Severe Viperidae envenomation complicated by a state of shock, acute kidney injury, and gangrene presenting late at the emergency department: a case report

Agnès Esiéné1,2, Paul Owono Etoundi1,2, Joel Noutakdie Tochie1,*, Arlette Junette Mbergon Metogo1 and Jacqueline Ze Minkande1,3

Abstract

Background: Snake envenomation is an underestimated pathology in sub-Saharan Africa associated with severe emergencies, and even death in case of late presentation. We herein present a case of severe envenomation managed at the surgical emergency department of the Yaoundé Central Hospital.

Case presentation: We report a case of a 47-year-old female farmer with no relevant past history who sustained a snakebite by an Echis occellatus viper during an agricultural activity. Her initial management consisted in visiting a traditional healer who administered her some herbal remedies orally and applied a white balm on the affected limb. Due to progressive deterioration of her condition, she was rushed to our surgical department where she arrived 20 h after the snakebite incident. On admission she presented in a state of shock (suggestive of an anaphylactic shock), coagulopathy, renal impairment, and gangrene of the entire right upper limb. Emergency management consisted of fluid resuscitation, repeated boluses of adrenaline, a total of three vials of polyvalent anti-venom sera, promethazine, analgesics, corticosteroids, and administration of fresh frozen plasma. Within four hours of emergency department hospitalisation she developed signs of sepsis and persistent hypotension refractory to fluid resuscitation, suggestive of an associated septic shock. Management pursued with antibiotherapy and administration of noradrenaline through an electric pump syringe to achieve a mean arterial blood pressure above 65 mmHg. The patient deceased at the 10th hour of hospitalisation in a state of circulatory collapse unresponsive to vasopressors, coagulopathy, renal failure, sepsis and gangrene of the right forearm.

Conclusion: The authors highlight this unusual presentation but equally pinpoint how late presentation to the emergency department, harmful tradition practices, poverty and cultural beliefs can adversely affect the prognosis of snakebite in our setting.

Keywords: Snake bite, Envenomation, Shock, Renal failure, Gangrene
societies [1, 4, 5]. Moreover, the management of snake envenomation is not optimal in several Cameroonian health centres, accurate species identification of most snakes is difficult and specific treatment (anti-venom serum) to stop signs of envenomation is scarce and financially unaffordable by many patients [6, 7].

Vipers are the most frequent cause of venomous snake bites in sub-Saharan Africa [8]. Their venoms are complex mixtures of enzymes, peptides and metalloproteins responsible for cardinal features of local pain, blisters, oedema or swelling, mild coagulation abnormalities and local necrosis [8, 9]. We herein discuss a case of unusual viperid envenomation presenting with a state of shock, acute kidney injury, coagulopathy, sepsis and gangrene of the entire upper limb in a Cameroonian farmer.

**Case presentation**

A 47-year-old female farmer residing in a semi-rural area of Yaounde was brought to the emergency department of the Yaounde Central hospital of Cameroon with complaint of a bite on the pulp of her right thumb 20 h prior to presentation, while working in her farm by an *Echis occellatus* viper. She killed and beheaded the snake (Fig. 1), then immediately tied a tourniquet round her right wrist, sought a traditional healer who removed the tourniquet and administered her some unknown complementary and alternative medicine both topically and orally. Due to no amelioration of her symptoms within 20 h following the bite incident, she was rushed the aforementioned emergency department and vomited twice during transportation. She complained of severe thirst, fatigue, dizziness, numbness of the entire right upper limb, anuria since the bite incident, but no complaint of haematuria, myalgia, difficult breathing or swallowing.

On examination, she was conscious, oriented, sweating profusely with moderate pallor and cold clammy extremities. Her blood pressure (BP) was undetectable, respiratory rate 28 breaths/minutes, temperature 36.4°C, and a thready pulse of 138 beats/minute. Two unclean puncture wounds were identified on the pulp of the right thumb. The right upper arm was reddish dark in colour with several ruptured blisters and covered by a white traditional balm (Fig. 2). This limb was oedematous, indurated, and painless, with loss of all movements and all range of active movements. She had no clinical sign of urinary retention. The rest of her physical examination was normal. A provisional diagnosis of severe envenomation complicated by anaphylactic shock, acute pre-renal kidney injury, and gangrene of the upper limb in an ASA IV patient was made.

She had a difficult peripheral venous access due to circulatory collapse. On admission, an urgent femoral venous access was achieved with the aid of a G 16 cannula, while waiting for central venous catheter. She received normal saline at 20 ml/kg, antivenom serum 1500 IU subcutaneously, ceftriaxone 2 g/24 h intravenously (IV), metronidazole 500 mg/8 h IV, adrenaline 1:1000 dilution at 0.2 mg every 5 min IV, promazine 25 mg/8 h IV, paracetamol 1 g/06 h IV, tramadol 100 mg/8 h IV, methylprednisolone 80 mg/kg IV, and two vials of polyvalent anti-venom sera IV. Shoulder disarticulation was envisaged after resuscitation.

Laboratory investigations on admission revealed; leucocytosis 18,800/mm3 (neutrophils 66% lymphocytes 24.6%), anaemia 9.9 g/dl, thrombocytopenia 109,000/mm3, altered renal function (serum urea 0.55 g/l and
serum creatinine 32.23mg/l), normal clotting profile and serum electrolytes.

At 4 h of hospitalisation she had received 31 of normal saline, but was still haemodynamically unstable with persistence of anuria. Her temperature rose to 38.9°C. Several echymoses and petechiae appeared on her limbs. A second laboratory panel showed increased leucocytosis at 26,800/mm3 (neutrophils 76% lymphocytes 20.6%), severe thrombocytopenia of 3500/mm3, haemoglobin of 9.6/dl. Here the diagnosis of an anaphylactic shock coupled with a septic shock was made. Noradrenaline was administered at 0.3/kg/min using an electric pump syringe with objectives to have a mean arterial pressure ≥ 65 mmHg). The management which was pursued was administration of a third vial of polyvalent anti-venom serum and transfusion of three units of fresh frozen plasma and continuation of the aforementioned antibiotics, analgesics and promethazine. All attempts of internal jugular and subclavian catheterisations failed due to severe circulatory collapse and marked oedema. After repeated attempts, a left femoral catheter was successfully placed. Blood obtained from the femoral catheterisation was non-coagulable.

At 7 h of hospitalisation her blood pressure was 102/68 mmHg, pulse 108 beats/minutes and of good volume, respiratory rate netly improved. She was fully conscious, less diaphoretic and had a diuresis of 0.35 ml/kg/h. The patient and her family refused shoulder disarticulation.

At 10 h of hospitalisation her level of consciousness dropped to a Glasgow Coma score scale of 9/15, with undetectable pulses, BP 88/42 mmHg. Resuscitation was continued. She deceased at 18 h of hospitalisation in a state of shock, sepsis, coagulopathy, renal failure and gangrene of the right forearm.

Discussion and conclusion

This case illustrates the potential problems associated with Viperidae bites: anaphylactic and septic shock, acute kidney injury, coagulopathy, and entire limb gangrene coupled with harmful cultural beliefs and poverty.

Five Cameroonian cases (Table 1), including our case, have recently been described in which patients developed severe envenomation and either presented early or late to the hospital after seeking traditional medicine. Only one out of these five patients completely recovered and did not die. Patient 1 was a healthy physician bitten in his bedroom by a cobra in an enclosed area of northern Cameroon [10]. Despite early hospital presentation and administration of one vial of anti-venom serum, his signs of envenomation worsened with severe respiratory distress warranting urgent endotracheal intubation and mechanical ventilation [10]. The lack of these equipment in his enclosed area ultimately led to his death [10]. Patient 2 was a 10-year old girl who presented with facial swelling and haematuria following a snake bite on her right temple by an unidentified snake species [11]. This case differed from ours (patient 5) by the timely administration of one vial of anti-venom serum, within eight hour of the snake bite incident despite seeking traditional medicine before. There was complete regression of her signs of envenomation within 72 h of hospital stay [11]. In another more recent case series, Tianyi et al. described an elderly patient (patient 3) and a three-year old girl (patient 4) with severe snake envenomation who both died [12]. The elderly patient sought first-line treatment from traditional medicine, which did not cure him. He ended up dying on his way to the hospital. In contrast to our patient, patient 4 presented early to the hospital without seeking the consult of a traditional healer [12]. However, she had a fatal outcome stemming from the unavailability of anti-venom serum, severe envenomation with a state of shock (despite fluid resuscitation) and neurological signs like inability to stand, talk, open her eye, breathing difficulties, and a convulsion [12]. The unavailability of anti-venom serum is a frequent challenge encountered in the management of snake envenomation in Cameroon [13].

The rising ill-health burden from snake envenoming led to a categorization as a neglected tropical disease by the World Health Organization in 2017 [13]. The true incidence of snakebites is difficult to assess because it is often under-reported [14]. In sub-Saharan Africa, recent estimates suggest that about one million bites by venomous snakes occur with 100,000 to 500,000 cases of envenimation and up to 30,000 deaths per year [9]. Populations in these regions face high morbidity and mortality due to the poor access to health services. As illustrated in our case, Viperidae (typical vipers and pit vipers) are responsible for majority of envenomation in sub-Saharan Africa [9]. Unlike envenomings by Elapidae (cobra, krait, coral snakes and sea snakes) which causes neurotoxicity (muscular weakness, spreading paralysis, dysphagia, dysphasia, ptosis, external ophthalmoplegia, respiratory arrest and convulsions) and myotoxicity (muscular pain, stiffness and myoglobinuria), envenomation by vipers mainly results in haemotoxicity (echymoses, petechial haemorrhage, epistaxis, haematemesis, melaena, haematuria), though overlapping symptoms are common between both snake families [15].

The diagnosis of the cause of her shock could be anaphylactic induced by the snake venom acting as an allergen. Although not a common presentation for snakebite, the incidence of anaphylaxis to snake venom has been underestimated. Anaphylactic shock is mediated through a variety of different mechanisms, including IgE-mediated hypersensitivity, a surge in bradykinin production, marked vasodilataion and potentiation of hypotension by haemorrhage [16, 17]. Also, septic shock can be evoked as the etiology of her shock or a compounding factor to her
| First author, year of publication, study design | Patient number, age, gender, profession | Region of Cameroon and site of the incident | Snake species | Delay before hospital presentation | Signs of envenomation | Management | Outcome |
|-----------------------------------------------|---------------------------------------|-------------------------------------------|--------------|-----------------------------------|----------------------|------------|---------|
| Nkwesheu [10], 2016, case report             | Patient 1; 28 year, male, physician    | Northern Cameroon, in bedroom             | Naja melanoleuca | Within an hour                     | Swollen hand, rigors, foaming at the mouth, loss of speech and severe respiratory distress. | One vial AVS, Fluid resuscitation, Atropine 1 mg IV, Ranitidine 50 mg IV, Paracetamol 500 mg IV. | fatal    |
| Tianyi, 2017 [11], case report               | Patient 2; 10 years, female, occupation not precised | Adamawa region, in the farm | Unidentified snake species | 12 h | Marked facial swelling, haematuria, pain, bledding from the wound and mouth, mild respiratory distress. | Topical application and oral ingestion of herbal concoctions, 1 vial of AVS, 1500 IU anti-tetanus serum SC, dexamethasone 4 mg IV every 8 h, ceftriaxone 450 mg every 12 h, wound dressing, Normal saline 100 ml/h. | Complete recovery |
| Tianyi, 2018[12], case series of two patients | Patient 3; 80 years, male, traditional healer | Adamawa region, in the bush | Naja melanoleuca | Died on the way to the hospital | Inability to stand, and difficulties in standing, loss of consciousness. | Application of traditional topical ointments on the wounds, ingestion of herbal concoctions, no AVS administered. | fatal    |
|                                              | Patient 4; 3 years, female             | Adamawa region, in the bush              | Unidentified snake species | Four hours | Inability to stand, talk and open her eyes, breathing difficulties, convulsion, a state of shock. | Tourniquet applied on left thigh, fluid resuscitation, 750 IU anti-tetanus serum SC, dexamethasone 4 mg IM, AVS not available. | fatal    |
| The present case report                      | Patient 5; 47 years old female farmer  | Centre region, in the farm               | Echis ocellatus   | 20 h | a state of shock, acute kidney injury, coagulopathy and gangrene. | Topical application and oral ingestion of herbal concoctions, fluid resuscitation, anti-tetanus serum 1500 IU SC, ceftriaxone 2 g/24 h IV, metronidazole 500 mg/8 h IV, adrenaline 1:1000 dilution at 0.2 mg every 5 min IV, promethazine 25 mg/8 h IV, B-Tamol 1 g/06 h IV, tramadol 20 mg/8 h IV, methylprednisolone 80mg/kg IV, three vials of polyvalent anti-venom sera IV, Noradrenaline 0.3/kg/min using EPS, and transfusion of units of fresh frozen plasma. | fatal    |

AVS: anti-venom serum; SC: subcutaneous; IV: intravenous; IM: intramuscular; EPS: Electric pump syringe
anaphylaxis given the fact that she had signs of sepsis (a SOFA score > 2 due to undectable blood pressure necessitating noradrenaline, platelet count of 109,000/mm3 and serum creatinine of 32.23mg/l on admission), persistent hypotension despite fluid resuscitation and requiring vaso-pressors to maintain a mean arterial pressure greater ≥65 mmHg, in line with Sepsis-3 definition [18].

Coagulopathy following a viperid bite is mainly due to haematotoxic effects of the venom [9]. The pathophysiology involves activation of prothrombin (factor II) by metalloprotein contained in the venom, inhibition of platelet aggre- gation, spontaneous activation of factor V and factor X by procoagulant enzymes present in the venom, disruption of fibrinolysis and induction of toxic vasculitis by toxin on the vascular epithelium [14, 17, 19, 20]. The manifestation of coagulopathy varies from isolated thrombocytopaenia to disseminated intravascular coagulopathy [21]. The indexed patient presented with several ecchymoses, petechiae, moderate thrombocytopaenia, and non-coagulable blood at four hours of hospitalisation. With the non-availability of fibrinogen degradation products, and a control clotting profile we could not affirm the diagnosis of disseminated intravascular coagulopathy.

Gangrene of the entire limb following a viper bite is a rare with few cases reported [22]. The pathogenesis involves marked oedema within a muscular compartment which compromises adequate limb perfusion [8, 23, 24]. The resultant ischaemic effect may be potentiated by vascular lesions caused by metalloprotein hemorrhagins (contained within the venom), inappropriate treatments (tourniquet) or severe anaemia caused by bleeding [8]. The diagnosis of compartment syndrome is confirmed by measuring the compartment pressures [25]. We de- plore the lack of such invaluable but expensive tools in our resource-limited setting. Also, the patient’s coagulopathy further posed a risk-benefit dilemma of limb amputation for necrosis.

Our patient was anuric for more than 24 h following the snake bite with an altered renal platelet. We hypothesized an acute kidney injury of multifactorial aetiologies; pre-renal acute kidney injury from shock and renal acute kidney injury from venom-induced nephrotoxicity leading to acute tubular or cortical necrosis, or cyclophosphamide [25–27].

Prompt recognition of systemic envenomation and timely administration of anti-venom serum are effective life saving measures aimed at neutralization of snake venom, reverses acute venom-induced inflammation, haemorrhagic syndrome [28–30], reversing severe coagulopathy [19], reduc- ing renal damage [10] and preventing necrosis. Currently, anti-venom serum is the only safe and efficacious specific treatment for snake envenomation [1, 31]. Generally, anti-venom serum should be administered as a matter of urgency in the presence of signs of envenomation [32, 33].

In the absence national guideline on the management of snake envenomation in Cameroon, the treatment advocated by some experts entails administration of two 10 ml vials of anti-venom serum either as intravenous injection over five minutes [30, 34] or as an infusion over 30 to 60 min [32]. The frequency of reinjections or re-infusions is guided by patient’s clinical conditions [30].

Besides anti-venom serum administration, the treatment of snake envenomation involves a number of first aids and adjuvant interventions. The most important first aid management entails non-aggressive analgesia, rapid wound dressing and immobilization of the bitten limb [32, 35]. Previously cited first-aid treatments such as incision, suction of the venom and application of tourniquets are currently condemned by experts due to the increase of potential adverse effects and the lack of effectiveness [36, 37]. Similarly, traditional treatments involving application of traditional balms and snake bitten area may be sources of infections [38]. Adjuvant treatments entail the administration of crystalloids and colloids to maintain hemodynamic stability, low fibrinolics drugs and transfusion of fresh frozen plasma to coagulopathy, anti-tetanus serum for tetanus prevention, antibiotics therapy for super-imposed wound infection, mechanical ventilation for respiratory dis- tress and dialytic treatment for acute kidney injury [32, 39]. However, the use of these ancillary measures in most resource-challenged settings is precluded by financial constraints of patients, the absence of the necessary drugs, limited health infrastructures [10, 38], and poor knowledge of health personnel on case management of snake envenomation [40]. Poor prognostic factors observed in the indexed patient were her poor health-seeking behaviour (seeking a traditional healer for first-line treatment), late presentation and signs of severe envenomation (shock, acute kidney injury, gangrene of the bitten limb and coagulopathy).

In conclusion, to the best of our knowledge we have presented a case of severe viperid envenomation complicated by a state of shock, acute kidney injury, coagulopathy, and gangrene of the affected limb in a female farmer managed in a Cameroonian emergency depart- ment. The authors highlight these severe presentation but equally pinpoint how late hospital presentation, harmful health-seeking behaviour, and cultural believes may worsen the clinical condition of the patient. Due to the risk of potential fatal complications from severe snake envenomation and the management challenges akin to resource-limited settings, we highlight the need to reinforce sensitization of the local population on timely presentation to the hospital; avoid ineffective and time-wasting traditional remedies that are potentially harmful. Moreover, first-aid knowledge should be improved. Lastly, the formulation of a national guideline may go a long way to improve treatment outcomes of patients.
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Authors’ contributions
AE and JNT: Study conception and design, acquisition of data, and interpretation, manuscript writing and critical revisions. POE, JAMM and JZM: acquisition of data, and interpretation, proof read the manuscript and critically revised it for intellectual content. All authors read and approved the final manuscript.

Ethics approval and consent to participate
Not applicable.

Consent to publication
Written informed consent was obtained from the patient’s husband for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Competing interests
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Author details
1. Department of Emergency Medicine, Anesthesiology and critical care, Faculty of Medicine and Biomedical Sciences, University of Yaoundé I, Yaoundé, Cameroon.
2. Department of Emergency Medicine, Anesthesiology and critical care, Yaounde Central Hospital, Yaoundé, Cameroon.
3. Department of Emergency medicine, Anesthesiology and critical care, Yaoundé Gynaeco-Obstetrics and Paediatric Hospital, Yaoundé, Cameroon.

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