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Black Mamba *Dendroaspis Polylepis* Bite: A Case Report

Závada J., Valenta J., Kopecký O., Stach Z., Leden P.
Department of Anesthesiology and Intensive Care, First Faculty of Medicine, Charles University in Prague and General University Hospital in Prague, Prague, Czech Republic

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Abstract: Although very rare in a European context, a bite from the black mamba *Dendroaspis polylepis* is an event that poses an immediate threat to life. Given the content of neurotoxins in the snake's venom, the mortality of envenomation reaches 100% in almost every case if ventilation is not provided in a timely manner and adequate therapy initiated. The report describes a case of a snake breeder being envenomed. This 31-year-old man was bitten by a black mamba on his finger, and who subsequently developed clinical symptoms of envenoming typical for the species. Thanks to mechanical ventilation being employed promptly, with myorelaxation during generalized muscle fasciculations, and particularly owing to the eventual antivenin therapy, the patient's condition settled without consequences. In addition to describing the given case in detail, the paper discusses the composition and mechanisms of action of black mamba venom, while providing guidelines for adequate therapy.

Mailing Address: Jiří Valenta, MD., Department of Anesthesiology and Intensive Care, First Faculty of Medicine, Charles University in Prague and General University Hospital in Prague, U Nemocnice 2, 128 08 Prague 2, Czech Republic; Phone: +420 224 962 248; e-mail: jiri.valenta@vfn.cz

Introduction

With an average length of 250–350 cm, and the maximum recorded length of 425 cm, the black mamba *Dendroaspis polylepis* is the longest venomous snake in Africa. In reality, this snake possesses an olive-brownish through to dark gray colour and a light belly; the name is actually derived from the black colour inside its mouth. Mambas are considered one of the fastest snakes either when moving or possibly striking when disturbed, which makes them highly dangerous creatures when combined with their short-tempered behaviour (Figure 1). The genus members compete with the African puff adder *Bitis arietans* and saw-scaled vipers *Echis* sp. for the dubious honour of supremacy in terms of mortality from bites in Africa, based on lethality reaching 100% if no therapy is available. However, the incidence of snake bites in typical places of envenoming is probably overstated (Warrell, 1995; Hodgson and Davidson, 1996; Valenta, 2010).

The black mamba's venom glands contain approximately 8–16 ml of liquid venom. In the freshly hatched young, the amount is 1–2 ml of venom, which is sufficient quantity for a lethal effect on a human. The key venom components involve highly effective neurotoxins. In this species, the venom contains neurotoxically acting nicotine acetylcholine receptor antagonists analogous to the postsynaptic neurotoxins of other elapids (*Elapidae*) classified as α, β, γ and δ neurotoxins (Hodgson and Davidson, 1996). The neurotoxins with the greatest effectiveness are dendrotoxins (DTX); blocking voltage potassium channels, these cause extension of the process of re-polarization of neurons (Harvey and Karlsson, 1980; Harvey, 2001; Harvey and Robertson, 2004). This way the substances support muscle paralysis by exhausting neuromuscular junctions via super-threshold stimulation. Other types of neurons include fasciculins, peptide acetylcholinesterase inhibitors. Originally isolated from the venom of the green mamba (Tox-C isolated from the venom of the black mamba), these substances increase the intrasynaptic quantity of

Figure 1 – Black mamba Dendroaspis polylepis *(photo: P. Velenský).*

acetylcholine, which results in muscle fasciculations (Karlsson et al., 1984; Warrell, 1995; Hrdina et al., 2004). Some of the peptides isolated from mamba venom act as muscarine acetylcholine receptor ligands and probably potentiate neural transmission in CNS (Jolkkonen et al., 1995).

The venom also contains a certain portion of components that are cardiotoxic (Naidoo et al., 1987). Hyaluronidases facilitate rapid propagation of venom components in the organism, plus there is the Dendroaspis natriuretic peptide (DNP), a substance analogous to the atrial natriuretic peptide in humans; it is responsible for causing diuresis through natriuresis and dilation of vessels (Lee and Burnett, 2007). Hemolytic, hemorrhagic and coagulation activities are almost completely absent from mamba venom (Warrell, 1995).

Case report

A 31-year-old Czech snake-breeding specialist and active sportsman experienced a snake bite from a black mamba on the tip of the third finger of his right hand; the bite occurred through the cloth of a snake transporting bag. First aid procedures were carried out by the patient, which involved cutting next to the bitten site and applying Sutherland's pressure immobilization bandage (whole extremity tight bandage). Being aware of the severity of his status, the man arranged for immediate transportation to the local hospital.

Fully conscious in the emergency room, the patient was showing tachycardia of 150–160 per minute, hypertension (systolic blood pressure of 200 mm Hg) and profusive sweating, with paresthesia in the lower limbs and dyspnea. Due to increasing respiratory failure, the patient was intubated and mechanical ventilation initiated with continual analgosedation; the man was admitted to ICU. Following the intubation, furosemide and manitol were administered due to signs of pulmonary edema, with a subsequent application of hydrocortisone and antitetanic prophylaxis. After consulting the Toxinology Center, the patient was transferred *par avion* to their ICU under continued sedation, ventilation, and intermittent muscle relaxation.

Upon admission to the ICU, which took place 4.5 hours after the bite, limb and body muscle fasciculations appeared upon reducing such relaxation, despite intense sedation using propofol and sufentanil. The patient was continually profusely perspiring and hemodynamically unstable, with a sinus tachycardia of 125 per minute, centralized circulation and decreased capillary refill. A slight decrease in blood pressure was treated by volumosubstitution and also temporarily by administering a low dose of norepinephrine (less than 0.1 μg/kg/min); at the same time, peripheral perfusion was improving. No pathological findings were found via echocardiography. Mechanical ventilation with a PEEP level of 6 cm H_2O and FiO_2 of 0.4 was sufficient to maintain normal levels of blood gases. Polyuria with diuresis was developing, as much as 500 ml per hour. The limb was without any hematoma and oedema and was kept bandaged until administering the antivenom – SAIMR polyvalent antivenin, South Africa – of which two doses were applied.

Despite the fact that two doses of antivenin had been applied, fasciculations became generalized nine hours following the bite, with increased CO_2 production and body temperature. The status did not change even when sedation was intensified using diazepam, midazolam, thiopental and after giving $MgSO_4$. Fasciculations receded only following relaxation by means of administering atracurium in the form of a bolus, and this at full dosage (0.5 mg/kg). Redness on the skin became apparent, which in this phase was not accompanied by perspiration, plus there were rather striking reddish bands around peripheral veins on the affected limb and a slight swelling developed on the injured finger. Even a third dose of antivenin did not result in mitigating the symptoms. Fears of potential development of rhabdomyolysis and myoglobinuria, with creatinkinase levels registering 10.81–20.80 μkat/l, meant relaxation of the patient had to be conducted on a continual basis. The levels of serum myoglobin did not exceed 407 mg/l.

Additional antivenin had to be brought in urgently from a foreign toxicological centre. 27 hours after the bite two more doses of antivenin were administered, the continual relaxation by atracurium halted and the dosage of analgosedation decreased. Later, the fasciculations stopped, 3 hours after administering the last dose of antivenin. 35 hours following the bite, respiratory muscle function recovered, the extent of which was, however, insufficient for the extubation. Mechanical ventilation was shifted to ventilatory support.

In laboratory testing, leukocytes were found to have increased during the envenomation, with 15.07×10^9/l being the maximum, plus progressive growth in CRP occurred, the levels ranging from 1.3 mg/l to 241.6 mg/l.

On day 4, i.e. the 58th hour following the bite, the patient was extubated, with muscular strength proving sufficient. The diffuse redness receded, with the limb's swelling temporarily progressing to the mid forearm. The patient was observed over the next 24 hours until full extent of mobilization was reached with the remission of neurological symptomatology and once hemodynamic stability was achieved and *per os* intake recovered. The oedema regressed with only localized extension on the finger. On day 5, the patient was transferred to the neurological department of his local hospital, after two days of observation dismissed home fully recovered.

Discussion

A bite by the mamba is a rare event within Europe and only involves snake enthusiasts. In fact, just one case of envenomation by a black mamba has been described and published in the past 30 years throughout the continent (Markwalder and Koller, 1987). Two case studies describe bites by a different member of the genus, the green mamba *Dendroaspis viridis* (Markwalder and Koller, 1987; Leclerc et al., 2008). In these, however, the effect of neurotoxins was not serious enough to result in paralysis of the respiratory muscles and

mechanical ventilation was not required. No antivenin was administered due to the mild progress experienced and prior recurrent exposure to a horse antivenin (Markwalder and Koller, 1987), whilst in the case described by Leclerc et al. (2008) progress also proved mild and no antivenin was available. Other than these, a few cases of envenoming by mamba bites have been published in Africa (Crisp, 1985; Harvey, 1985; Hilligan, 1987).

The high efficiency of toxins contained in black mamba's venom causes life-threatening muscular paralysis to develop even when the quantity of venom injected is low, and this within several minutes following the bite. If symptoms develop, arrangements for mechanical ventilation and subsequent final treatment by administering the respective antivenin are, in a European context, requirements for successful therapy. When there is a lack of options to ensure ventilation for the affected person, very timely application of a sufficient dose of antivenin is essential, which may prevent the effects of neurotoxins from fully developing, as well as avoiding paralysis of the respiratory muscles and ventilatory failure (Warrell, 1995).

Even though the injury occurred through a transporting bag and just a single fang was employed, and assuming that only a minor quantity of venom had been transferred, the severity of the envenomation is confirmed through the possible lethal effect of just a fraction of the quantity of venom that an adult black mamba can release. Symptoms of affliction were developing as early as during the patient's transfer. The autonomic and circulatory symptoms that occurred can be attributed to the effects of venom components, but also in part to the current mental state of the person affected. Nausea, vomiting, abdominal pain, headache, perspiration, and vasomotoric disorders are conditions generally described in cases of envenoming by a snake bite, which applies to one from the mamba as well (Warrell, 1995).

The onset of neurological symptoms usually begins with paresthesia and paralysis in the area of the cranial nerves, with subsequent progression craniocaudally. The elimination of respiratory muscles and respiratory insufficiency usually occurs while maintaining full consciousness. In the case described, the development of this life-threatening symptomatology took place within 30 minutes.

The progression of neurotoxic effects with apparent and persisting fasciculations, despite administering the first allocation of the available antivenin, heightened concerns about damage to the neuromuscular plate and axons in the instance of long-term, excessive stimulation by dendrotoxin (DTX) and fasciculins. Due to the reasons above, additional doses of antivenin were ordered urgently from abroad. Potential damage to muscle cells by fasciculations was another concern. Continual myorelaxation to eliminate ongoing muscle fasciculations proved to be temporarily sufficient therapy to protect the muscular tissue and bought some time before the other doses of antivenin were supplied.

Administering cholinesterase inhibitors, like edrofonium or neostigmine (Warrell, 1995; Hodgson and Davidson, 1996), effective in cases of postsynaptic neurotoxin effects and as recommended by some authors, was not applied because it was not

indicated under the action of neurotoxins that increase acetylcholine supply on neuromuscular junctions, i.e. DTX, fasciculins, with the potential consequence of intensifying the effects of these.

The high diuresis in the initial phase of envenomation can be associated with the presence of DNP, a polypeptide with natriuretic effects, and even with administration of furosemide and manitol during treatment at the local hospital due to suspected development of pulmonary oedema and prevention of tissue oedema. The cause of the occurrence of the pulmonary oedema is not explained by the presence of any of the described components of the black mamba's venom; it, however, might be associated with severe autonomic responses and hemodynamic instability, or the possible content of some enzymatic components of the metalloprotease type that may generally interfere with the endothelial structure and that of its junctions.

Conclusion

The case described above illustrates a typical severe progress in envenoming by the black mamba. The total quantity of antivenin used for neutralizing the venom components indicates, as well as the mechanism of the bite, that the quantity of venom released was rather small. Despite the facts above, severe envenomation posing an immediate threat to life developed, which is consistent with the toxicity considered and described in the black mamba venom. A key moment in the case of snake bite from the black mamba is timely reaching a medical facility that can arrange for securing the airways and mechanical ventilation, plus the adequate antivenin must be available.

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