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Viper snakebite causing symptomatic intracerebral haemorrhage

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Sirs: Venomous snakebites are associated with high morbidity and mortality. Although rare in Western industrialized countries, venomous snakebites represent a serious health problem in tropical developing areas [2, 8]. Snake venoms are complex mixtures of proteins and biologically active polypeptides [9]. Depending on the snake species, local symptoms at the site of the bite, central nervous system, neuromuscular, cardiovascular, respiratory and/or haematological manifestations may arise. In particular, venoms from Viperidae species contain polypeptides which may interfere with haemostasis, thus leading to ischaemic or haemorrhagic neurovascular complications [4, 6, 7].

Herein, we report a 22-year-old patient originating from Mali in Western Africa who was bitten by a snake in his left foot while performing agricultural work in the savannah. Soon after the snakebite, marked oedema of the left leg developed. As he had no access to a medical facility, no antivenom administration or other medical treatments were possible. Within the following hours, he developed signs of a severe envenomation with drowsiness and vomiting, and he was later reported to have suffered from a generalized haemorrhagic syndrome with epistaxis and macrohaematuria. Over several weeks, he recovered from the general symptoms of the envenomation. As he was able to get back to his feet, he realized that the muscle strength of his left leg was markedly diminished. During the following months, the weakness did not improve and a pronounced muscular atrophy of the left leg developed. At the age of 24 years, he came to Switzerland seeking political asylum. After arrival, he was admitted to our department. Neurological examination demonstrated a distally pronounced monoparesis of the left leg, ranging from M1 to M4, with a generalized left leg muscle atrophy. In contrast, the muscle tone of the left leg was markedly increased, tendon reflexes were brisk, but plantar responses were flexor. Sensory testing of the left leg, the remaining neurological examination, and a general medical examination were normal. An extended laboratory investigation including differential blood cell count, haemostasis parameters, renal, thyroid and liver cell function tests, and HIV testing was normal.

Based on the clinical findings, a central monoparesis of the left leg, most probably caused by a cortical lesion, was presumed. A peripheral neurogenic palsy as local sequelae of the snakebite was further ruled out by normal electromyographic examinations. In addition, motor evoked potentials demonstrated a prolonged central motor latency (CML) to the left anterior tibial muscle (27.2 ms; normal < 20.3 ms). CMLs to the right leg and both arms were normal, without pathological side differences in the latter. Hence cerebral MRI was performed, that demonstrated a circumscribed lesion in the right lobulus paracentralis including the parasaggital motor cortex (Fig. 1A). The lesion was hypointense in T1-weighted images, and hyperintense in T2-weighted images with a rim of decreased signal intensity, corresponding to an intracerebral haemorrhage in a chronic stage (Fig. 1B). Upon confrontation to illustrations of different candidate snakes, the patient could identify without doubt the one that had bitten him as a saw-

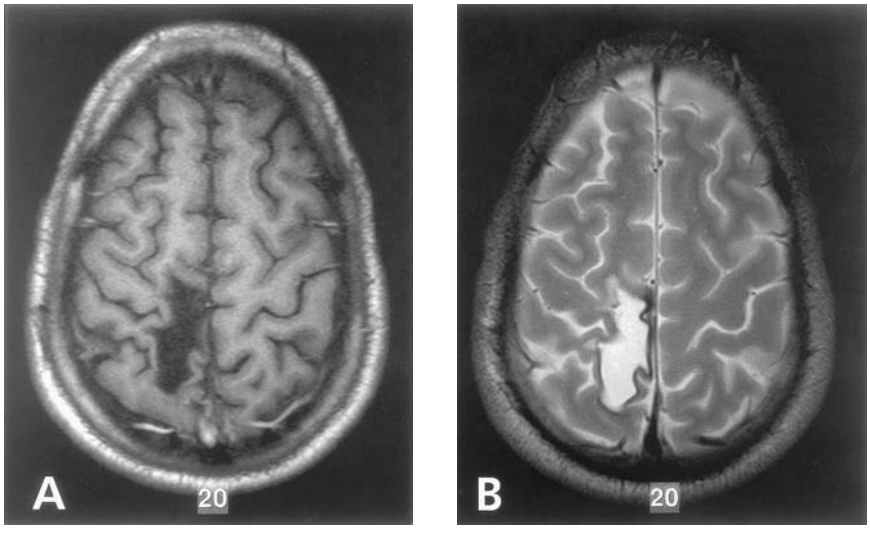

Fig. 1 **A** T1-weighted magnetic resonance imaging demonstrates a hypointense signal abnormality in the lobulus paracentralis including the right parasaggital motor cortex. **B** T2-weighted magnetic resonance imaging demonstrates a hyperintense signal abnormality surrounded by a rim of hypointense signal, thus the imaging characteristics of an intracerebral haemorrhage in the chronic stage

scaled viper (*Echis carinatus*; Fig. 2). Since haemostatic failure is a known complication of *Echis carinatus* bites, the intracerebral haemorrhage was interpreted as a direct consequence of the viper bite.

True vipers (Viperidae; *Viperinae*) are found in Africa, Europe, Middle East, the Indian subcontinent and Southeast Asia. Saw-scaled vipers (*Echis* spp.) consist of different species and subspecies, which are spread from Western Africa to the Indian subcontinent. *Echis* spp. are considered to be one of the most dangerous venomous snakes. Their bites regularly cause severe local symptoms such as oedema, blistering and necrosis. The leading clinical symptom, however, is haemostatic failure. Up to 50 % of patients with *Echis* spp. bite envenomation developed severe spontaneous haemorrhage, resulting in a mortality rate ranging between 10 to 20 % if no antivenom serum was applied [10].

Haemorrhagic diathesis induced by the *Echis* spp. venom may be caused by different mechanisms. Some active venom proteins have metalloproteinase-like properties and induce destruction of the basement membrane and extracellular matrix surrounding capillaries and small vessels [5]. Other venom proteins directly interfere with coagulation factors or platelet function. Echistatin, a polypeptide purified from the *Echis carinatus* venom, acts directly on platelet aggregation [1]. Echistatin belongs to the family of disintegrins and acts as a fibrinogen receptor (GPIIb/IIIa) antagonist, thus inhibiting the final common pathway of platelet aggregation. Because of its potential as a therapeutic agent, echistatin has received a lot of attention [1]. Another well-characterized *Echis* venom polypeptide is echicetin, a C-type lectin that binds to the platelet GPIb receptor, thus blocking the interaction of platelets with thrombin and the von Willebrand factor. It is noteworthy that echicetin has also been shown to activate platelet aggregation [1]. These findings support the clinical observation that viper venoms may exhibit both coagulant and anticoagulant properties.

Cerebrovascular complications due to Viperidae snakebites, although rare in Western countries, represent a significant health problem in developing countries. From over 300 Viperidae *Bothrops* spp. snakebite victims in Ecuador, 7 patients developed haemorrhagic, and one patient ischaemic cerebrovascular complications [6]. Other clinical reports including different snake species and performing less detailed clinical evaluation suggest that 5 to 12 % of snakebite victims might develop cerebrovascular complications [3, 7]. The present case report illustrates the potentially lethal effects of viper venoms on the haemostatic system, and is an instructive example of a neurological complication that is rarely encountered in Western countries. The increasing knowledge about snake venoms and their possibly deleterious interference with the molecular cascades of the haemostatic system might lead to new treatment strategies of snakebites apart from the established therapies with specific antivenoms. In addition, constituents of snake venoms represent attractive molecules for the ongoing pharmacological research of the haemostatic system.

Fig. 2 Saw-scaled or carpet viper (*Echis carinatus*)

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