

Vipera berus bites in Eastern Poland – a retrospective analysis of 15 case studies

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Abstract

Introduction and objective: The common European adder (*Vipera berus*) is the only venomous snake that is found naturally in Poland. This study presents the epidemiological and clinical characteristics of *V.berus* bites in Eastern Poland and describes the methods of poisoning treatment.

Materials and methods: Medical documentation of 15 patients hospitalized at the Department of Infectious Diseases and Neuroinfections of the Medical University of Białystok between 1998-2010 because of *V.berus* bite was analyzed retrospectively.

Results: Most of the snakebites were accidental (86.7% of the cases). The bites usually took place in forests (66.7% of the cases). The majority of patients were bitten in the lower extremity (8 cases, 53.3%), most often in the area of ankle joint. The severity of poisoning was usually minor to moderate. The most common local symptom was oedema (93.3% of the cases) and associated extravasations (73.3% of the cases). One patient experienced shock. Transient hypertension was observed in 3 cases. Mild coagulation disorders were present in 4 cases. In 4 cases, leukocytosis was observed. 86.7% of patients received the specific antivenom. No fatal outcome and no adverse reactions after antivenom administration were reported.

Conclusions: In the majority cases of poisoning with *V.berus* venom, the poisoning takes a mild course, limited to local oedema, but sometimes it may lead to severe complications. The only specific method of the treatment is antivenom administration.

Key words

Vipera berus, bite, venom, poisoning, antivenom

INTRODUCTION

It is estimated that worldwide 5.4-5.5 million people are bitten by snakes each year, resulting in about 400,000 amputations and between 20,000 and 125,000 deaths [1].

In European countries, the incidence of snake bites varies from 0.1-4.1 per 100,000 inhabitants [2], and in the case fatality – 0.1-1.8% (mortality 0.0001-0.029 per 100,000 inhabitants). The common European adder (*V.berus*) is the only venomous snake found in Poland. Many regions inhabited by *V.berus* are popular recreation centers; therefore, tourists are at risk of adder bites.

The most distinguishing morphological feature of the adder is the dark zigzag pattern running along its back [3]. *V.berus* venom is composed of protein enzymes with cytotoxic activity, such as hyaluronidase, proteases and phospholipase. These compounds lead to endothelium damage, oedema and hypovolemia in the course of poisoning. One of the most known venom components is phospholipase A₂ (PLA₂), which transforms phospholipids of the erythrocytes' and thrombocytes' membranes into lysophospholipids, which

results in hemolysis and trombocytopenia. Miotoxic activity of PLA₂ may lead to rhabdomyolysis and acute kidney injury [3, 4, 5].

Objectives. The study presents epidemiological and clinical characteristics of *V.berus* bites in Eastern Poland, and describes the methods of poisoning treatment.

MATERIAL AND METHODS

Retrospective analysis of the medical documentation of 15 patients bitten by *V.berus berus* in the Podlaskie Province of Poland, and treated in the Department of Infectious Diseases and Neuroinfections of the Medical University of Białystok between July 1998 – July 2010 was performed.

During that time, 19 patients bitten by adders were hospitalized; however, 4 patients were excluded from the study due to the lack of some clinical data. The parameters analyzed were as follows: geographical location, month and moment of the day the bite took place, age, gender, anatomical location of the bite, presence of fang marks, time between the bite and admission to hospital, local and general symptoms, laboratory results, treatment and duration of hospitalization. Each patient underwent assessment of the severity of poisoning according to the Poisoning Severity

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Score – PSS [6], which grades poisoning into five categories: 1) none (absence of symptoms or the presence of fang marks only), 2) minor (local oedema around the bite, mild, transient and spontaneously resolving general symptoms), 3) moderate (oedema involving the whole extremity, pronounced or prolonged general symptoms), 4) severe (oedema involving the whole extremity and a part of the trunk, severe and life-threatening general symptoms), 5) fatal (death).

RESULTS

Epidemiology of bites. The examined group consisted of 10 males and 5 females. Mean age of the patients was 49.7 years (range 22-81 years). 8 patients (53.3%) lived in the country (villages with less than 5,000 inhabitants).

The bites were mostly accidental – 13 cases (86.7%), usually by stepping on an unnoticed snake; 2 patients were bitten while attempting to catch an adder. The majority of analyzed patients were bitten in May – 5 cases (33.3%) and July – 5 cases (33.3%).

13 bites took place between 08:00-15:00, with the peak at midday, the remaining two cases between 16:30-19:00. The patients were usually bitten while in the forest – 10 cases (66.7%), 3 patients – in the country (including 1 indoors), 2 patients – in a meadow located in the city. The majority of patients were bitten in the lower extremity (8 cases, 53.3%), most often in the area of the ankle joint. Bite location did not influence the severity of poisoning. Two patients drank alcohol after a bite; 1 patient cut the skin at the site of the bite; another patient squeezed the blood from the site of the fang marks.

Clinical manifestation. The severity of poisoning is presented in Table 1. The dominating form was minor poisoning (46.7%). At the moment of admission to the department, all the patients had fang marks visible, and all patients complained of severe pain which appeared just after the bite. 14 patients (93.3%) had oedema immediately

Table 1. Severity of poisoning

Severity of poisoning	No. of patients (%)
None	0
Minor	7 (46.7)
Moderate	6 (40.0)
Severe	2 (13.3)
Fatal	0

Table 2. Location of bites and area of edema

Anatomical location of bite	No. of patients (%)
Upper limb	7 (46.7)
Lower limb	8 (53.3)
Edema area	No. of patients (%)
Local	1 (6.7)
Hand and forearm	1 (6.7)
Whole upper limb	4 (26.7)
Foot	1 (6.7)
Foot and shank	6 (40)
Whole lower limb	1 (6.7)

after the bite; oedema was absent in 1 patient edema (6.7%); in 5 cases (33.3%), the whole extremity was affected (Tab. 2). Oedema lasted for 3-13 days (mean duration – 8 days); in 2 patients such a period could not be precisely defined as the patients were discharged at their own request. In 1 case, oedema of upper extremity was accompanied by enlargement of the axillary lymph nodes, and 1 patient had symptoms of lymphangitis. Subcutaneous blood extravasations were present in 11 cases (73.3%); 3 patients had mobility problems due to a massive lower extremity oedema (Fig. 1). General symptoms, such as diarrhea, abdominal pain, nausea and vomiting were present in 5 patients (33.3%); in 3 patients the body temperature was mildly elevated (37-38°C); and 3 patients had fever (>38°C).



Figure 1. *Vipera berus* bite in the area of ankle with visible fang marks. Edema and bruising of the foot, shank and distal part of thigh

Hypotonia was present in 3 patients (20%): 1 patient presented with shock, loss of consciousness, and an indeterminate blood pressure. Another patient experienced fatigue, bradycardia, blurred vision, chills, joint and muscle pain, and severe dyspnea soon after the bite. 3 patients with no history of hypertension had high blood pressure (on admission 190/80, 185/100, 170/80mmHg, and on the next day 140/85, 180/110, 155/98 mmHg, respectively). 2 patients had bradycardia (<60/min), 4 patients had tachycardia (>90/min). Abnormal ECGs were present in 4 patients (26.7%): 2 patients had nonspecific ST-T segment changes, 2 patients had intraventricular conduction defects.

Laboratory findings. 4 patients (26.7%) had leukocytosis >10,000/ μ L and neutrophilia. 1 patient had anaemia with thrombocytopenia within 24 hours after the bite (RBC $3.19 \times 10^6/\mu$ L, HGB 10.6 g/dL, HCT 32.2%, PLT 90,000/ μ L) with no concomitant coagulation disorders; additionally, there was 1 case of slight thrombocytopenia (133,000/ μ L). Coagulation disorders were present in 4 cases (26.7%): in 2 cases it was prolonged PT (PT>16 s), in 1 case prolonged APTT (APTT>40 s), in 1 case prolonged APTT with elevated D-dimer (>0.5 mg/l) and decreased fibrinogen (<200 mg/l).

2 patients had elevated CRP. In 4 cases (26.7%) the level of creatine phosphokinase (CPK >200 U/L) was elevated – in 2 cases there was more than a two-fold increase. Creatinine concentration was elevated in 2 cases (>1.3mg/dL); 1 patient with no diabetes had transient hyperglycaemia (233 mg/dL); in 1 case the aminotransferases activity was elevated; in 4 cases (26.7%) haematuria was observed, in 1 case – proteinuria; and in 1 case hyponatraemia was observed.

Treatment. The average time between the bite and admission to hospital was 5 hours (range 1-24 hours); 6 patients were admitted within 2 hours of the bite. There was no correlation between the severity of poisoning and the time between the bite and admission to hospital. 13 patients (86.7%) had specific antivenom against *V.berus* (*Immunoserum contra venena viperarum europaeorum*, Biomed, Warsaw, Poland) administered, each patient with a single dose of 500 antitoxic units due to the significantly exacerbated local lesions in the form of rapidly enlarging oedema and/or general symptoms. In 2 cases, antivenom treatment was not implemented due to the fact that the local lesions were slightly marked with no general symptoms. Each patient had an intracutaneous test to detect antivenom hypersensitivity. In 1 case, the test was positive; however, within a short period of time, three-quarters of the extremity was swollen and the antivenom was administered with hydrocortisone. After the administration of antivenom the swollen extremities of all patients were immobilized. There were no adverse reactions connected with the administration of the serum in any of the patients. In 6 cases (40%) the antitetanus prophylaxis was administered; in 10 patients (66.7%) hydrocortisone i.v. was administered.

The aforementioned patient with dyspnea after a bite had teophylline and hydrocortisone administered intravenously, with rapid resolution of symptoms. In 1 case it was necessary to administer dopamine and fluids infusion due to hypovolemic shock after the bite. All patients with oedema had symptomatic treatment, e.g. compresses with aluminium acetotartrate (Altacet) and/or sodium bicarbonate. Episodes of hypertension were treated with enalapryl (an Angiotensin-converting Enzyme Inhibitor – ACEI). 12 patients (80%) had NSAID administered due to severe pain of the extremity. The majority of patients were given phlebotropic drugs: diosmine, venescin, rutinascorbin. 9 patients (60%) had antibiotic prophylaxis (most often amoxycylin with clavulonic acid). The average duration of hospitalization was 8 days (range 1-17 days); 2 patients were discharged at their own request, even though discharge was contraindicated. All patients were discharged in good general condition with no ailments.

DISCUSSION

Epidemiology of bites. In the presented study, the majority of bites occurred between March – October, during the activity period of adders [7]. In Poland, adder bites are not mandatorily reported; therefore, only some data from individual centers are available: between 2000-2008, 26 patients were hospitalized in the Toxicological Unit in Wrocław, due to adder bite [8]; between 1999-2003, 26 patients were hospitalized in the Department of Infectious Diseases at the Medical University of Silesia in Bytom [9]. For comparison, in Sweden in 1995, there were 231 cases of bites [6]. Analysis of the group in the presented study revealed that men were bitten more often which is similar to other observations. According to the majority of analyses, the lower extremity is affected most often, especially in the area of ankle joint. In the case of the upper extremity, the fingers are most commonly affected. In the analysed group, bites of the lower and upper extremity accounted for 53.3% and 46.7% of cases, respectively [6, 8, 10, 11]. The bites were usually accidental, as a result of carelessness (accidentally stepping on a adder or disturbing it).

Results of bites. The analyzed patients presented with both local and general symptoms of venom poisoning. In 53.3% of cases the poisoning was moderate or severe; there was no asymptomatic bites. In the majority of cases, fang marks were present after a bite. In the study they were present in all the analysed patients. The most common symptom of poisoning was oedema, present in almost every patient; the patient who did not present with oedema had general symptoms of poisoning in the form of abdominal pain and increase in CRP and ESR. The most common local symptom of a bite was pain, with tingling and oedema painful on palpation which may spread, and usually appeared within a few minutes (up to 2 hours). In most cases, the oedema was accompanied by redness and subcutaneous blood extravasation. Regional lymph nodes enlargement or lymphangitis occurred less frequently [3, 12, 13].

Anxiety, nausea, vomiting, diarrhea, abdominal pain and elevated body temperature were the most common general symptoms of poisoning in this study. Anaphylactic reaction is not common, the possibility of such phenomenon is higher in people with hymenoptera allergy as a result of cross-reactivity with adder's venom [14]. Severe poisoning manifests with hypotonia and shock [3], while the most dangerous poisonings occur after direct injection of venom into the blood vessels [15]. To date, the presence of neurotoxin in the venom of *V.berus berus* has not been confirmed. There are single reports of ptosis and blurred vision; these, however, were most probably the result of a bite in the area of the head, and not the neurotoxic activity of venom. Neurotoxin, however, is present in another subgenus of *V.berus* – *V.berus bosniensis* [10, 16, 17].

It has been confirmed that the venom of *V.berus* contains cardiotoxines, the activity of which may be reflected in changes in ECG (T-wave inversion, ST segment elevation/depression, atrial fibrillation, second-degree AV block, brady and tachyarrhythmias). ECG abnormalities may be present in either mild or severe poisonings [7, 12, 18]. In the analyzed group there were 3 cases of ECG abnormalities in the mild poisonings, and in 1 case of severe poisoning. Taking into consideration that ECG changes due to adder bite are rare, it should be pointed that 1 patient in the presented study with intraventricular conduction defect, had ischaemic heart disease, which seems to be more a probable explanation of the ECG abnormalities than the influence of venom.

In the literature there are case studies concerning patients presenting with high blood pressure after *V.berus* bite, which also has been observed in the study group. This is possibly the result of a cardiotoxic venom component which leads to the release of catecholamines from the nerve synapses. Hyperglycaemia, present in 1 patient, was most probably induced by the catecholamines and the administration of glucocorticosteroids [10, 16, 17].

Biochemical tests may reveal leukocytosis with neutrophilia, anaemia, thrombocytopenia, elevated total bilirubin, creatinine and urea concentrations, and increased activity of CPK, ALT, AST. Coagulation results present with prolonged PT, APTT, increased INR, hypofibrinogenemia and the increase of D-dimer [12]. The anemia with thrombocytopenia in 1 patient, with massive oedema of the extremity, was the result of extravasation of the plasma to the vascular area and hemolysis.

Some bites are described as 'dry bites', in which there is no injection of venom into the body; nevertheless,

it is recommended that patients with no symptoms of poisoning except fang marks should undergo 2-4-hour hospital observation. Patients with slight oedema, with no accompanying general symptoms, should be observed for 48 hours. A mild course at the beginning may develop into life-threatening hypotonia or arrhythmia within a few or several hours after a bite. An initially asymptomatic bite may develop into moderate or severe poisoning [13, 19].

Treatment. The person bitten by an adder should be transported to hospital as quickly as possible. Directly after the bite, the patient should be tranquilized, the wound disinfected, and the extremity immobilized which slows the process of venom transportation in the body. A tourniquet above the area of a bite, ice compresses; sucking the venom or any cut in the area of a bite are not recommended. Due to the lack of precise data in the history of the patients it could not be defined how many patients had ice compresses or a tourniquet applied. The treatment for symptoms of shock were in accordance with standards [3, 12, 15].

The only specific method for the treatment of poisoning is the antivenom (antitoxin), which neutralizes the activity of venom, reduces the risk of death, and shortens the period of hospitalization and reconvalescence. Due to the fact that antivenom contains a foreign protein and its administration may cause allergic reactions, such as anaphylactic shock or postserum disease (*Morbus postsericus*), it should be administered in the hospital [4, 12, 20]. In Poland to date, only horse-derived antivenom (*Immunoserum contra venena viperarum europaeorum*, Biomed, Warsaw, Poland) has been available [21]. Since May 2011, sheep-derived antivenom is also available (Institute of Immunology, Zagreb, Croatia). Horse-derived antivenom is effective in neutralizing venom; however, there is a higher risk of adverse allergic reactions than in the case of sheep-derived antivenom [22]. Clinical analysis by *Karlson-Stiber and Persson* revealed that allergic reactions after the administration of horse-derived antivenom accounted for 10% of patients (in the form of urticaria or postserum disease) [20]. In comparison, in a retrospective study by the same authors, the administration of sheep antivenom did not promote any allergic reactions [23]. Sheep antivenom has better kinetics and distribution in the body and may be administered intravenously with better effectiveness [23]. According to *British National Formulary* it is recommended in hypotonia, vomiting, ECG abnormalities, coagulation disorders and rapidly spreading oedema (exceeding the wrist/ ankle within 4 hours) [24]. Other indications are: trombocytopenia, haemolysis, leukocytosis with neutrophilia, increase of CPK activity, metabolic acidosis and consciousness disorders [3, 7, 12, 15]. Before the administration of antivenom, the performance of an allergy test is recommended [19].

In the presented study, antivenom was administered in 13 patients (86.7%). 60% of the patients had prophylactic doses of antibiotics and 40% of cases had antitetanus prophylaxis introduced. The necessity of antibiotic and antitetanus prophylaxis should be considered in each case. The majority of authors recommend antibiotics only in patients with the symptoms of infection due to the introduction of the bacteria into the wound by the fangs; however, they should not be treated as a routine [13, 15]. *Kerrigan et al.* divided 114 patients bitten by snakes into 2 groups: those who had prophylaxis doses of antibiotics and those who did not receive antibiotics.

There were no statistically significant differences between either group [25]. The majority of patients analysed had hydrocortisone administered before the specific treatment. Glucocorticosteroids, recommended in the past, are still very popular in cases of venom poisoning.

Analysis of a group of 136 cases of bites, compared patients who had glucocorticosteroids administered before the admission to hospital with patients who did not receive glucocorticosteroids, showed no difference in the severity of symptoms between the groups. Nowadays, glucocorticosteroids are not recommended unless allergic reactions induced by the venom or antivenom are present (anaphylactic shock, postserum disease) [26, 27].

Symptomatic treatment is usually sufficient – the administration analgesics, antiemetics, sedatives, phlebotropics drugs and compresses.

CONCLUSIONS

In Poland *V.berus* bites are not so rare. Usually, the event take place in a forest, in the middle of the day. In most cases, the severity of poisoning with *V.berus berus* venom is minor to moderate, limited to local oedema. Most often lower limb is affected. Indications for antivenom treatment should be restricted, as its administration may provoke adverse allergic reactions, including life-threatening anaphylactic shock. Routine administration of corticosteroids and antibiotics is not recommended.

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