Fatal acute disseminated encephalomyelitis following treated snake bite in India

P Malhotra, N Sharma, A Awasthi, R K Vasishta

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Snake bite is an important cause of mortality and morbidity in India, with an estimated 35 000 to 50 000 fatal bites occurring annually. The neurological consequences of snake bite are predominantly the result of inhibition of neuromuscular transmission. We describe the first documented case of autopsy proven acute disseminated encephalomyelitis following treated snake bite in a young female.

A 27 year old woman was brought to the emergency department with a history of ptosis, weakness of all four limbs, and oliguria following a snake bite on the dorsum of her left foot 10 days previously. She was initially seen at a local medical college 6 hours after envenomation where 100 ml of polyvalent antivenin was administered 8 hourly, and one session of haemodialysis was given. There was an initial improvement in muscle power from grade 2/5 to 4+/5; however, there was a recurrence of weakness from day 8 after envenomation, and in view of progressive neuroparalysis and impending respiratory failure, she was referred to our institute. There was no history of blurred vision, dysphagia, dysphonia, haematuria, or dark coloured urine.

On physical examination she was conscious, oriented, and anxious, with a pulse rate of 104 beats/min, a blood pressure of 150/100 mmHg, and a respiratory rate of 26 breaths/min. There was generalised oedema, and fang marks were present on her left foot. On neurological review, bilateral external ophthalmoplegia and flaccid, hyporeflexic quadriparesis were noted. Investigations revealed normal haemogram (Hb 122 g/l (normal range 120–160 g/l), platelets 1.9×10^5/μl ($1.5–4\times10^5$), total leucocyte count 8.9×10^3/μl ($4–11\times10^3$), normocytic normochromic peripheral smear) and coagulation profile (prothrombin time 14 seconds (13–15), prothrombin time index 87%, activated partial thromboplastin time 37 seconds (35–40 seconds)), advanced renal failure (blood urea 38 g/l (2–4), serum creatinine 71 mg/l (4–12)), granular casts on urine microscopy and metabolic acidosis. Creatine kinase level was 21 U/l (normal 10–70). Plasma haemoglobin was 130 mg/l (normal <60), while urine was negative for both haemoglobin and myoglobin. Administration of antivenin and maintenance haemodialysis were continued, but the neuroparalysis persisted and a nerve conduction study revealed slowed conduction velocities, decreased amplitude of motor and sensory action potentials, and absence of F waves. The patient's sensorium gradually deteriorated over the next few days and she developed signs of raised intracranial tension (hypertension, blurring of optic discs) despite optimum haemodialysis and controlled hyperventilation. Broad spectrum antibiotics were added for ventilator associated pneumonia.

A CT scan of the brain revealed diffuse hypointensity of the white matter (fig 1) and there were 40 cells, predominantly lymphocytes, elevated protein (510 mg/l), and normal sugar on CSF examination. Oligoclonal bands were not detected. Intravenous methylprednisolone (1 g once daily for 3 days) followed by intravenous immunoglobulin (0.4 g/kg once daily for 5 days) were administered assuming a diagnosis of acute disseminated encephalomyelitis (ADEM); however there was no improvement in encephalopathy, and the patient finally died.

An autopsy was performed after informed consent from the relatives. The brain was normal on gross examination; however, there was microscopic evidence of extensive perivascular demyelination (fig 1B) and lymphocyte cuffing confrmed by solochrome cyanin stain. Lesions of similar age were distributed throughout the cerebral hemispheres, cerebellum, and brain stem. The kidneys revealed acute tubular necrosis; other organs were grossly and microscopically normal.

DISCUSSION

ADEM is an acute widespread demyelinating condition characterised by the rapid development of focal or multifocal neurological dysfunction. It usually follows 4–21 days after an infection or vaccination, and results from a transient autoimmune response against myelin or other autoantigens either by molecular mimicry or non-specific activation of an autoreactive T cell clone.[1]

More than 200 000 cases of snake bite are reported in India annually and it is estimated that between 35 000 and 50 000 of these are fatal.[2] Four clinically important types of snake are found in India: cobras (*Naja naja and Naja kaouthia*), the common krait (*Bungarus caeruleus*), Russell's viper (*Daboia russelii*), and the saw scaled viper (*Echis carinatus*).[3] The neurological consequences of snake bite are predominantly the result of inhibition of neuromuscular transmission.[4] In addition, there are reports in the literature of Guillain-Barré syndrome[5] and delayed neuropathy[6] following snake bite. To the best of our knowledge, this case represents the first report of demyelination involving both central and peripheral nervous systems following snake bite. ADEM was confirmed on autopsy, while the nerve conduction study performed antemortem was suggestive of demyelination.

The immunopathogenesis of demyelination following snake bite may be related to molecular mimicry between one of the components of snake venom and myelin and subsequent generation of pathogenetic auto-antibodies causing myelin damage. In this patient, it may also have developed as a consequence of a serum sickness-like reaction to the initial administration of antivenin, as neuroparalysis recurred a few days after definite clinical improvement. Late reactions to antivenin are immune complex diseases and present in the form of serum sickness syndrome usually 5–24 days after antivenom administration. Clinical features include fever, arthralgias, mononeuritis multiplex, and rarely,

Abbreviations: ADEM, acute disseminated encephalomyelitis

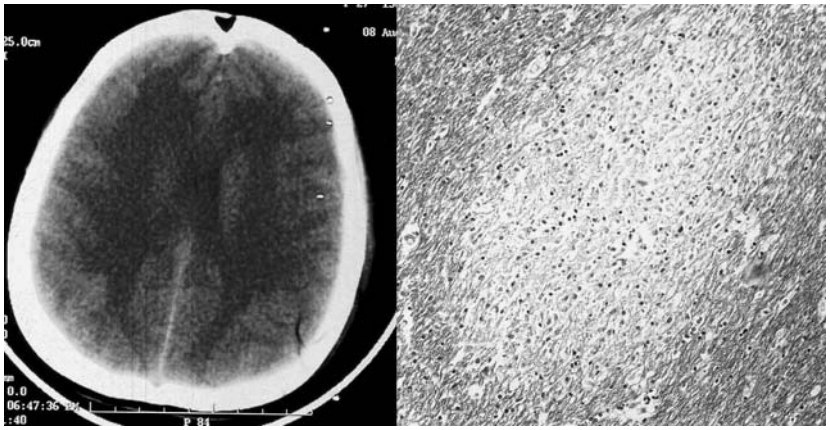

Figure 1 (A) CT scan showing diffuse white matter hypointensity; (B) solochrome cyanin stain demonstrating myelin loss and a mild lymphocytic infiltrate (original magnification × 32).

encephalopathy.[3] A reversible osmotic demyelination syndrome and demyelinating neuropathy have also been reported as a complication of dialysis in patients of advanced renal failure, and this may have been a third mechanism of demyelination in the index case; however such cases are rarely fatal.[7 8]

To conclude, we have described a previously unreported complication of treated snake bite and, if similar cases are seen by other physicians in countries where snake bite is a common problem, ADEM may be added to the list of neurological complications of snake bite. We suggest that patients with snake bite who develop unexplained encephalopathy should be screened for ADEM. Even though this is the first report of such a case, it is possible that if CT/MRI scans of the brain are ordered more often in patients with snake bite, this complication may be recognised more often and appropriate therapy instituted. Up to two thirds of patients with ADEM treated with corticoseroids benefit clinically, especially those who are treated early,[1 9] while intravenous immunoglobulin and plasmapheresis have been shown to produce dramatic improvement in steroid non-responsive cases.[10 11]

Authors' affiliations

P Malhotra, Department of Pulmonary Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh-160012, India
N Sharma, Department of Internal Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh-160012, India
A Awasthi, R K Vasishta, Department of Histopathology, Postgraduate Institute of Medical Education and Research, Chandigarh-160012, India

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Correspondence to: Dr P Malhotra, Department of Pulmonary Medicine, PGIMER, Chandigarh-160012, India; dranshupuneet@yahoo.com

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