Black Mamba Death

Venom Versus Antivenom?

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Abstract

We present the case of a male adult who was admitted to an emergency department after having sustained envenomation from a black mamba (*Dendroaspis polylepis*). According to the available history, a single fang hooked his right index finger, post venom extraction. After administering antivenom in the accident and emergency department, further vials were transfused in the intensive care unit. An urticarial rash was noted, which was thought to be related to the antivenom. The victim remained in a coma for 3 days, after which he was declared dead. A medicolegal postmortem examination was performed 4 days after death because of logistical reasons. The complexities of differentiating acute envenomation from black mamba versus early acute reactions to polyvalent antivenom administration are highlighted in this case study.

Keywords:

antivenom; autopsy; black mamba; *Dendroaspis polylepis*; dendrotoxins; early acute reaction; anaphylaxis; forensic; fatality; neurotoxic; snake bite

There is limited literature on the pathology of trauma of black mamba (*Dendroaspis polylepis*) bites. The black mamba is a venomous snake found in southern Africa with neurotoxic venom. It is a front-fanged elapid with neurotoxic venom.[1] Although often becoming very dark with age, it is rarely truly black, but usually dark brown, olive brown, or gunmetal in color. Black mambas may reach 4.3 m in length "in exceptional cases"[2] (Fig. 1).

Figure 1: Black mamba (Dendroaspis polylepis). Photograph courtesy of Thomas Birkenbach.

Of all venomous snakes, it is the largest and most feared, being of somewhat uncertain temper and often displaying great truculence and readiness to attack if suddenly disturbed or otherwise molested. This readiness to attack is particularly evident during the mating season, that is, spring or early summer, when it is more irritable and aggressive than usual.[2]

As an example of the lethal potentialities of the mamba, one can quote many cases when one of these snakes has been flushed by a pack of inexperienced dogs and 4 or more of the attackers have been bitten in rapid succession and have subsequently succumbed before the snake has been torn to pieces.[2]

As may be gathered from the above account, there is no doubt that the mamba is fully deserving of its reputation as being “king” of African snakes, a position comparable only to that of the king cobra in Asia.[2]

The maximum venom yield of a large black mamba is often given as 400 mg but is probably closer to 280 mg. Approximately 15 to 20 mg of venom is required for a fatal bite on a human. Although this snake has a reputation as being the most dangerous snake in Africa, it is actually a shy and elusive snake that will endeavor to avoid humans.[3]

Elapid venom interferes with transmission across the motor end-plate.[4] Toxin C from black mamba venom contains 61 amino acid residues in a single polypeptide chain, cross-linked by 4 intrachain disulfide bridges. The complete primary structure of toxin C has been elucidated. The amino acid sequence and the invariant amino acid residues of toxin C resemble the corresponding properties of the angusticeps-type proteins.[5]

Neurotoxic venom is composed of polypeptides that bind to the postsynaptic nicotinic receptors that would normally bind acetylcholine. These receptors are located at the skeletal muscle nerve junctions and therefore will result in paralysis. Specifically, mamba venom additionally contains dendrotoxins that promote the release of acetylcholine from nerve endings. The venom also inhibits synaptic acetylcholinesterases.[6]

CASE REPORT

An unconscious victim of a snakebite reportedly less than 20 minutes previously was admitted to the accident and emergency department of a major hospital in a large urban area. The victim, a 27-year-old man, was accompanied by coworkers who were able to supply valuable information to the personnel on duty. It was verbally reported that the victim, who worked as a snake handler, in a facility where venomous snakes were milked for their venom for the production of snake antivenom, had sustained a bite. Their account further related that the victim had apparently finished milking a black mamba. The coworkers were certain that the snake was a black mamba.

After safely securing the snake in its cage, the victim apparently walked over to a washbasin and proceeded to wash his hands. He then walked over to his colleague and reported that he felt dizzy and that the snake may have bitten him when he released it in its cage. According to the one coworker, the victim was holding his right hand and was bleeding from the index finger.

Emergency measures were instituted by his coworker, who placed a blood pressure cuff around the arm, to stop the venom from entering the circulation. A private car was used to transport the victim to the nearest hospital. The victim reported feeling faint and was "rubbing his lips on top of one another." They called the accident and emergency department on their way to inform them that they were rushing a snakebite victim to hospital and that they would in all likelihood require antivenom.

The hospital pharmacy prepared all available antivenom and acquired more should the need have arisen. On arrival, the emergency doctors and personnel assessed the patient, finding no pulse or spontaneous breathing; they commenced with immediate cardiopulmonary resuscitation, which comprised tracheal intubation, manual ventilation with high-flow 100% oxygen, and manual chest compressions. Intravenous access was obtained to administer fluids and inotropic support. Shortly after commencing cardiopulmonary resuscitation, a recordable ventricular fibrillation on electrocardiography was obtained, with no regular rhythm returning.

The accident and emergency department doctor then consulted the extracorporeal membrane oxygenation (ECMO) team of the hospital to consider the patient for ECMO as their efforts had no lasting effect on the patient's cardiac rhythm or output. Also known as extracorporeal life support, ECMO is an extracorporeal technique of providing prolonged cardiac and respiratory support to persons whose heart and lungs are unable to provide an adequate amount of gas exchange or perfusion to sustain life. Extracorporeal membrane oxygenation is fast becoming part of the armamentarium for the physician treating catastrophic life-threatening emergencies.

Sinus rhythm did occur, but repeatedly converted to ventricular fibrillation. Extracorporeal membrane oxygenation was initialized during active cardiopulmonary resuscitation in approximately 45 minutes. Access to the vascular system was achieved with venous cannulation of the right femoral vein and arterially through the left femoral artery, which included a 7F distal perfusion cannula.

Upon commencement of extracorporeal flow, the victim's heart rate returned to a fast sinus tachycardia, and chest compressions were halted. During this time, the administration of polyvalent antivenom was commenced, shortly after which signs of anaphylaxis were evident. The victim required high dosages of continuous inotropic support, intravenous short-acting steroids were administered, and hemodialysis was commenced upon arrival in the intensive care unit.

Hemodynamically, the victim could be supported adequately with a flow on the ECMO of between 3.5 and 4.2 L/m. After administering 20 vials of antivenom in the accident and emergency department, a further 20 vials were transfused upon arrival in the intensive care unit. The first 12 hours were critical in stabilizing all parameters, and constant vigilance was applied to maintain all systems. Neurological assessment was acquired less than 24 hours after admission. The results were not promising.

The peripheral resistance remained low, and adequate circulation could be maintained only through high dosages of peripheral vasoconstrictors, resulting in a steady low perfusion state and severe compounding metabolic acidosis. No neurological activity could be recorded on electrocardiography, and maintaining the circulation became increasingly difficult. No further escalation in treatment was possible, and all cardiac activity ceased 72 hours after admission to hospital.

Autopsy Examination

A medicolegal autopsy was performed 4 days after death because of logistical reasons. External examination showed a male adult with a single “puncture mark” located approximately 0.5 cm from the fingernail on the lateral aspect of the right index finger. No obvious swelling could be seen in relation to the wound. Surrounding subcutaneous hemorrhage was present, which measured approximately 1.0 cm in diameter (Fig. 2).

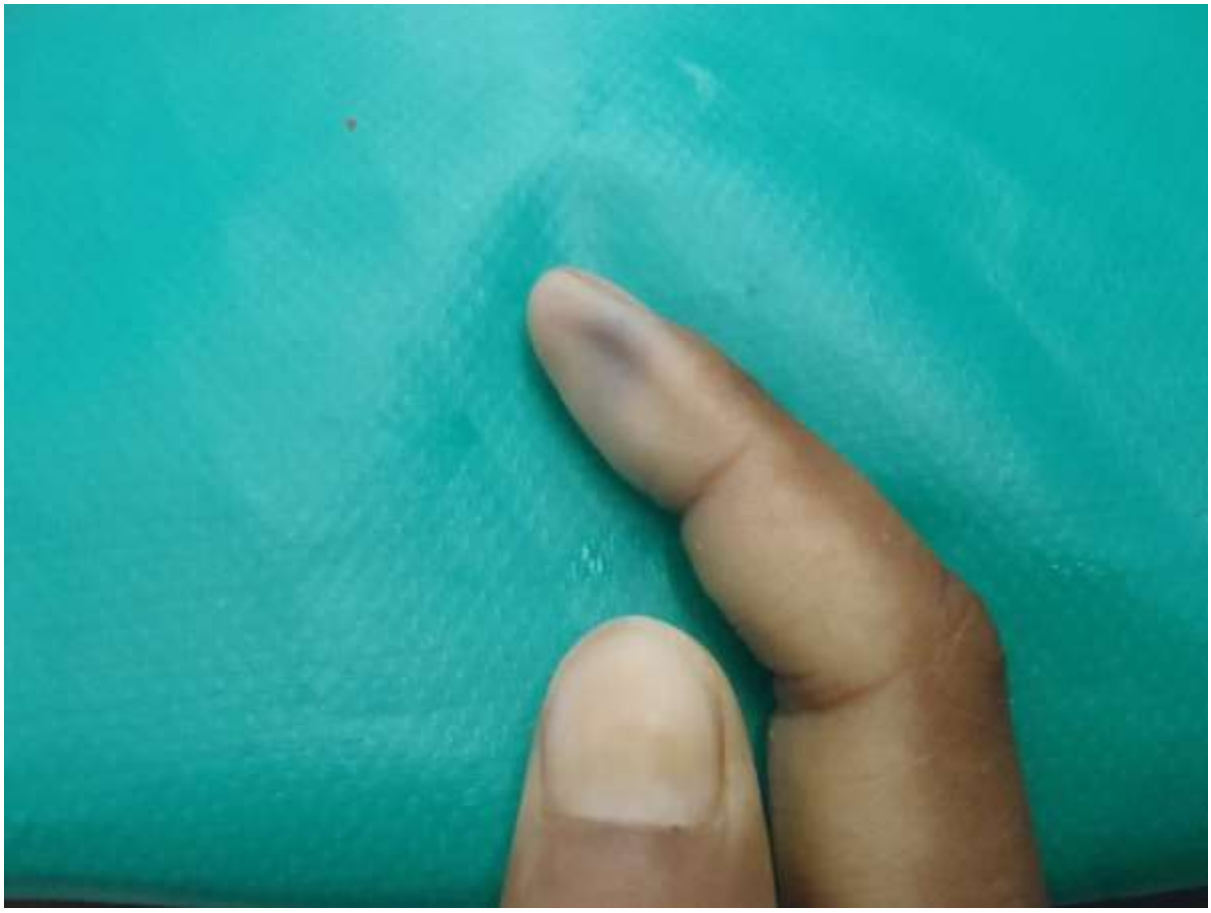

Figure 2: Puncture wound on the lateral aspect of the right index finger.

The body showed signs consistent with prolonged hospitalization, multiple organ failure, and disseminated intravascular coagulation. Surgical incision wounds were present within both inguinal fossae regions, in keeping with the available history of ECMO. Multiple needle puncture marks, in various stages of healing, were also present on the body.

Both conjunctivae showed chemosis and jaundice. The right eye showed a subconjunctival petechial hemorrhage. Purpuric hemorrhages were located overlying the anterior and medial aspects of the right upper arm (Fig. 3). Fresh subcutaneous hemorrhages were located on the anterior aspect of the right thigh and the suprapubic region.

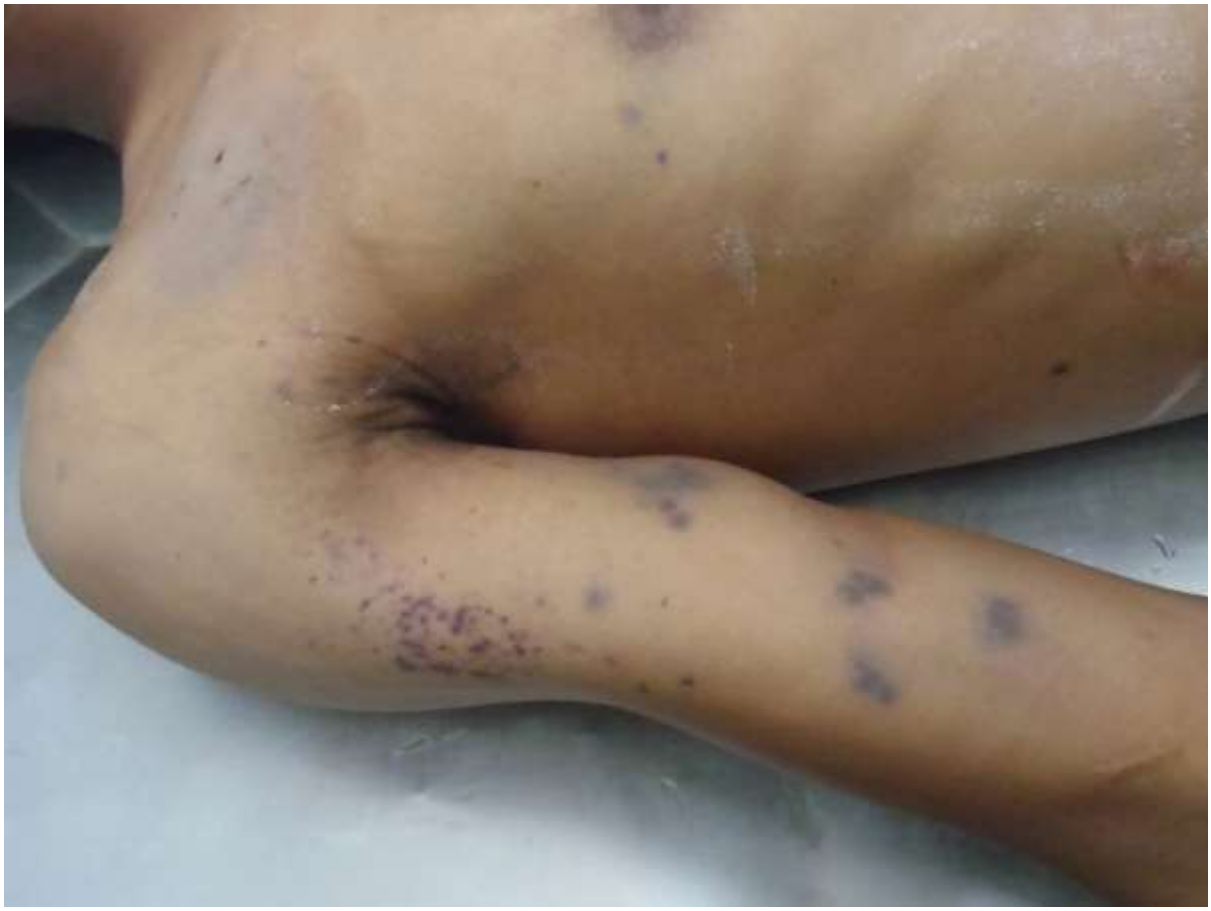

Figure 3: Purpuric haemorrhages found on the victim at autopsy.

Discolored regions, probably urticarial in nature, were present overlying the left side of the hip, buttocks, left thigh region, left lower leg, and right lower leg.

Internal examination showed multiple, fresh, submucosal hemorrhages located in and around the vocal cords and overlying the epiglottis (Fig. 4).

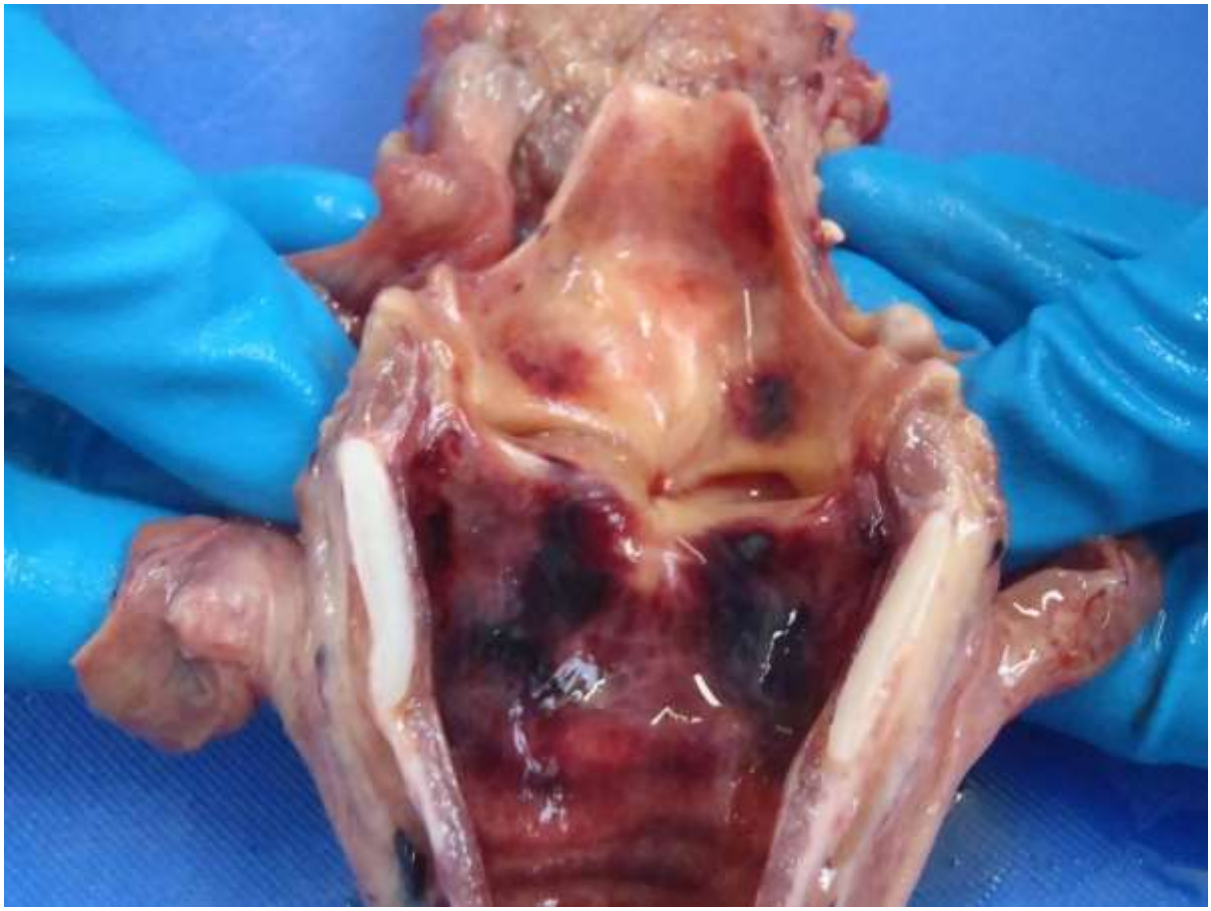

Figure 4: Fresh sub-mucolsal haemorrhages located in and around the vocal cords.

Examination of the thoracic cavity showed fresh intercostal hemorrhages, in keeping with fresh cardiopulmonary resuscitation injuries.

Both lungs were relatively heavy. The left lung weighed 828 g, and the right lung weighed 926 g. There was a 6 × 5-cm ecchymotic hemorrhage located on the posterior aspect of the left lung lower lobe. Shower petechiae were present within the fissures of the lungs. Cut sections of the lungs showed hemorrhagic “mottling” of the pulmonary parenchyma. The pulmonary parenchyma was friable, bilaterally.

The heart showed shower petechiae overlying the anterior and posterior epicardial surfaces. Fresh hemorrhages were present within the right atrium and right ventricle. A fresh 3 × 2-cm subendocardial hemorrhage was present at the left ventricular outflow tract, which extended approximately 0.5 cm deep. The coronary arteries were patent. The valves were normal. The heart weighed 264 g (Fig. 6).

Perivesicular hemorrhage was present. Multiple catheter irritation marks were present on the bladder wall mucosa. The bladder contained approximately 20 mL of blood-stained urine.

Histological Examination

Histology of the “fang” puncture mark on the finger showed vital reaction, with associated hemorrhage noted at the skin puncture site. There was minimal skin necrosis seen at the bite mark (Fig. 5).

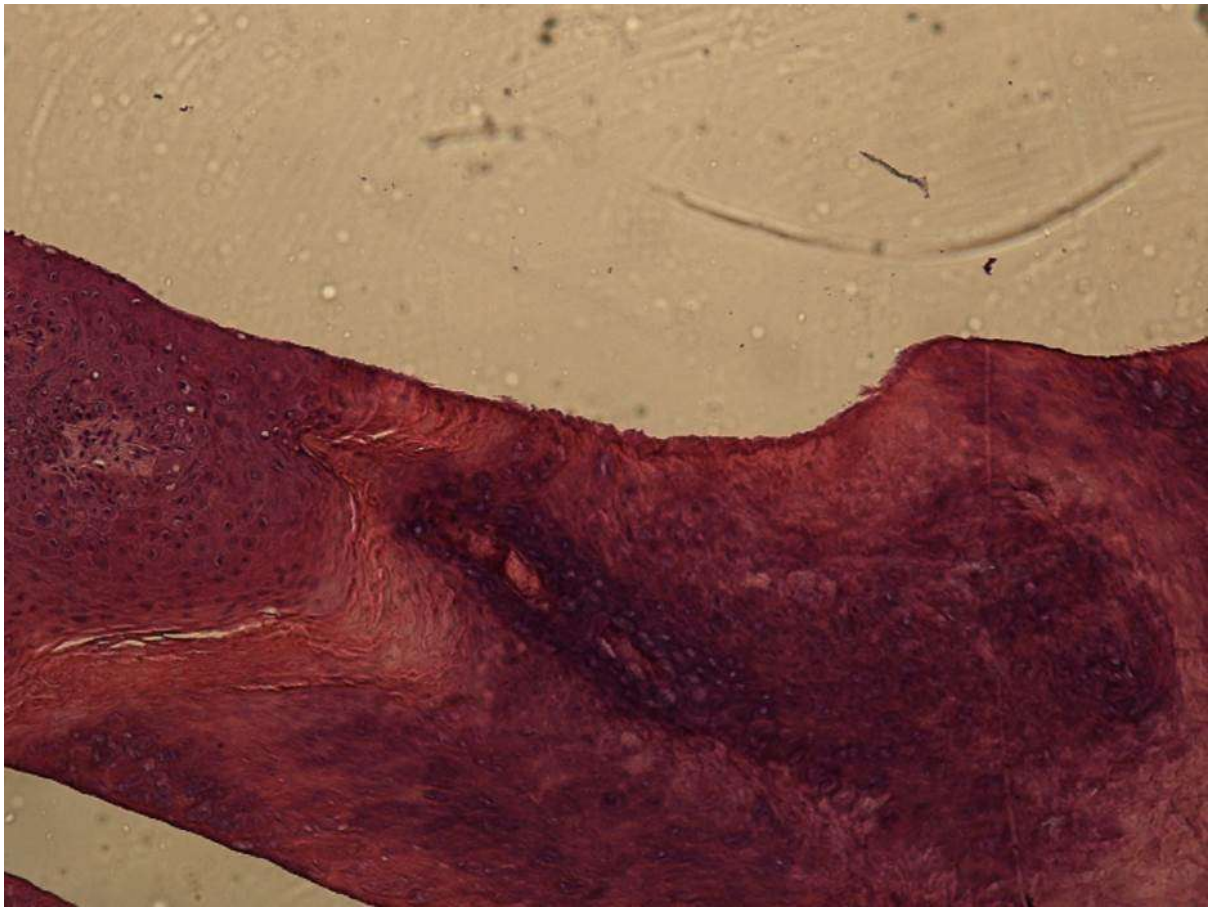

Figure 5: Microscopic demonstration of necrotic skin found in relation to the fang puncture site.

Histology of the lungs showed features in keeping with early fibrinosuppurative consolidation. Microscopic examination of the heart showed diffuse intramyocardial hemorrhages, with extensive interfiber free-lying erythrocytes. A subendocardial hemorrhage was confirmed at the left ventricular outflow tract. Papillary muscle hemorrhage was confirmed (Fig. 6 and Fig. 7).

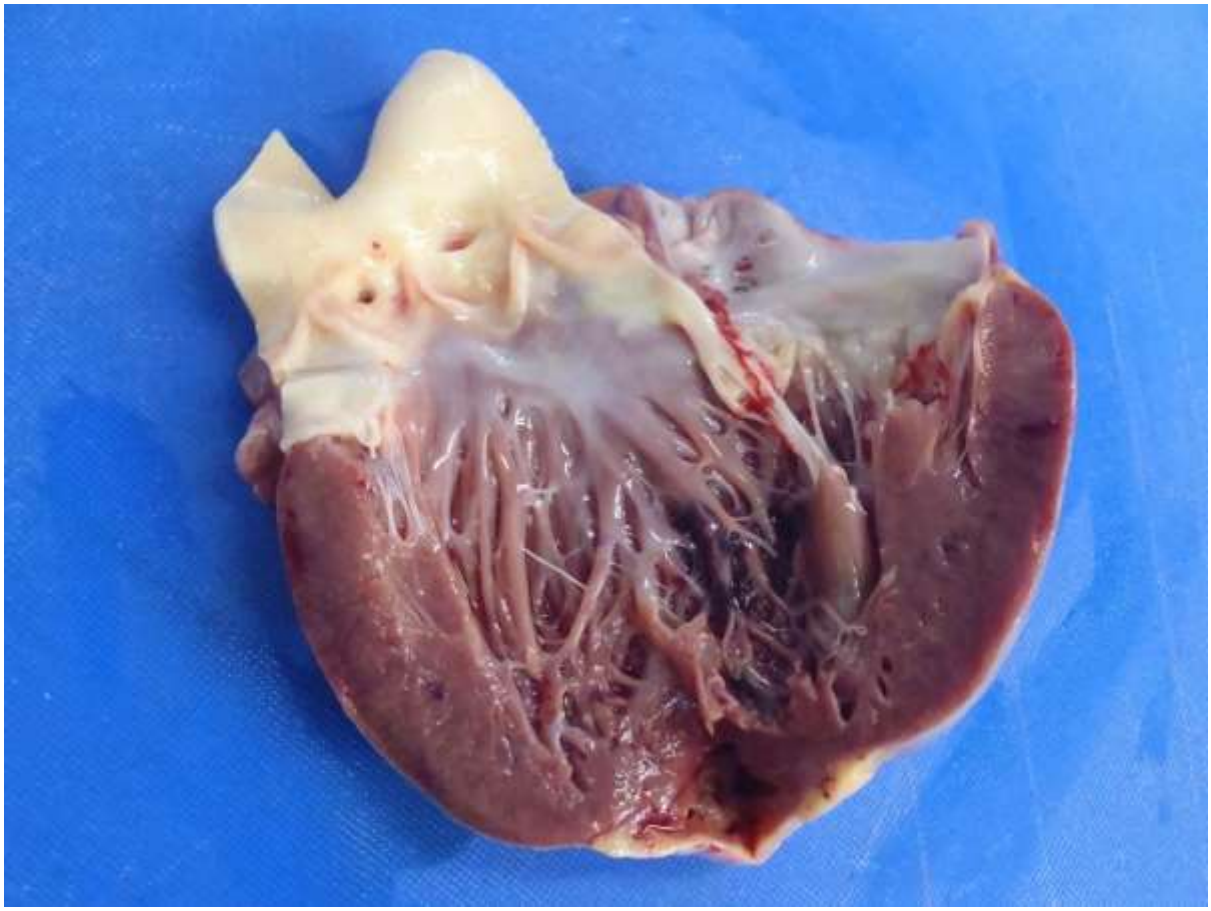

Figure 6: Subendocardial haemorrhage at the left ventricular outflow tract.

Figure 7: Microscopic demonstration of the fresh inter- and intra-fibre haemorrhages located within the cardiac muscle.

Histology of the brain showed features suggestive of hypoxic-ischemic encephalopathy. Postmortem toxicology and serum-tryptase levels were not performed because of the prolonged in-hospital management.

DISCUSSION

Mambas belong to the family Elapidae, which includes cobras and coral snakes.[7]

According to Hilligan,[8] the mamba is born with 2 to 3 drops of venom per fang (an adult having 12–20 drops per fang), and 2 drops of venom only are required to kill an adult human, thus making even the young mamba a very dangerous snake.

Strover[9] reported on the death of an African male adult who was admitted after having been bitten by a black mamba. The victim was admitted into hospital 3 hours after having been bitten on the right thumb. There was practically no swelling in the region of the bite and no signs of bleeding at the site or any hemolytic symptoms. There was a most profuse sweating reaction. The victim was alert and struggling until just before death. There was the presence of ptosis, but not paralytic strabismus.[9] Sweating and struggling were not reported in the records of this particular case.

A case of envenomation was described following a bite to a finger by *Atractaspis corpulenta*, which resulted in sudden death approximately 2½ hours later, in the Republic of Congo.[10]

A report of a black mamba bite was published in *The Central African Journal of Medicine* in June 1980.[11] The victim, a medical colleague of the author, survived because of 4 reasons: the bite was in a favorable location (below the left elbow); a tight above-elbow tourniquet was applied; the excellence of the South African Institute of Medical Research (SAIMR) polyvalent serum in adequate doses; and the protective doses of steroid and small doses of intravenous adrenaline in staving off anaphylaxis.

Hilligan[8] reported 2 cases of black mamba bites. One involved a 14-month-old child, and the other a 34-year-old man. Both victims survived because of early aggressive treatment. Several factors influenced the successful result; first, the child arrived within 15 minutes of being bitten, and an intravenous line was quickly established. The first dose of antivenom was given within 35 minutes of the child being bitten. Second, there was no hypersensitivity reaction to the antivenom. In the second case, the patient arrived to the clinic within 35 minutes of being bitten, and he was treated quickly and aggressively and showed no evidence of hypersensitivity reaction.

Krengel and Walton[4] reported the case of a 34-year-old man bitten through his trousers and socks on the medial aspect of the left leg, just above the ankle, in 1967. The victim survived because of the polyvalent mamba antivenom and intravenous cortisone to counteract any adverse effects from the serum. The polyvalent antivenom used was created by the SAIMR and was specific to the venoms of *Dendroaspis angusticeps*, *D. polylepis*, and *Dendroaspis jamesoni*.

A 24-year-old black man was bitten by a black mamba in 1985 in Durban. He had been bitten twice by the snake at the same site in quick succession as his arm brushed the boughs of a tree overhanging the river bank. A tourniquet had been applied immediately, and he was brought to hospital. This patient made a good recovery with no residual cardiac damage. A probable direct toxic effect of elapid venom on the myocardium as evidenced by transient electrocardiogram changes and transiently elevated cardiac enzyme levels was described by Naidoo and Naiker,[12] following black mamba bite.

Upon reviewing this case, it is believed that the patient arrived at the hospital after having suffered cardiac arrest with accompanying hypoxic brain injury. The initial injury, the envenomation by the toxin of a black mamba, apparently put all events in motion, which contributed to multiple organ failure in a very short period. The administration of antivenom with the complication of anaphylaxis further compounded matters. The application of ECMO was a team decision, based solely on available information at the time during active resuscitation.

Polyvalent snakebite antiserum is effective against the venom of most of the cytotoxic and neurotoxic snakes in South Africa. It is noted that there is a risk of allergic reaction when using horse serum–derived antivenoms. According to the literature, 10% to 30% of patients may be expected to show allergic reactions, including acute anaphylaxis. Skin testing for sensitivity is not recommended because it is unreliable and only delays urgent

administration of antivenom. Premedication with antihistamines and steroids is recommended in sensitive individuals. Although these agents may dampen reactions, they will not prevent an anaphylactic (anaphylactoid) reaction.[13]

Antivenom production began at the SAIMR (now known as National Health Laboratory Service) as early as 1928. Polyvalent antivenom is effective against the venom of a number of snakes including black mamba, green mamba, Jameson mamba, cape cobra, snouted cobra, Egyptian cobra, forest cobra, Gaboon adder, Mozambique spitting cobra, puff adder, and Rinkhals. The antivenom consists of equine antibodies. South African Vaccine Producers (SAVP) is situated in Johannesburg and is the only South African manufacturer of antivenom for the treatment of snake, scorpion, and spider envenomation.[14]

It is well known that serum reactions can be serious.[1] In this case, an urticarial rash was noted, which probably was related to the antivenom. Urticarial rash is one of the common manifestations of the early acute reactions to SAVP (SAIMR) polyvalent antivenom.[15]

Elevated mast cell tryptase levels have been used as an indicator of anaphylaxis, but because mast cell degradation postmortem also results in raised levels, levels should be tested within a postmortem interval of 3 days.[16] In the current case, no reliable analysis was deemed possible at the time of autopsy examination.

The purpuric skin rash may have been due to diffuse intravascular coagulation. The hemorrhages in the heart may have been due to cardiopulmonary resuscitation injuries, diffuse intravascular coagulation, a precipitous drop in blood pressure (the subendocardial hemorrhage), or a direct effect of the black mamba venom on the heart.[12]

Although beyond the scope of this article, the first-aid treatment of black mamba bites includes lymphatic retardation with the pressure immobilization technique. Medical management comprises continuous monitoring, securing patency of the airway, ensuring adequate ventilation, symptomatic measures, and administration of antivenom.[17]

Treatment can be challenging, particularly if the rapid administration of antivenom fails.[17]

The most likely causes of death are considered to be due to either the direct effects of the venom or medications administered. This case report demonstrates the complexities in assessing toxic elapid envenomation versus polyvalent antiserum hypersensitivity reaction.

Although it cannot confidently be excluded, anaphylaxis resulting from antivenom is considered to be the less likely of the potential causes due to the relatively long interval between administration and death. It cannot, however, be entirely ruled out as a contributory cause of death (Supplemental Digital Content, http://links.lww.com/FMP/A28; http://links.lww.com/FMP/A29; http://links.lww.com/FMP/A30).

Ethical Consideration

Consent was obtained from the next-of-kin, the director of public prosecutions, and the mortuary manager. Consent to publish was obtained from the University of Pretoria's Ethics and Integrity Committee (ethics reference no. 718/2018).

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