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Case Report

Multiple thromboembolic strokes in a toddler associated with Australian Eastern Brown snake envenomation

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ABSTRACT

Venomous snakes are found in every state and territory in Australia and are amongst the most dangerous in the world. Of Australia's snakes the Eastern Brown snake (*Pseudonaja textilis*) is responsible for the majority of the cases of envenomation and death. We describe a case of thromboembolic stroke associated with Eastern Brown snake envenomation in a 2-year-old boy. Following the incident, the boy has made a good recovery.

Case report

In a remote Australian town, a 2-year old boy was witnessed by his mother to run towards her in the yard then begin crying and collapse and become unresponsive. He was taken to the local hospital with a persistently alerted level of conscious. Physical examination showed normal vital signs, dual heart sounds, a clear chest, a soft and nontender abdomen but generalized poor tone. There were no other neurological deficits. There was no significant medical or antenatal history and no regular medications. The child had not recently been unwell.

He was commenced on intravenous ceftriaxone and aciclovir empirically to treat encephalomeningitis. An initial blood panel showed a mild neutrophilia (12.4×10^9 cells/L), hypokalaemia (2.7 mmol/L) and a metabolic acidosis (pH 7.21). His level of consciousness gradually improved but after discussion with the specialist pediatrics team he was transferred to the nearest tertiary center. The differentials at this stage included sepsis, meningitis, and atypical seizures.

On arrival to the tertiary center, he was noted to have developed marked dysmetria and dysphagia. His coagulation profile was also significantly deranged with an international-normalized ratio of 1.7 (1.0-1.2), activated-partial thromboplastin time of 62 (30-40 seconds), and a fibrinogen level of 0.9 (1.9-4.3 g/L). Further tests including blood cultures, infectious serology, an autoimmune and vasculitic screen, and a lumbar puncture were taken. Given the sudden onset of symptoms in an otherwise well child, envenomation was considered a possibility. The treating physicians also noted a possible bite mark on the lip of the boy. Serum samples for snake venom-specific enzyme immunoassay were also taken. This immunoassay is more sensitive at lower venom concentrations than older techniques which suffer from poorer sensitivity and higher background absorbance leading to high false positive rates [1].

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Whilst on the pediatrics ward he developed acute respiratory distress. He was transferred to the pediatric intensive care unit where he became encephalopathic shortly later, he was intubated and ventilated. He was given cryoprecipitate to attempt to reverse his coagulopathic state and was continued on aciclovir and ceftriaxone, methylprednisolone was commenced to treat a possible vasculitis. An echocardiogram was performed which was normal.

He underwent an urgent MRI with contrast of the brain. This revealed multiple supra and infratentorial anterior and posterior circulation infarcts involving the white matter, deep grey matter, nuclei, and cerebellar hemispheres (Fig. 1) with no associated hemorrhage.

The patient was managed conservatively with supportive treatment. His antibiotics, antivirals, and corticosteroids were ceased. He was extubated a day after this. Specialized testing of his blood sample had by this time returned a positive result for Eastern Brown snake venom. He was returned to the pediatrics ward and by this time his dysmetria and dysphagia had resolved. He was discharged 4 days later with near normal function. He received ongoing rehabilitation, physical therapy, and occupational therapy in the community and has made a good recovery and is meeting all his developmental milestones.

Discussion

Snake envenomation has been reported to be cause a variety of neurological conditions and MRI findings depending on the species of snake (Table 1) [2–13]. In Australia there are approximately 80 snake envenomations per year with 40% of these being from the Eastern Brown snake. The majority of the 3 deaths per year from snake bites in Australia are due to the Eastern Brown snake as well. Brown snake venom leads to a state of venom-induced consumptive coagulopathy in 99% of envenomations, myotoxicity in 4%, nephrotoxicity in 18%, microangiopathic hemolytic anemia in 14%, cardiac arrest in 6%, major hemorrhage in 3%, and death in 5% [14].

Brown snake venom contains proteases which mimic the action of the prothrombinase complex consuming clotting factors and classically leads to a prohemorrhagic state through the consumption of these clotting factors [15]. Intracranial hemorrhage from the Eastern Brown snake envenomation is a well appreciated but rare phenomenon occurring in only 1% of cases in 1 study [16]. However, there are no reported cases of thromboembolic stroke occurring in association with Eastern Brown snake envenomation.

Most reported cases of stroke associated with snake bites originate from India and involve the viper family of snakes in particular Russel's viper snake (*Dabois russelii*) and from South America and the Caribbean with the *Bothrops* spp. of snake [17–20]. Mechanisms leading to thromboembolic stroke in snake bite are multiple and depend on the species of the snake, but may include [21]:

- cardiotoxic effects of the venom could cause cardiac dysfunction and arrhythmias leading to cardiac thromboembolism [21].
- coagulopathy due to alterations in the clotting system leading to microthrombus formation causing thromboembolic events [22].
- vasculitis due to the venom causing vascular spasm, endothelial injury, and inflammation [23].
- hypotension and circulatory dysfunction from envenomation can further worsen thrombosis [24].

The patient is this case had a deranged coagulation profile supporting the theory that microembolism formation resulted in the stroke. The fact patient was normotensive throughout the events and the infarcts did not occur in watershed areas makes the role of hypotension less likely. Antivenom was not administered in this case given the large delay in the diagnosis of envenomation. It is uncertain what effect antivenom may have had in this case.

Patients with signs of clinical evenomation are generally given antivenom. The use of polyvalent antivenom has been described in cases of stroke associated with snake bite [8]. In one study dealing with *Bothrops* spp. envenomation, antivenom use was associated with a lower rate of serious

Table 1. – Common MRI findings following envenomation and the species of snake implicated.

MRI findings	Common species of snake implicated
Acute disseminated encephalomyelitis [2–4]	Chinese moccasin (*Deinagkistrodon acutus*)
	Krait snake (*Bungarus caeruleus*)
	Russell's viper (*Daboia russelii*)
Cerebral venous thrombosis [5]	Russell's viper
Hemorrhagic leukoencephalitis [6]	Russell's viper
Intracerebral hemorrhage [7–9]	*Bothrops* spp.
	Russell's viper
	Australian Eastern Brown snake (*Pseudonaja textilis*)
Leukoencephalopathy [10]	Russell's viper
	Saw scaled viper (*Echis carinatus*)
Posterior reversible encephalopathy syndrome [11–12]	*Bothrops* spp.
	Indian pit viper
	Horned viper (*Cerastes cerastes*)
Thromboembolic stroke [13]	*Bothrops* spp.
	Horned viper
	Russell's viper

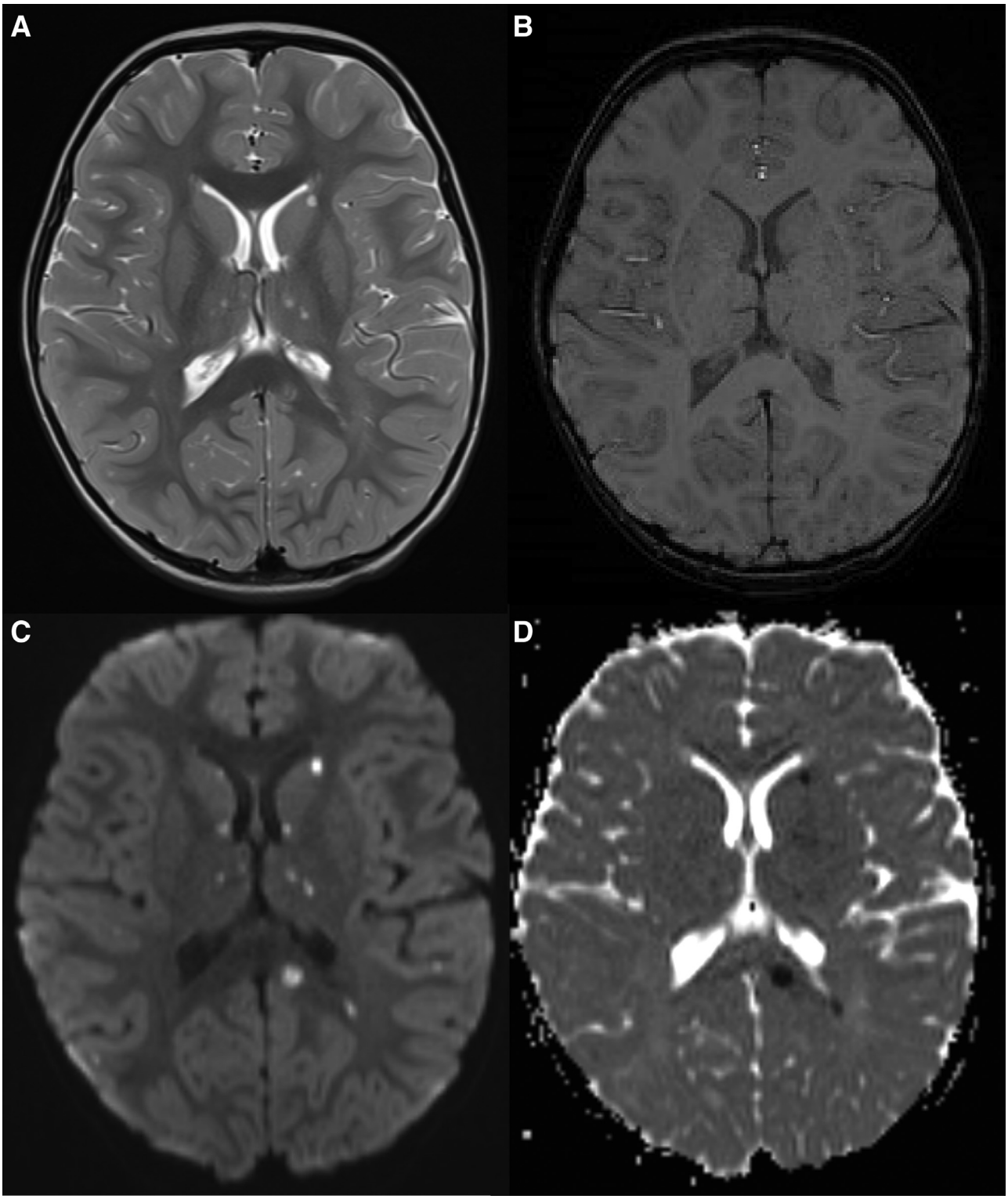

Fig. 1 – Two-year-old boy bitten by an Australian Eastern Brown snake. (A) Axial T2 weighted MRI image showing multiple diffuse hyperintense regions throughout the thalami, head of the caudate nuclei, and in the splenium of the corpus callosum. (B) Axial SWI image shows no associated hemorrhage. (C) Axial DWI (b1000 s/mm^2) image showing areas of restricted diffusion in the hyperintense regions described above. (D) Axial ADC image shows hypointense regions correlating with the hyperintense regions seen on the DWI image, this confirms that these represent areas of true diffusion. Overall the findings are consistent with multiple acute ischemic infarctions.

thrombotic events, including stroke, than no antivenom use [24]. However, antivenom is not effective in preventing thromboembolic stroke in all cases [25]. Envenomation should be considered as a differential in people living in snake endemic regions presenting with a stroke where no other obvious cause can be found.

Conflicts of interest

The authors have no conflicts of interest to declare.

Supplementary material

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.radcr.2019.05.034.

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