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Case report

A Severe Case of Snakebite Envenoming by *Vipera ammodytes* in Winter

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SUMMARY

Introduction. Venomous snakebites in Serbia are neither too frequent nor extremely dangerous. Nevertheless, some can lead to complications or even death.
Case report. On December 24, 2023, a young man was admitted to hospital after being bitten by a snake, believed to be *Vipera ammodytes*. He was in a state of shock, unconscious, with unmeasurable blood pressure. Having received the proper treatment, the patient fully recovered.
Conclusion. The case described herein was the most severe clinical manifestation resulting from snakebite treated in the Užice General Hospital thus far and one of the most severe among the rare published cases of snakebites in Serbia. In our country, barely any information is available regarding venomous snake bites, so every peculiar case should be made public. We consider publishing this case even more important because it occurred at the beginning of winter when snakes should be inactive. To ensure better prevention and more efficient treatment of snakebites, appropriate transdisciplinary education has to be provided both to laypeople and medical workers.

Keywords: ***Vipera ammodytes*, shock, snake, treatment**

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INTRODUCTION

Snakebite is a special type of injury that occurs almost globally and is an especially severe issue in rural, low-income regions of (sub)tropical countries (1, 2). The injected venom causes a wide range of toxic effects, from local tissue damage to multi-organ failure or, finally, permanent disabilities or death (2–4).

In Serbia, as in other parts of the Balkan Peninsula and Europe, snakebites are neither too common nor extremely dangerous (5–7). Nevertheless, they do occur—only in the Užice General Hospital, 249 snakebite patients were admitted between 2006 and 2018 (8), and 64 people were treated for snakebites between 2019 and 2023 (unpublished). Unfortunately, data on snakebites are still not properly collected and systematized, not only in Serbia but in most of Europe (6, 9).

There are only three venomous snake species in Serbia, all protected by national and international legislation (10). The nose-horned viper, *Vipera ammodytes* (*V. ammodytes*), is widely distributed in our country, covering altitudes between 160 and 1,620 meters above the sea level (11). Reaching up to a meter, it is the largest viper in Europe and potentially the most dangerous (9, 12).

CASE REPORT

A 19-year-old male was admitted to the Užice General Hospital on December 24 at 4:18 p.m. due to a snake bite on his left hand. The bite happened approximately 40 minutes before admission, while he was hiking on the Cerovo hill near Arilje, a town in Western Serbia. Since the patient was unconscious, we obtained the hetero-anamnestic data from the accompanying person. The patient had no previous medical history and no known food or drug allergies. He was regularly vaccinated, including the tetanus vaccine five years before.

While climbing a steep slope, when he put his hands on the ground, our patient suddenly felt pain in the back of his left hand and saw a snake which he identified as *V. ammodytes*. An accompanying person immediately started the initial management of the bite injury by squeezing venom and blood out of the bite site. The patient experienced sweating and nausea, combined with abdominal pain in the first 15 minutes after the bite. He felt a tingling sensation and could not stretch his fingers. The patient was transported by car (about 30 minutes) to the nearest emergency room, where he received intramuscularly a single dose (5 ml) of the equine viper venom antiserum Viekvin® (13). Within 10 minutes, he was transported to the hospital. The patient vomited three times during the transport.

On admission, the patient was pale and unconscious. The vital parameters were as follows: blood pressure unmeasurable, heart rate 140/min, SO_2 95%, body temperature 36.5 °C. There was no hemorrhage.

The auscultatory findings of the lungs were normal. Clinical examination of the abdomen was normal. There was a visible bite mark between the index and middle finger of the left hand and oedema on the entire back of that hand.

The patient was immediately given single doses of adrenaline (0.5 mg/kg bw i.m.) and methylprednisolone (0.5 mg/kg bw i.m.). After 15–20 seconds the patient regained consciousness but was still disoriented. Spontaneous diuresis occurred after rehydration (fluid resuscitation with 20 mL/kg 0.9% sodium chloride i.v.). After 30 minutes the patient became oriented, and complained of pain in the hand, a tingling sensation, and paralysis of the fingers. An electrocardiogram revealed sinus tachycardia.

Laboratory findings upon admission to the hospital are given in Table 1.

Six hours after admission, the patient still felt weak with increased pain in his hand. The oedema extended, accompanied by pallor, bruising, and tenderness. Repeated laboratory findings indicated increases in CK (206 units/L) and LDH (310 units/L).

The patient was treated with antibiotic (ampicillin 500 mg/6 h PO) and symptomatic therapy.

Hospitalization lasted three days. Clinical and control laboratory findings before discharge were in the normal ranges of values. The local changes at the place of bite were in regression.

Table 1. *Results of laboratory tests upon admission to hospital. Boldface values are above and italicized below reference ranges*

Laboratory test	Result	Reference range
Hemoglobin	145 g/L	138–172 g/L
White blood cells (WBC)	**17.5 × 10^9/L**	4.5–1.0 × 10^9/L
Absolute neutrophil count (ANC)	**10.200 neutrophils/μl**	1.500–7.700 neutrophils/μl
Platelets	*133.000/μl*	150.000–450.000 platelets/μl
Erythrocytes	4.9 × 10^{12}/L	4.3–5.9 × 10^{12}/L
Blood sodium	*129 mEq/L*	135–145 mEq/L
Serum potassium	*3.2 mmol/l*	3.5–5.5 mEq/L
Calcium	**2.9 mmol/L**	2.2–2.7 mmol/L
Phosphorus	**4.8 mg/dL**	4.2–4.5 mg/dL
Blood glucose	**6.4 mmol/L**	3.9–5.6 mmol/L
Blood urea nitrogen (BUN)	6.2 mmol/L	1.8–7.1 mmol/L
Creatinine	98 μmol/L	61.9–114.9 μmol/L
Alanine aminotransferase (ALT)	25 units/L	0–35 U/L
Aspartate aminotransferase (AST)	21 U/L	0–35 U/L
Creatine kinase (CK)	180 U/L	33–211 U/L
CK–MB (creatine kinase-myocardial band)	12 U/L	< 24
Lactate dehydrogenase (LDH)	**260 U/L**	105–233 U/L
Fibrinogen	230 mg/dL	200–400 mg/dL
Prothrombin time	**14 seconds**	11–13.5 seconds

DISCUSSION

Evolved as a hunting/feeding aid and defense tool, snake venoms are virtually infinitely variable mixtures of inorganic components, enzymes, large proteins, toxic polypeptides, etc. that lead to a wide range of inflammatory, pharmacological, and toxicological effects (9, 14–18). They can cause a variety of potentially fatal clinical toxic syndromes affecting the nervous system (neurotoxicity), musculoskeletal system (myotoxicity), cardiovascular (cardiotoxicity), and blood clotting systems (hemotoxicity) (2, 19). Snakes from the genus *Vipera* produce venoms with predominating hemotoxic and cytotoxic but also necrotoxic components (9, 20). In Europe, potentially the most dangerous snake is the nose-horned viper, *V. ammodytes*, with four subspecies (21), listed by the World Health Organization as both Category 1 and 2 medically important (9). The venom of *V. ammodytes*, contrary to other members of the genus, was shown to have strong procoagulant potential (22), in addition to neurotoxic components (23, 24). Its bite, causing "local and systemic hemorrhage, tissue damage and neurotoxicity", can be fatal; the lethal potential of the venoms of *V. ammodytes* subspecies differs (9, 21, 25), as does the composition of venom within subspecies (16).

Our patient was admitted in a state of shock, which is not common for the clinical manifestations of snake bites in the Balkans (7), however, it occurs occasionally (26). The patient had tachycardia, but there was no arrhythmia, and there were no changes in the ECG. Since IgE was not elevated, the patient's condition resembled an anaphylactoid reaction.

One among only several published instances of snakebites in Serbia (27) was very severe, but in that case, the patient had been consuming alcohol, and several hours passed between the bite and admission to hospital. In the southernmost portions of Serbia (28), there were approximately 1/3 severe cases and one fatality among 264 patients. As in other reported complicated and fatal cases in the region (29, 30), these authors suspected a direct bite to the blood vessel without pronounced local signs but with a strong systemic reaction. There are also reports of severe complications resulting from *V. ammodytes* bite from Bulgaria and Greece (25, 31).

On admission, the blood pressure could not be measured in our patient. This was, however, quickly resolved with injections of adrenaline and methylprednisolone.

Our patient had thrombocytopenia, similar to cases described in the region (32). Major inducers of thrombocytopenia in *V. ammodytes* venom are snaclecs that cause platelet aggregation or their adhesion to blood vessel walls (23).

Venoms of Balkan vipers can cause transient renal failure and liver damage (26). Our patient had mild serum electrolyte imbalance which was quickly normalized.

The subjective sensation of tingling, paresthesia, and paralysis of the fingers in our patient can be explained by the neurotoxic effect of snake venom. Due to the presence of ammodytoxins, the venom of *V. ammodytes* affects even cranial nerves and directly the central nervous system, causing ptosis, ophthalmoplegia, dysphonia, dysphagia, swelling problems, neuromuscular weakness, unconsciousness, etc. (23).

Local manifestations of snakebite include excruciating pain and the appearance of immovable, tensely swollen, cold, and seemingly pulseless extremities. In our patient, local changes gradually regressed spontaneously.

Snake venom composition (and consequently its effect) varies geographically, individually, ontogenetically, depending on the dominant available prey, etc. (9, 33–35). There is a widespread belief that snake venom is more potent in spring than in other periods of the year (28), however, such assumptions of seasonal variations in venom yield and potency have rarely been confirmed (36, 37). Other investigations revealed only individual differences among snakes in the amount of produced venom (38).

Reactions to snake venoms depend on the snake (species, age, size), location of the bite, age, body mass index, health status of the bitten person, etc. (39). In our case, the patient was young and healthy hence such a strong reaction to venom was not expected.

Vipers are not uncommon in the Balkans. In Serbia, *V. ammodytes* has the widest distribution and has been recorded in the vicinity of Arilje (11). As ectotherms, reptiles are adapted to local climate and they respond to weather conditions. In temperate regions, snakes experience "winter dormancy", i.e. brumation. In *V. ammodytes*, this inactivity phase can last from September to April (40). Therefore, encounters with vipers at the beginning of winter are not expected. Nevertheless, there are reports to the media (41) or to/from our colleague herpetologists about snakes active during winter months (e-mail communication with R. Ajtić, PhD (rastko.ajtic@pmf.kg.ac.rs) on December 28, 2023, and A. Simović (alexandar.simovic@gmail.com) on December 29, 2023). Even if awakened from a hole covered with snow, a viper can quickly become agitated (42). In the neighboring countries somewhat warmer than Serbia—Croatia and Bosnia and Herzegovina—snake bites were recorded in January, November, and December (26, 43–45).

The correlation between weather/climate and snakebite incidence was shown previously (44, 46) and more thoroughly addressed recently (47–49). Climate changes influence both the snakes' distribution and annual activity rhythm, one of the changes being late brumation (50). Bearing in mind that the entire 2023 was globally "the warmest on record", and the second warmest in Europe, that we had "the warmest boreal autumn" (51), it is not surprising that reptiles delayed entering brumation.

Regarding snake bites, incomparably more published information exists for the neighboring countries than for Serbia (7). Also, for decades it has been suggested that reporting snakebites should be mandatory and all information should be collected in one place (9, 28, 52, 53). In Central and South-Eastern Europe (including Serbia), the initial steps were made (6), but with limitations. The most obvious is the low quantity of the obtained information. For the entire Serbia, the National Poison Centre collected data on 56 bites in three years. In the Užice region alone, 64 bites were recorded in four years.

Certain groups of nature-loving people are comparatively well-informed regarding venomous snakes (54), but we fear that most modern tourists do not possess enough quality information. To minimize the risk of snakebites and improve their treatment, it is necessary to initiate targeted transdisciplinary investigations into snake distribution, ecology, and behavior and to combine and publicize such information, to educate both residents and visitors in regions inhabited by venomous snakes (17, 49, 55, 56). Also, a guide for the clinical management of snakebites in Serbia could be produced, similar to that recently published for Italy (21). In addition, the media should be taught not to spread panic but to objectively report cases of snakebites.

CONCLUSION

Venomous snakebites occur in Serbia every year, but they are still not appropriately covered in the national scientific literature. The majority of the cases are mild or of medium severity, but sometimes, life-threatening symptoms develop. To better understand and treat such cases, it is necessary to publish reports of envenomations whenever possible.

The patient presented herein was young and healthy, but his reaction to venom was violent, which is not usual. Thanks to his companion and to timely and appropriate treatment by medical doctors, he fully recovered. This case highlights the fact that every snake bite should be treated individually, which demands experience.

Our patient was hiking as a tourist. Considering the increase in the presence of people in nature, often inexperienced, the education of hikers and tourist/mountain guides should be seriously considered. Communication between biologists and medical workers is essential. In "critical" regions, medical doctors should be educated to promptly recognize and deal with snakebites, and antivenom must be available. Also, the media should be educated not to spread panic but to objectively report cases of snakebites. With proper organization and wide cooperation, much can be done in snakebite prevention and treatment.

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Težak slučaj trovanja usled ujeda poskoka (*Vipera ammodytes*) u toku zime

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SAŽETAK

Uvod. Ujedi otrovnih zmija u Srbiji nisu ni preterano česti ni naročito opasni. Ipak, pojedini mogu dovesti do komplikacija ili čak smrti.
Prikaz slučaja. Dvadeset četvrtog decembra 2023. godine u bolnicu je primljen mladić koga je ujela zmija, najverovatnije poskok (*Vipera ammodytes*). Mladić je bio u stanju šoka, bez svesti, a njegov krvni pritisak nije mogao biti izmeren. Nakon adekvatnog zbrinjavanja i praćenja stanja, bolesnik se potpuno oporavio.
Zaključak. Opisani slučaj predstavlja najozbiljniju kliničku manifestaciju ujeda zmije koja je do sada tretirana u Opštoj bolnici Užice i jedan od najozbiljnijih, među retkim objavljenim slučajevima, ujeda otrovnica u Srbiji. Kako u našoj zemlji nema mnogo podataka povezanih sa ujedom otrovnih zmija, svaki neuobičajen slučaj treba objaviti. Objavljivanje slučaja koji ovde opisujemo dodatno dobija na značaju pošto se desio početkom zime, u periodu kada bi zmije trebalo da budu neaktivne. Kako bi se obezbedili bolja prevencija i efikasnije tretiranje ujeda otrovnica, potrebno je pružiti odgovarajuće obrazovanje i opštoj populaciji i medicinskim radnicima.

Ključne reči: **poskok, šok, zmija, lečenje**