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Posterior Reversible Encephalopathy Syndrome As A Rare Manifestation Of Vasculotoxic Snake Bite

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Abstract:
Snake envenomation often leads to various neurological complications but the incidence of leuko-encephalopathy is quite rare. A 25-year-old male presented following a viperidae snake bite with progressive lower limb swelling. He was treated with anti-snake venom and hemodialysis but on the fifth day of hospitalization he experienced multiple episodes of generalised tonic clonic type of seizures. MRI brain revealed features of Posterior reversible encephalopathy syndrome (PRES). Treatment was mostly supportive and patient was discharged after resolution of clinical symptoms. A repeat MRI after two weeks suggested normal study suggesting radiological resolution. Hence, this case highlights PRES as a possible complication of snake bite.

Keywords: *PRES - Posterior reversible encephalopathy syndrome, CBC – Complete blood count, LFT – Liver function test, RFT – Renal function test, PT INR – Pro-thrombin time and International normalized ratio, WBCT- Whole blood clotting time, ASV– Anti snake venom, MRI – Magnetic resonance imaging, FLAIR – Fluid attenuated inversion recovery, MRA - Magnetic resonance Angiography, Leuco encephalopathy.*

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I. Introduction

The approximate number of snake bites worldwide has been estimated as 5.4 million, resulting in 2.5 million envenomation and around 81,000–138,000 deaths, annually. In India alone, it is estimated that there are over 1,000,000 snakebites causing 58,000 deaths annually and significant disability in almost four times the number [1]. Most of the fatalities occur due to the delay in reaching hospital in time, which are often preventable. Hence, identification of early symptoms and signs of envenomation are needed to prevent the further complications. The neurotoxic features of a snake envenomation is quite well known but the incidence of posterior reversible encephalopathy syndrome following snake envenomation is quite rare. Posterior reversible encephalopathy syndrome (PRES) is a clinico-radiological syndrome manifested characteristically as symmetrical white matter edema predominantly involving the watershed areas of parietal and posterior occipital lobe [2]. It is a neurological disorder which can present clinically in various ways like visual disturbances, seizures, headache, and altered mental status. Till now, only six cases in the literature have described the occurrence of PRES following snake bites in india [3,4].

Summary of clinical and outcome data of six reported cases (including the present one) of snake bite envenomation induced Posterior reversible encephalopathy syndrome in India. Adapted from R. Ghosh et al. 2023 [3], Ibrahim et al. 2017 [4].

Author and year of publication	Type of snake	Onset	Anti-venom given	coagulopathy	Renal impairment	Respiratory failure	Hypertension	Seizure	Visual disturbance	Motor disorder	Reversibility
Ibrahim et al. 2017 [4]	ceraste scerastes	Within 7 days	Yes,before symptoms	yes	no	No	no	no	yes	no	partially

Chaudhary et al. 2013 [5]	Not identified	30 min	Yes,after symptoms	yes	no	no	no	no	no	yes	Partially
Varalaxmi et al. 2014 [6]	Pit viper	2 days	no	no	yes	no	no	no	yes	no	yes
Kaushik et al. 2014 [7]	bungaruscaeruleus	hours	Yes,after symptoms	Not clear	Not clear	yes	yes	yes	yes	yes	yes
R. Ghosh et al. 2023[3]	Daboia ruselli	hours	Yes,after symptoms	no	yes	no	yes	no	yes	no	yes
Kumaravel KS et al.2020 [2]	Not identified	Within minutes	Yes,before symptoms	yes	yes	yes	no	no	no	yes	partially
Present case	Pit viper	5 days	Yes,before symptoms	Yes	yes	no	yes	yes	no	no	yes

II. Case Report

History

A 25 year old male presented with a history of snake envenomation at left lower leg while he was doing his routine work in a paddy field. He initially presented with complaints of left lower limb swelling and decreased urine output. There was bleeding and presence of local tenderness at the site of bite. There was no ptosis, external ophthalmoplegia, or any other of signs of neurotoxic snake envenomation. Hence, a provisional diagnosis of vasculo toxic snake envenomation was made and patient was admitted in intensive care unit.

General Examination and Blood Investigation

All routine blood investigations were sent with simultaneous monitoring of whole blood clotting time (WBCT) was done 6 hourly. At the time of admission, the vitals and routine investigations of the patient were as follows:

Blood Pressure was 130/90 mm hg, pulse was 78 beats per minute, Saturation was 97 % on room air and no focal neurological deficit was elicited. CBC, LFT, PT INR and RFT parameters on the day of admission was within normal limit (Baseline serum creatinine - 1.25 mg/dl, Baseline blood urea – 29.85 mg/dl). Whole blood clotting time (WBCT) was more than 20 minutes.

Course of illness and treatment history

The treatment was started with Anti-snake venom (ASV) and antibiotics, however, the cellulitis was progressive and had reached up to his mid- thigh region crossing his knee joint within one day of admission. Serum creatinine increased to 3.86 mg/dl and repeat WBCT was still greater than 20 min. Hence, hemodialysis was planned and 2 cycles of hemodialysis was done over the next 4 days. There was improvement in RFT parameters, decrease in limb swelling and increase in urine output. However, on the fifth day of hospitalization, patient experienced multiple episodes of generalized tonic clonic type of seizures associated with up rolling of eyeball and clenching of teeth. Patient had a BP of 154/100 mm hg, with normal blood glucose and serum electrolyte level during the ictal phase. Therefore, patient was started on anti-epileptic and anti-hypertensive drugs.

Magnetic imaging resonance was done which showed ill-defined hyper intense areas in bilateral frontal and parieto-occipital region, bilateral cerebellar hemisphere predominantly in white matter on T2 FLAIR image suggesting of posterior reversible encephalopathy syndrome (PRES). EEG and fundus study was within normal limit. There was gradual improvement from the post-ictal confusion state with normalization of blood pressure over the next 2 days. The patient was discharged on oral medication with the advise of repeat imaging study on follow-up after 2 weeks.

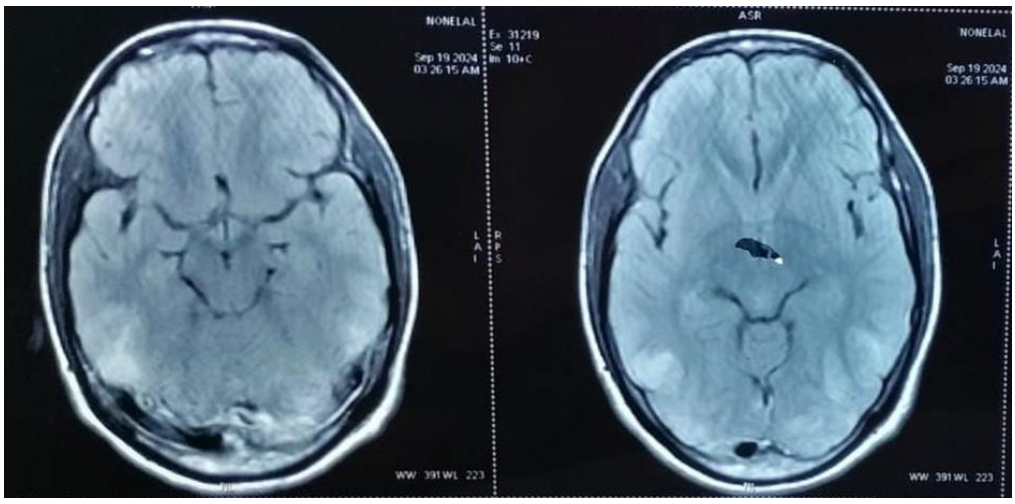

Figure 1 : T2 FLAIR image showing hyper intensities over bilateral parieto-occipital region

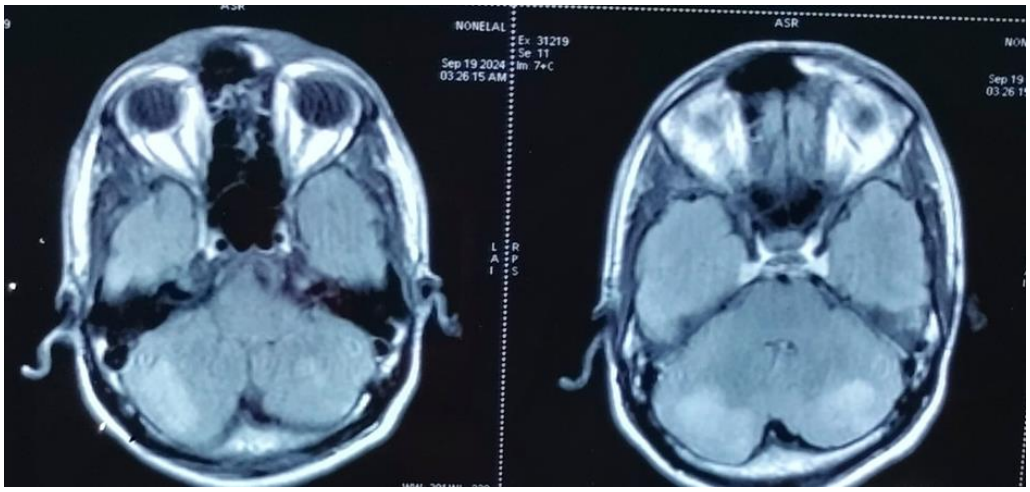

Figure 2 : T2 FLAIR image showing hyper intensities over bilateral cerebellar hemispheres

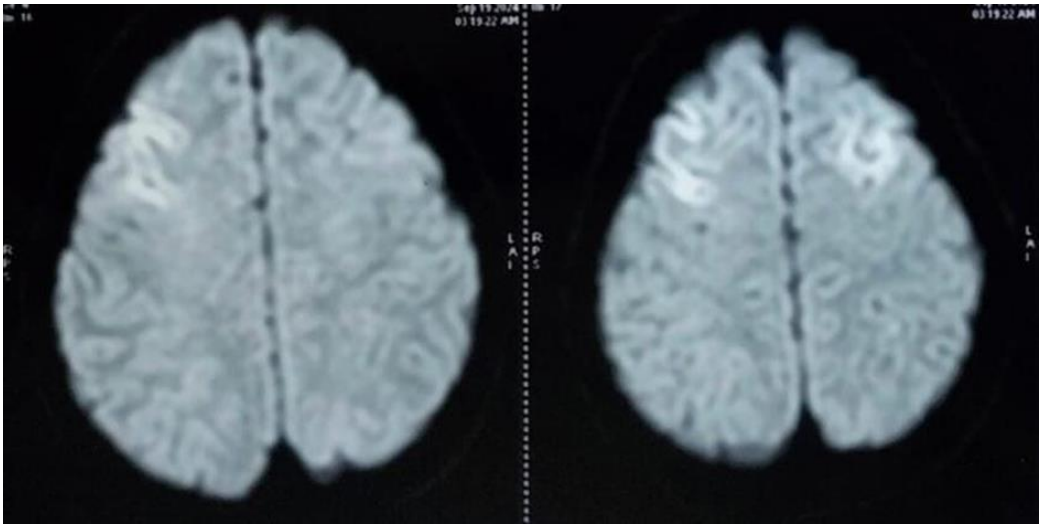

Figure 3 : Diffusion weighted magnetic resonance image showing lesion in both frontal lobe (right > left)

Follow-up study

The patient was called up for a follow-up visit after 2 weeks in which a repeat imaging of MRI Brain with MR Angiography was done. The repeat imaging study suggested a normal scan. There was also significant clinical improvement along with normal laboratory parameters without any appearance of further seizure episodes in the patient.

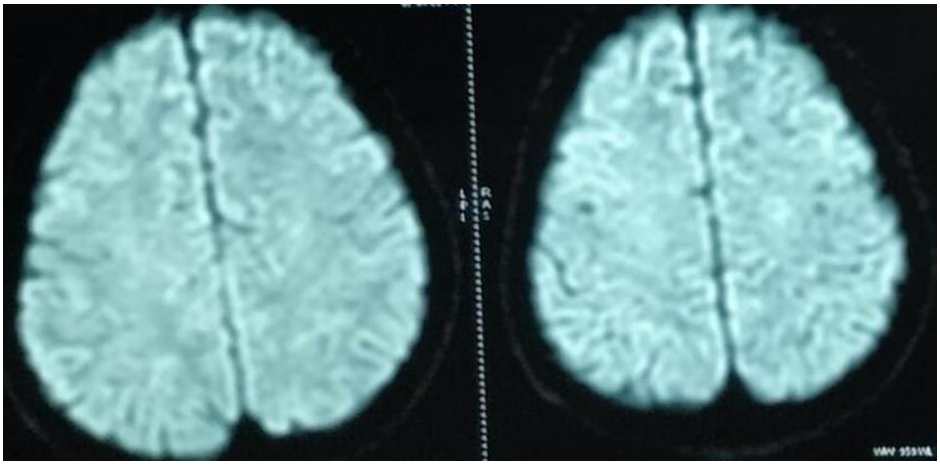

Figure 4 : Diffusion weighted magnetic resonance image showing normal scan during follow-up study

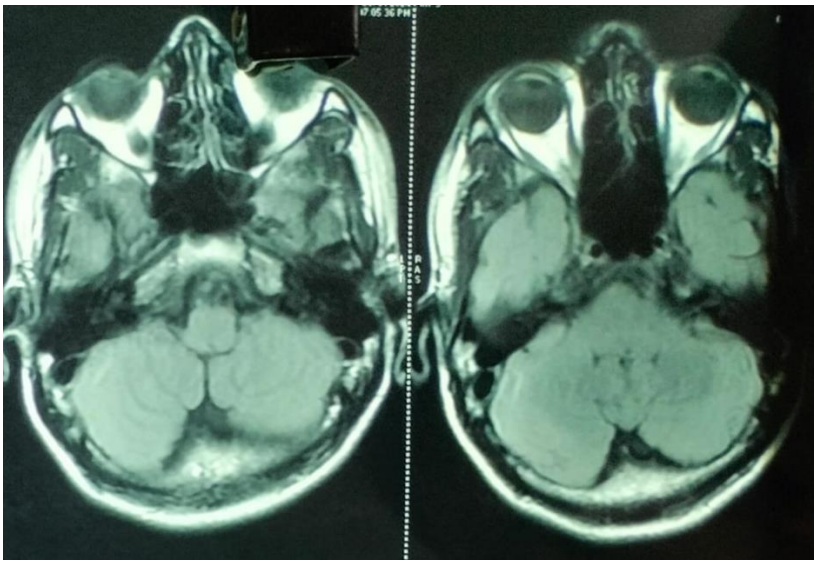

Figure 5 : T2 FLAIR image showing normal scan of bilateral cerebellar hemispheres during follow-up study

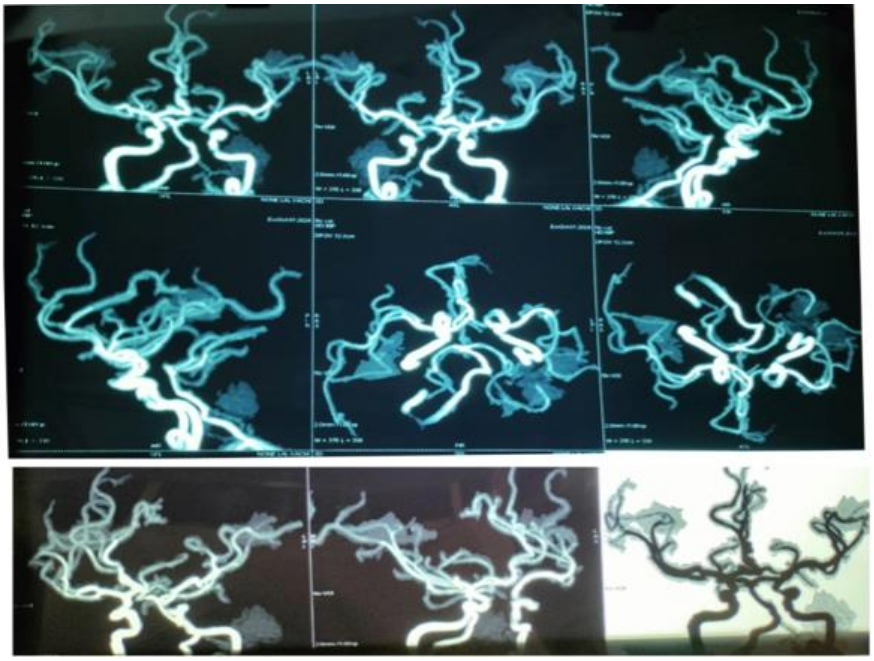

Figure 6 : MR Angiogram showing normal arterial territory and architecture during follow-up study

III. Discussion

Leuco encephalopathies are a heterogeneous group of disorders characterized by degeneration of white matter of central nervous system. There may be various etiological factors responsible for this condition like vascular, inflammatory, infection, trauma, toxin, nutritional, neoplastic etc. PRES is a reversible leuco encephalopathy and is also known with some other names like Reversible Posterior Leuco encephalopathy Syndrome, hyper-perfusion encephalopathy, brain capillary leak syndrome, hypertensive encephalopathy etc [2]. The PRES is a clinico-radiological syndrome characterized by bilateral white matter edema affecting predominantly the vascular watershed areas of the posterior occipital and parietal lobe [8,9] but asymmetrical involvement of thalamus, basal ganglia, cerebellum, brain stem and frontal lobe has also been reported in many instances. It usually involves the posterior portions of the brain because of a lower threshold for auto regulatory breakthrough in the posterior circulation as compared to the anterior part [10]. It is usually mediated by two mechanisms :

i) Disorders with systemic hypertension with increased capillary pressure leading to capillary leakage into the interstitium

ii)Toxin mediated direct endothelial dysfunction causing impairment of blood brain barrier leading to vasogenic edema. The venom has complex substances which includes peptides, proteins, biogenic amines, lipids and polysaccharides which has cytotoxic, neurotoxic, anticoagulant and pro-coagulant activities. The venom also contains metallo proteinases and C- type lectin which activate platelets exhibiting pro inflammatory activity called as thrombo-inflammation.[11] The venom causes increased vascular permeability which in turn induces abnormal release of tumour necrosis factors and cytokines causing endothelial dysfunction leading to vasogenic edema.[2]

However, the symptoms of neurological dysfunction in our patient appeared after 5 days of the snake envenomation and blood pressure also being raised during the acute episode indicate that renal failure leading to reno-vascular hypertension could be the most probable etiology in our case. PRES is commonly reported as a result of hypertension but around 30% of patients have normal blood pressure [12,13,14]. Neurological symptoms of this syndrome includes headache, dizziness, mental confusion, visual disturbances and seizures [15]. If the insult is recognized quickly and the triggering factor is withdrawn, clinical symptoms usually resolves within 1-2 weeks [12].

The characteristic radiological finding in PRES syndrome suggests symmetrical cortical and sub-cortical hyper intense signals on T2 weighted and FLAIR images in the parieto-occipital regions, not respecting any particular single vascular territory [16]. Similar findings were also observed in our case. However, the patient had complete resolution of clinical symptoms and a repeat MRI brain with MR angiogram after 2 weeks showed complete resolution of the radiological findings signifying the reversible nature of the disease.

IV. Conclusion

Snake bite induced leuco encephalopathy is a rare entity. Hence, in patients with snake envenomation, the development of symptoms of PRES should be recognized promptly and has also to be distinguished from venom induced neurological manifestations. The characteristic MRI findings along with spontaneous clinical and radiological resolution favours a diagnosis of PRES, whereas a presentation with ptosis or external ophthalmoplegia usually favour the diagnosis of neurotoxic envenomation. The clinical syndrome of PRES following snake envenomation is quite uncommon and early detection along with proper treatment can reduce the morbidity to a significant extent.

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