Case Report: Reversible Posterior Leukoencephalopathy in a Venomous Snake (*Bothrops asper*) Bite Victim

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Abstract. An 18-year-old man developed posterior reversible leukoencephalopathy after being bitten by a venomous snake (*Bothrops asper*). It is possible that this previously unrecognized neurological complication of snake bite envenoming occurred as the result of endothelial dysfunction induced by the venom of the offending snake. This pathogenetic mechanism has also been implicated as the cause of cerebral infarctions in snake bite victims. Alternatively, the leukoencephalopathy might have been a complication of antivenom therapy.

INTRODUCTION

Snake bite envenoming is a neglected tropical disease killing thousands of people living in tropical regions of the developing world. According to conservative estimates, about 5 million people are bitten by snakes every year, resulting in more than 2 million cases of envenoming and from 20,000 to 125,000 deaths.^{1,2} Venom components may have cytotoxic, hypotensive, neurotoxic, and anticoagulant or procoagulant effects, which account for the local and systemic clinical manifestations of snake bites.³ 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).⁴

Neurological manifestations are the most feared complications of venomous snake bites, because they add significant morbidity and mortality to the victims.⁵ 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,⁶ and abnormalities in the coagulation cascade (or other more complex pathogenetic mechanisms), producing cerebrovascular events.⁷ 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.^{5,7,8} Alternatively, venom-induced endothelial damage may be the cause of ischemic strokes in these patients.⁹ This case is the first case of posterior reversible 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

An 18-year-old farmer was bitten in the left foot by a snake while working in a rice paddy. He was taken to a rural hospi-

tal, where the attending physician recorded severe pain and edema in the bitten foot. The victim and witnesses recognized the offending snake as an equis. Because one of the witnesses killed the snake and brought it to the rural hospital, a local expert recognized it as a *Bothrops asper* (Figure 1), the most common venomous snake in the coastal region of southern Ecuador.¹⁰ The bite occurred near a rural village named Camital (Naranjal County, Province of Guayas).

The patient received local care of the wound and two intravenous vials of polyvalent anti-*Bothrops* antivenin (elaborated by the Minister of Public Health of Ecuador; www.inh.gob.ec). He remained stable for 2 days, when he developed breathing dysfunction, headache, and cloudiness of consciousness. He underwent endotracheal intubation and was transferred to the intensive care unit of our institution. On admission, the patient was stuporous, with evidence of respiratory distress. The edema (originally confined to the left foot and ankle) had extended up to the knee, and there was associated blistering in the edematous region. Laboratory testing showed normal white blood cell (WBC; 9,400 per mm³), red blood cell (RBC; 3,960,000 per mm³), and platelet counts (250,000 per mm³) and hematocrit levels (36%), but coagulation studies revealed increased prothrombin (17/12 in) and thromboplastine (46/32 in) times. Four more vials of antivenin were administered, and ventilatory support was continued. On the next hospital day, he had a generalized tonic clonic seizure. Computed tomography (CT) of the head showed bilateral symmetrical hypodense occipital lesions extending to the frontal lobes that did not enhance after contrast medium administration (Figure 2). The patient continued with assisted ventilatory support for 2 more weeks, showing progressive improvement in his general and neurologic status. The blood pressure of the patient remained lower than 140/90 mmHg during his stay at the intensive care unit. He was discharged asymptomatic 1 month later, and CT scan performed after 6 months was completely normal (Figure 3).

COMMENT

Posterior reversible encephalopathy was first associated with eclampsia, renal disease, and use of immunosuppressive agents.¹¹ 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.^{12,13} Although the hallmark of

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FIGURE 1. Photo taken of the offending snake showing characteristics of *B. asper*, including its length and the typical X-like dorsal marks.

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.¹⁴ 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.¹⁵

FIGURE 3. Normal plain CT performed 6 months after discharge.

A recent review of the systemic alterations induced by the venom of *Bothrops asper* suggested that the complex toxicity of venom components goes beyond their effects on the coagulation cascade and the number and function of platelets, at least in animal models.¹⁶ Other toxic effects of the venom include an increase in vascular permeability, an induction of abnormal release of tumor necrosis factor and cytokines, and most importantly, a systemic endothelial dysfunction. The latter may be the pathophysiological substrate to explain the development of posterior reversible encephalopathy in our patient, because he never developed systemic hypertension or hypovolemic shock, which would explain a primary loss of autoregulation of cerebral blood vessels. That cerebral infarction occurring in venomous snake bite victims may be the result of such pathogenetic mechanism is a plausible explanation, because most of these patients have developed the infarct in the absence of hypovolemic shock.⁵ Our patient received polyvalent antivenon, a compound that is not free of adverse reactions, and it is also possible that antivenin was the cause of the posterior reversible encephalopathy. Antivenin-related damage of the central nervous system has been reported in the form of optic nerve damage or demyelination.¹⁷⁻¹⁹

FIGURE 2. Contrast-enhanced CT on admission showing bilateral symmetrical hypodense occipital lesions extending up to the frontal lobes.

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