

# Severe Allergic Reaction Following Administration of Antivenom Serum for Snakebite: A Case Report from Togo

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## Abstract

**Background:** Ophidian envenomation is common in Sub-Saharan Africa, and its management is hampered by the lack of access to healthcare services in rural areas, in particular the availability and appropriate use of antivenom. Rare cases of serious side effects following the administration of antivenom have been reported. This is the case for a young farmer from the central region of Togo, who experienced a second snake bite within four years, and in whom antivenom serotherapy led to severe allergic manifestations. **Case presentation:** This 24-year-old patient, with a history of antivenom and tetanus serotherapy, was admitted to the Centre Hospitalier Régional (CHR) of Sokodé for a snakebite that occurred 45 minutes earlier while working in the field. Clinical assessment on admission revealed grade 1 envenomation, characterized by local pain in the right upper limb, with no sign of complication. He received an intravenous infusion of antivenom serotherapy, which rapidly relieved the pain, allowing him to be discharged after 24 hours of hospital monitoring. However, he was readmitted five days later for a skin rash associated with generalized pruritus and edema of the face and the neck, which prompted his evacuation to the Sylvanus Olympio University Hospital. He was diagnosed with a hypersensitivity-type allergic reaction to antivenom serum. Symptomatic treatment with antihistamines resulted in a favourable outcome after five days in the hospital. **Conclusion:** This young farmer developed a severe allergic reaction following a second course of antivenom serotherapy for low-grade ophidian envenomation. Although the efficacy of an-

tivenom serum is undeniable in the management of snakebites, its use should be guided by a sound clinical assessment and framed by rigorous monitoring, especially in people sensitized to antivenom or antitoxin serotherapy. This highlights the importance of training healthcare staff alongside the availability of anti-venomous sera at peripheral healthcare centres.

## Keywords

Snakebite, Antivenom, Allergic Reaction, Sub-Saharan Africa, Togo

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## 1. Introduction

Snakebites are common in Sub-Saharan Africa, and the severity of the resulting envenomations often justifies the use of polyvalent antivenomous serum in the management of the victims [1]-[3]. Previous reports have shown that ophidian envenomations are a real public health problem in Togo, both in paediatric and adult population [4]-[6]. The problem is particularly crucial in the central region, where a hospital frequency of 5.7% was reported in a retrospective study in 2016, leading to a high mortality of 9%. In most cases, these bites occur in rural or semi-rural areas and affect poor people, so their management is confronted with delays in consultation and limited access to antivenom [5] [6]. While these serums undeniably have a beneficial effect on the outcomes of envenomations, the potential risk of a severe allergic reaction should not be ignored. Indeed, rare cases of serious side effects have been reported following the injection of an anti-venomous serum [2] [7]. We report the case of a 24-year-old man who experienced an allergic reaction following repeated administration of antivenom serum for a second snakebite within four years. This report aims to raise the attention of practitioners on the importance of reasonable assessment of the benefits and risks of antivenom use in the management of snakebite cases.

## 2. Observation

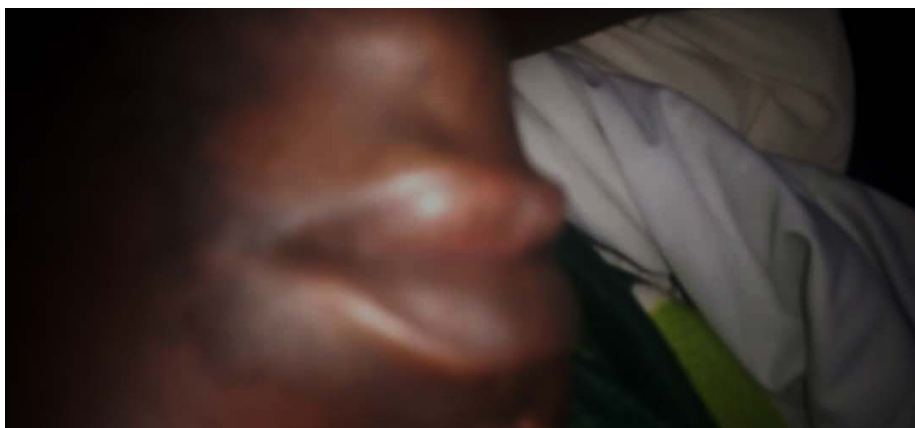
This 24-year-old farmer was evacuated from Centre Hospitalier Régional (CHR) Sokodé to the Centre Hospitalier Universitaire (CHU) Sylvanus Olympio of Lomé on July 25, 2023, for envenomation management. The medical history revealed that he had been bitten on the right hand by a «green mamba» on July 16, 2023, while out in the fields. Transported by motorbike to CHR Sokodé, the initial clinical assessment concluded to a grade 1 envenomation. Based on the presence of fang marks on the finger and localized pain in the right upper limb. He immediately received two vials of INOSERP, a polyvalent antivenom serum (F(ab)<sup>2</sup>-equine) infused over 30 minutes, as well as cleaning and antiseptics of the bite area. He also received an intramuscular injection of a dose of anti-tetanus serum (equine tetanus immunoglobulin fragments F(ab)<sup>2</sup>) combined with an ampoule of betamethasone and a dose of anti-tetanus vaccine. Finally, analgesics consisting of combined para-

cetamol + codeine and antibiotics (amoxicillin + clavulanic acid) were administered orally, resulting in a favourable clinical outcome and discharge after 24 hours of monitoring. However, five days later, the patient presented again with ferocious generalized pruritus skin rash and oedema of the face and neck, prompting his referral to CHU Sylvanus Olympio in the capital.

Examination of his health record revealed a history of maculopapular rash associated with generalized pruritus in July 2019, occurring three days after initial administration of antivenom serum (INOSERP) combined with antitetanus sero-anatoxin therapy following a white snake bite. His history also included tetanus sero-anatoxin therapy on three occasions between April 2020 and February 2023, a rabies vaccination (VERORAB) in December 2022, and repeated use of a combination of paracetamol + codeine and amoxicillin + clavulanic acid without any allergic reaction. The physical examination revealed insomnia, anxiety, fierce pruritus with scratching lesions (**Figure 1**), oedematous maxillofacial and labial infiltration (**Figure 2** and **Figure 3**). Blood pressure was normal at 130/80 mmHg, heart rate at 80 bpm, respiratory rate at 18 cpm, and temperature at 37.2°C. There was no local or general sign of envenomation. Coagulation tests, blood count, liver and renal function tests were normal.



**Figure 1.** Scratch marks on the body.



**Figure 2.** Edematous infiltration of the lips.



**Figure 3.** Cervicofacial oedema in the resorption phase.

The diagnosis of a WHO grade 2 allergic reactions to antivenom was made based on:

- The onset of generalized rash and edema of the face and neck six days after administration of the antivenom, whereas a regression of envenomation symptoms was rapidly observed within 24 hours.
- The absence of any obvious cause of this symptomatology.
- The history of sensitization to the antivenom in 2019.
- The absence of a history of allergy to the associated medications, namely anti-tetanus serum, antibiotics, and analgesics despite the administration of the latter several times.

The patient was admitted to the hospital for better management. He received injectable promethazine (25 mg twice daily), and psychosocial support. Careful monitoring of respiratory and hemodynamic conditions revealed no further complications. The patient completely recovered within 72 hours and was discharged after reporting pharmacovigilance. He also received awareness of snakebite prevention measures.

### 3. Discussion

This patient had presented with Grade 1 envenomation following a snakebite for the second time; the occurrence of serious side effects linked to the administration of antivenom serum necessitated his evacuation to a tertiary-level hospital. The socio-demographic profile of the patient and the circumstances of the bite are typical of the situation usually observed in Sub-Saharan Africa [1] [4]-[6] [8] [9]. Indeed, snake bites are more frequent in rural areas, often occurring during field work [4]-[6] [8] [9]. In addition, access to adequate health care, particularly antivenom serum, remains marginal in most African countries [6] [10]. The care pathway followed by this patient who reached a health facility in less than an hour to receive antivenom serum, contrasts with that typically observed in resource-limited countries where traditional pre-hospital practices are sometimes inappropriate and a source of delays in healthcare [6] [8] [9]. This reflects a renewed interest in this neglected tropical disease, as evidenced by a subsidy for

antivenom serum in Togo [11] [12]. It's therefore understandable that this farmer should have benefited from antivenom serotherapy at each of these two exposures. According to Chippaux, antivenom or antitetanus serotherapy is a major factor in sensitization to allergic reactions [2]. Admittedly, given the limited knowledge of the ophidian ecology in Sub-Saharan Africa and the sometimes unpredictable outcomes of envenomations, clinical assessment, indication of antivenom serum serotherapy, and hospital monitoring of snakebite victims must be carried out with a certain degree of caution [6]. However, the fact remains that not all snakebites are followed envenomation, and consequently serotherapy should not be routine, once the patient has reached an equipped hospital [1] [2]. The management of this patient, whose only symptom was localized limb pain, could be limited to symptomatic treatment and monitoring; the administration of antivenom serum in this patient with a history of allergy to this product represented a high risk of serious side effects. Indeed, allergic reactions have been reported following administration of antivenom serum, which can lead to anaphylactic shock [6] [7]. In a descriptive retrospective study conducted in the central region of Togo in 2016, eight cases of anaphylactic shock and one case of facial oedema were reported by Bawe *et al* [6]. However, the risk factors for these allergic reactions were not specified. It must be acknowledged that there are some limitations in the imputability of antivenom serum in our case, namely the lack of details on the types of serum and vaccine batches used, and on the conditions of administration of these products. Indeed, it has been also reported that allergic reactions depend on the type, quality, and dose of serum administered [13]. Notwithstanding these limitations, it seems likely that antivenom serotherapy was responsible for this allergic reaction, given the patient's history, the chronology of signs, and the list of essential medicines comprising a single antivenom serum subsidized by the state in Togo public health facilities. This calls the attention of hospital practitioners to a better assessment of the benefit-risk ratio for any snakebite case admitted to a health facility.

#### **4. Conclusion**

We reported the case of a patient who had been snake-bitten twice within 4 years and had received antivenom serotherapy on both occasions, without any real signs of severe envenomation. This administration caused a generalized allergic reaction. Although the benefit of antivenom serotherapy is undeniable in the management of severe envenomations, its administration should not be systematic in all cases of snakebites. This observation highlights the importance of training staff in the clinical assessment and monitoring of snakebite patients and in the judicious use of antivenom serotherapy. Moreover, a comprehensive study is necessary to identify the risk factors for these reactions in our context.

#### **Ethics Approval and Consent to Participate**

All procedures performed in this report were in accordance with the ethical

standards of the Faculté des Sciences de la Santé de l'Université de Lomé research committee and with the Helsinki Declaration (as revised in 2013).

### Consent for Publication

Written informed consent for publication of the case report was obtained from the patient. A copy of the consent is available from the corresponding author for the review.

### Availability of Data and Materials

The datasets generated and/or analyzed during this study are not publicly available due to [THEIR MEDICAL CONFIDENTIALITY RELATING TO A SINGLE INDIVIDUAL] but are available from the corresponding author upon reasonable request.

### Authors' Contributions

Awèréou Kotosso designed the study. Awèréou Kotosso, Lidaw Deassoua Bawe, Lampouguini Nebona, Cici Amouzou, and Ezzo-Essinam Félix Pissang collected the data. Awèréou Kotosso drafted the manuscript. Bawoubadi Abaltou, Gnimdou Tchamdja, Akouda Akessiwe Patassi, Magnoudewa Poko, Hassimou Bramah and Majesté Ihou Wateba contributed to the interpretation of the results and critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript.

### Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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## Abbreviations

CHR: Centre Hospitalier Régional; CHU: Centre Hospitalier Universitaire; WHO: World Health Organization.