. Patient received 10 more vials of polyvalent ASV. Investigations revealed haemoglobin of 12 g/dl, total leucocyte count 12800 /mm^3 differential leucocyte count $P_{72}L_{25}E_2M_1$ and platelet count 200000 /mm^3. Twenty minutes whole blood clot test was positive. Random blood sugar was 160 mg/dl. Urine routine examination revealed 1-2 pus cells and 2-3 RBC's/HPF. His total serum bilirubin was 0.5 mg/dl, serum alanine aminotransferase 38 U/l, serum aspartate aminotransferase 35 U/l, serum alkaline phosphatase 74 U/l, total serum protein 5.7 g/dl (albumin 2.4 g/dl), prothrombin time 20 s, International Randomised Ratio (INR) 1.65, blood urea 30 mg/dl, serum creatinine 0.8 mg/dl, serum sodium 138 mEq/l and serum potassium was 4.2 mEq/l. Malarial parasite was negative. Hepatitis B surface antigen, hepatitis C virus antibody and ELISA for HIV were non-reactive. Chest x-ray was within normal limit. Patient was started

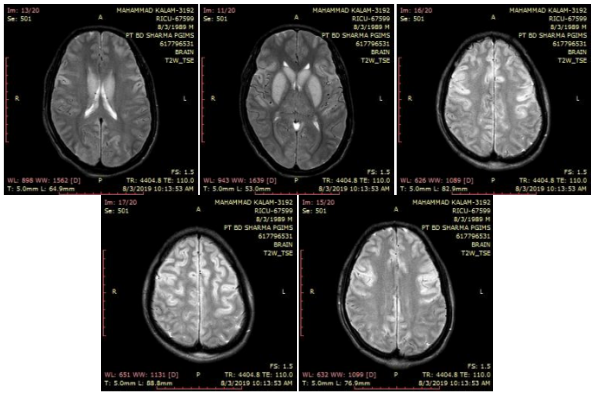
on following antibiotics Inj. Augmentin 625 mg BD, Inj. Metrogyl 500 mg TDS and further course of antibiotics were changed according to culture sensitivity reports. On day 8 of admission patient developed generalised tonic clonic seizures on stimulus to light, sound and touch. MRI Brain was done on which T2 and FLAIR Symmetrical hyperintensities noted in B/L lentiform nuclei, B/L caudate nuclei and B/L Cortical Rim. No evidence of (e/o) blooming on FFE images. There is e/o diffuse white matter diffusion restriction noted on DWI and ADC sequences. No e/o midline shift. B/L thalamus and internal capsule appear normal. Ventricular system, cortical sulci and sylvian fissure appear normal. There is subtle hyperintensity in midbrain especially B/L substantia nigra on T2 and FLAIR images which shows diffusion restriction on DWI and ADC images. MRI brain was suggestive of snake bite induced leukoencephalopathy. On consultation with neurologist patient was started on inj. Midazolam, inj. Phenobarbitone 50 mg BD, inj. Sodium Valproate 250 mg BD. Patient improved with myoclonus reduced to face and thighs intermittently. Patient was put thrice on inj. MgSO4 2 g for 3 days with a gap of 3 days between each session. Patient slowly improved and myoclonus disappeared. Patient was tracheostomised on day 9 of admission and after the above symptoms disappeared patient was weaned from the ventilator in 10 days with GCS improving to E3VtM6 and pupils becoming B/L normal size and normally reactive. Patient was maintaining SpO_2 100% on room air.



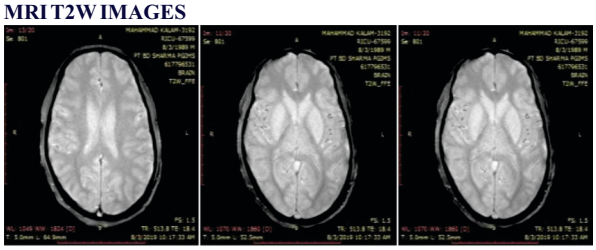
MRI FLAIR IMAGES



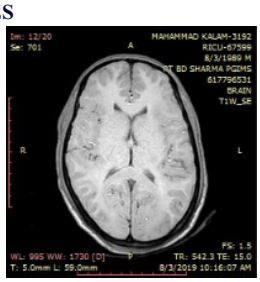
MRI DWI AND ADC IMAGES



MRI T2W IMAGES



MRI FFE IMAGES



MRI T1W IMAGE

DISCUSSION

Posterior reversible leukoencephalopathy was first associated with eclampsia, renal disease, and use of immunosuppressive agents.[13] Thereafter, this syndrome has been linked to a number of systemic and toxic conditions, leading to vasogenic and less often, cytotoxic edema predominantly located in the posterior circulation territory.[14,15] Although the hallmark of posterior reversible encephalopathy is the presence of bilateral and symmetrical lesions confined to the occipital and parietal lobes, forms with additional asymmetrical affection of thalamus, basal ganglia, cerebellum, brainstem, or even frontal lobes are increasingly recognized.[16] Predominance of involvement of the posterior circulation has been associated with a reduced sympathetic innervation at this level, making these vessels more susceptible to dysfunction of the normal mechanisms of autoregulation under circumstances of abnormal cerebral perfusion. Another less well-investigated possibility is that endothelial damage with subsequent vasoconstriction causes the reversible brain damage.[17]

Neurological signs and symptoms after a venomous snake bite are most often related to the toxic effects of venom, that is, anticoagulant/procoagulant activity or neurotoxicity. Some patients develop neurological complications related to cerebral hypoxia, which, in turn, are related to hypotensive shock that may accompany some snake bite envenomations. Neuromuscular disorders, that is, damage of the peripheral nervous system occurs most often after the bite of elapids, but may also occur following a viper bite. The effect of neurotoxins may start from minutes to a few hours after the inoculation of venom, causing weakness related to a blockage of synaptic transmission, at either presynaptic or postsynaptic levels.[2]

Adverse reactions to antivenom appear in two forms; early and late. Early reactions tend to occur within 10-180 min after treatment and range from urticaria to anaphylactic shock. Late reactions are immune complex diseases and present in the form of serum sickness syndrome usually 5-24 days after antivenom administration. Both central and peripheral nervous system manifestations are seen in association with serum sickness.[18] Generalised myokymia, syndrome of continuous and

spontaneous muscular activity, resembling fasciculations following snake bite has also been reported.[3]

Neurological features of viper bite include drowsiness, confusion, fainting, dizziness, blurred vision, loss of muscle coordination and convulsions.[19] The most common and serious central nervous system complication following vasculotoxic snake bite is intracranial haemorrhage. Ischaemic strokes involving various arterial territories[8-10] of the brain, including brain stem[11] and fatal ADEM[12] have also been described. In most of the cases, infarction is multifactorial. Occasionally, cerebral infarction may be unrelated to bite and could be due to underlying medical illness.[19] Altered sensorium following an hour after the bite is probably related to direct arterial endothelial injuries caused by the venom itself. The diffuse cerebral disturbances may be caused by toxic encephalopathy due to toxins in venom.

ASV remains the mainstay of therapy and suspected snake envenomation should be treated empirically with intravenous polyvalent ASV as early as possible. It may reverse systemic envenoming even when this has persisted for several days or, in the case of haemostatic abnormalities, for two or more weeks. However, when there are signs of local envenoming, without systemic envenoming, antivenom will be effective only if it can be given within the first few hours after the bite. Neurotoxic envenoming of the postsynaptic type (cobra bites) may begin to improve as early as 30 mins after antivenom, but usually takes several hours. Envenoming with presynaptic toxins (kraits and sea snakes) is unlikely to respond to ASV.[20]

In our patient respiratory distress due to respiratory muscle paralysis was managed promptly in the emergency department and patient immediately shifted to intensive care unit for further management after giving supportive antibiotics, tetanus toxoid, neostigmine. Hence the generalised tonic clonic seizures which the patient developed due to snakebite induced leukoencephalopathy as suggested on MRI could be due to snake venom toxins. This was managed by Phenobarbitone, Sodium valproate, Midazolam and MgSO4 which significantly reduced symptoms to myoclonus and ultimately to no seizure state and improvement in consciousness and respiratory muscle power of patient which enabled weaning of patient from ventilator.

CONCLUSION

Since leukoencephalopathy is not a common presentation in snakebite patients, imaging studies should be carried out in patients presenting with seizures to rule out other causes and for early diagnoses and appropriate management to reduce morbidity and mortality hence also for improved outcome.

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