Cerebral Infarction in a Young Female Following Snake Bite

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SUMMARY We present a normal 13-year old female who developed left cerebral infarction following envenomation by the carpet viper (Echis carinatus). We have read of only one other case of cerebral infarction following viper envenomation (Viperi russelli). Possible mechanisms for cerebral infarction in these circumstances are discussed. It is believed that this complication may be more common than is reported in the literature.

ECHIS CARINATUS, the saw-scaled viper, occurs throughout the Middle East and there have been sightings in many areas of Saudi Arabia. Envenomation by this snake causes local swelling and severe tissue necrosis. Systemic complications are primarily related to bleeding due to blood depleted of fibrinogen and factors V, VII, II and XIII. This is manifested as hemorrhage in different parts of the body including the gums, nasopharynx, gastrointestinal tract, urinary tract and central nervous system. The neurological symptoms include drowsiness, confusion and convulsions. Subarachnoid hemorrhage was seen in three of 115 patients reported from Nigeria, two of whom died. Arterial thrombotic complications in vessels near the site of some viper bites have been well described, but arterial thromboses at distant sites are quite rare. We are aware of only two such instances reported in the literature. In this communication, a Saudi Arabian patient who had cerebral infarction after a bite from Echis carinatus is described, and possible mechanisms for this phenomenon are discussed.

Case History

A 13-year old right-handed Saudi Arabian female was clearing the ground for her sheep when she was bitten on her hand by a snake. She described the snake as being 50 centimetres long. When we showed her colored pictures of different snakes, she consistently pointed out Echis carinatus. A few minutes after the bite the patient developed severe pain and swelling in the right arm. She was taken to a nearby infirmary where she was given three 10 ml intravenous injections of polyvalent anti-snake serum (Behringwerke). She showed no immediate reaction to the antivenom and bleeding studies and prothrombin time, were normal. She received two more 10 ml injections of polyvalent anti-snake serum with no change in condition.

Seventeen days later she was transferred to the King Faisal Specialist Hospital for investigation. The fang marks on the right middle finger were visible and healing, and there was mild swelling of the right arm. She had non-fluent aphasia with difficulty in expression and understanding. She also had right spastic hemiparesis involving the face and the arm, and to a lesser degree the leg.

A pre- and post-contrast computed tomographic cranial scan performed three weeks after the snake bite demonstrated areas of low density in the left parietal region (fig. 1a, 1b) which enhanced irregularly following contrast administration with a serpiginous pattern (fig. 1c, 1d). This is compatible with an enhancing insult to this region and most consistent with infarct. A digital subtraction angiogram performed subsequently demonstrated non-filling of the left supraclinoid internal carotid artery and delayed flow within the multiple left middle cerebral artery branches as compared with the normal right side (fig. 2). This suggests thrombosis of the supraclinoid internal carotid artery with attendant slowed flow in the left middle cerebral artery as collateral flow perfuses the left hemisphere.

Hemoglobin, white blood cell and platelet counts demonstrated no abnormality, neither did the prothrombin time, partial thromboplastin time and bleeding time. Fibrinogen degradation products, antinuclear antibody test and antithrombin III activity were all within the normal range. Platelet aggregability studies were normal, as were chest X-ray, electrocardiogram and echocardiogram.

The patient underwent physical therapy and was seen a few months later, at which time she showed only moderate improvement.

Discussion

The clinical and radiological presentation of our patient strongly suggests a vascular thrombosis as a cause for her deficit. The occurrence of vascular thromboses...
in vessels adjacent to the site of envenomation by some vipers has been well described; however, it is extremely rare for thromboses to occur in distant vessels. No clinical thrombosis was seen in 115 patients reported from Nigeria and only one out of 300 patients reported from India developed a remote thrombosis. That patient was bitten on a leg by *Echis carinatus* and developed gangrene of an arm. Another patient, reported from Ceylon, was bitten on the leg by *Vipera russelli* and developed thrombosis of the middle cerebral artery, demonstrated by angiography. That patient did not receive snake anti-venom injections, and the stroke developed three to four hours after she had been bitten.

The rarity of thrombotic events in distant vessels following *Echis carinatus* bites is not surprising. The venom contains endopeptidases that deplete the circulation of fibrinogen, factors V, VII, II and XIII leading to a state of hypocoagulability. Ancrod, a purified protein from the venom of the Malayan pit viper (*Agkistrodon rhodostoma*), produces defibrination in vivo by converting plasma fibrinogen into a soluble, non-cross-linked form of fibrin. Because of this property Ancrod has been used in clinical trials for the treatment of thrombotic stroke.

As a result of defibrination, high titres of fibrinogen degradation products are seen in some patients. There is evidence that thrombin formed when *Echis carinatus* procoagulant acts on prothrombin is unlike physiological thrombin. This observation may explain why thrombocytopenia and microangiopathic hemolysis are seen in only a few of the more seriously envenomated patients: 10 out of 115 cases in Warrell's study.

FIGURES 1a and 1b. Precontrast computerized tomography: demonstrates an ill-defined area of low density in the left parietal region.

FIGURES 1c and 1d. Post intravenous contrast computerized tomography: demonstrates irregular, serpiginous areas of high density corresponding to the low density areas seen on the precontrast computerized tomography compatible with enhancing infarct.
This diffuse intravascular consumptive coagulopathy could lead to small, and possibly large, occlusions, explaining cerebral infarction in the absence of heart disease in our patients. However, the bleeding studies and platelet count being normal the day our patient had an infarct contravenes this possibility. Studies done at this hospital 17 days later showed no evidence of disseminated intravascular coagulopathy or pre-existing coagulopathy. Heart disease was also excluded.

The venom of *Echis carinatus* contains a vessel damaging factor "hemorrhagin" which is complement dependent and can cause leakage across endothelial cells of cerebral capillaries. This factor could have contributed to our patient’s catastrophe but the fact that the insult was only in one hemisphere argues against this hypothesis unless there was a pre-existing vascular problem on that side. Digital substraction angiography did not show an arteriovenous malformation or other gross vascular lesion in the cerebral circulation, however this technique cannot rule out the presence of subtle lesions.

Our patient received three 10 ml injections of snake anti-venom at a local infirmary immediately after being bitten. About 13 percent of recipients have an immediate reaction to the Behringwerke antivenom which includes fever, urticaria, coughing, sneezing, itching, vomiting and hypotension. Profound hypotension could possibly lead to cerebral infarction, but the distribution of the infarct in our patient is not the typical watershed infarct seen in hypotension. Furthermore, as far as could be determined from the treating physician, the patient was not hypotensive before or after the catastrophe.

The cause of this rare incident of cerebral infarction is intriguing. It could be related to the vessel damaging toxin in the snake’s venom possibly acting on a pre-existing abnormality in a blood vessel wall; or it could be due to a low grade disseminated intravascular coagulopathy. An episode of hypotension that was unnoticed after the anti-venom injection might have contributed to the patient’s problem. Most envenomations from *Echis carinatus* occur in the third world, and so the possible introduction of computed tomography into these countries may lead to more reports of cerebral infarction following snake bite. A contributing factor to this apparent rarity may also be inefficient or inaccurate reporting of snake bites and their complications in areas of high incidence. Therefore, with advanced diagnostic equipment and more careful reporting in the future, the true frequency of this particular sequel to snake bite may be realized.

References
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