

# Acute Pancreatitis after Viperid Snake *Cerastes Cerastes* Envenoming: A Case Report

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**Abstract:** Snakebites by the viper snake *Cerastes cerastes* are quite common across the world but rarely published with regard to their mostly benign course. The reported case study depicts the envenoming of a 36-year-old Czech man, a private herpetologist, who suffered snakebite to his finger. He developed a painful local reaction with hemorrhagic oedema. Subsequently, consumption coagulopathy with thrombocytopenia and haemolysis, colicky pain in the epigastrium and acute renal failure developed. Acute exudative pancreatitis was diagnosed on the third day after envenoming. Hemorrhagic oedema of the arm was complicated by a phlegmon. Symptomatic treatment including haemodialysis, fresh frozen plasma and thrombocytes was administered. Antivenom was not administered due to the delay in referral to the specialized unit. The patient recovered within one month, only postnecrotic defects of the finger persisted.

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## Introduction

*Cerastes cerastes* Linneatus, 1758 (Sahara, African, Egyptian, Desert, Sand, Horned Viper) is a common viper snake, which occurs mainly in the sandy and rocky regions of North Africa, from south-eastern Morocco to Egypt, the southern to the central regions of Mali, Niger, Chad and Somalia. Eastwards, the habitation extends through Israel and the Arabian Peninsula to south-western Iran. The length of the *Cerastes* viper does not exceed 70 cm, the colour pattern consists of a gray-brownish or greyish colour, the head is large with supraorbital horns. The viper hides itself in the sand, showing only part of its head. It moves about by side winding which leaves typical impressions in the sand (Figure 1). They are popular among snake-keepers and thus encountering snakebite is not rare outside the area of its original distribution.

The venom of the *Cerastes* viper contains predominantly enzymatic components with proteolytic activities which affect the coagulation system. The venom components have inter alia direct fibrinolytic activity (afaacytin, cerastes F-4), thrombin-like activity (cerastocytin, cerastobin); they activate factor X and induce platelet aggregation (afaacytin, protein IVa) (Basheer et al., 1995; Marrakchi et al., 1995; Warrell, 1995). The venom causes local tissue destruction, coagulopathy, frequently of the consumption type and renal failure.

Envenoming is usually characterized by mild systemic symptoms, local swelling with lymphadenopathy and laboratory changes predominantly in coagulation tests. A severe course of intoxication is rare (Lifshitz et al., 1995, 2000, 2002; Schneemann et al., 2004), with no fatal cases described in recent literature. There are a few reports of fatal cases in the French Colonial literature from the end of the 19<sup>th</sup> century (Warrell, 1995).

In the last six years, nine patients have been treated for snakebite by the horned viper *C. cerastes* in the Czech Republic. In one of these cases, there were no signs of intoxication, in four cases only local reaction and in four cases systemic intoxication occurred. Two cases of systemic reaction were of a remarkable severity (Valenta, 2008).



Figure 1 – *Cerastes cerastes* (photo Velenský).

### Case report

A 36-year-old man, a Czech amateur snake-breeder, suffered two fang punctures to the distal phalanx of the first finger of his right hand during manipulation of an adult specimen of *Cerastes cerastes*. He was referred to the internal department of the local hospital. Local findings included a bite and progressive hemorrhagic swelling of the finger and hand. Laboratory tests revealed signs of haemolysis and consumption coagulopathy (disseminated intravascular coagulation – DIC). Symptomatic and replacement therapy was initiated: hydrocortisone, intravenous fluids, 2 transfusion units (TU) of fresh frozen plasma (FFP), 1000 IU of antithrombin (AT). The Toxicology service was not consulted, antivenom was not administered. The patient was referred to a specialized unit for the progression of local damage, renal insufficiency (blood urea 17.6–24.0 mmol, creatinine 504–712  $\mu\text{mol/l}$ ), persisting coagulopathy with thrombocytopenia  $23 \times 10^9/l$  and mild haemolysis without hemoglobinuria (signs of haemolysis in the initial tests).

On admission, three days after envenoming, the right upper extremity was swollen up to the elbow with numerous hematomas which extended in bands to the armpit. Axillary lymphadenopathy was present. The patient suffered from colicky pain in his epigastrium. Laboratory findings showed severe thrombocytopenia ( $23 \times 10^9/l$ ), high D-dimer level (6452  $\mu\text{g/l}$ ) and evidence of renal insufficiency (oligoanuria 30 ml per hour, blood urea 17.6 mmol/l, creatinine 504 mmol/l, kalium 6.2 mmol/l) which progressed to anuria. A high level of amylase in serum (30.69  $\mu\text{kat/l}$ ) and urine (51.15  $\mu\text{kat/l}$ ) was present (Table 1). Abdominal ultrasound from the previous hospital showed free fluid in the retro- and intraperitoneal spaces, subcapsular hematoma of the right kidney and diffuse renal parenchymal lesions. CT scan of the abdomen done after admission revealed signs of acute pancreatitis in the head of the pancreas with a fluid collection in adjacent tissue and in the right perirenal region.

Thrombocytopenia and consumption coagulopathy were corrected with the administration of 2 TU of thrombocyte concentrate, 3 TU of fresh frozen plasma, AT was replaced slightly up to 100% of the activity and hematocrit was corrected with 2 TU of erythrocyte concentrate (Figure 2). Administration of continuous intravenous unfractionated heparin (UFH) 310 IU/h was started. The antivenom was not administered due to the time delay from the envenoming and taking into account that secondary complications had already developed. A nasojejunal catheter was placed for enteral feeding due to evidence of pancreatitis and, after correction of hemocoagulation, an epidural catheter was placed for analgesia. Meropenem was administered as antibiotic treatment. Continuous veno-veno hemodiafiltration (CVVHDF) with heparin anticoagulation was used for renal failure. Persisting respiratory insufficiency was treated with oxygenotherapy, later with continuous positive airway pressure 10 cm  $\text{H}_2\text{O}$ . Mechanical ventilation was started on the 8<sup>th</sup> day for further impairment of ventilation and oxygenation parameters. Repeat

**Table 1 – Haemocoagulation and serum AMS laboratory findings**

Parameters	normal range (units)	Day of envenoming					
		3	4	5	6	7	8
INR		1.6	1.4	1.2	1.1	1.2	1.3
APTT	25.9–40 (s)	42.4	42.2	62.8	42	45.8	96.4
TT	12.0–18.0 (s)	15.5	13.7	29	16.4	16.2	61.6
FBG	2.0–4.0 (g/l)	2.7	4.7	5.2	4.6	4.6	4.7
AT	70–140 (%)	96	114	99	98	103	91
D-DIM	0–190 (µg/l)	5524	4555	6452	6044	4063	3222
PLT	150–300 (10 <sup>9</sup> /l)	23	63	50	68	74	130
PLT replacement	TU	2	4	n/a	n/a	n/a	n/a
AT replacement	IU	2000	1000	n/a	1000	n/a	n/a
AMS panc. isoен.	0–0.8 (µkat/l)	30.7	21.3	9.33	4.9	3.95	3.67

CT scan on the 9<sup>th</sup> day showed persisting evidence of acute pancreatitis in the region of the pancreatic head with oedema of adjacent structures.

Hemorrhagic swelling of the upper extremity persisted, with developing phlegmon of the hand and erythema of the arm extending up to the neck. Incisions with drainage were performed on the 10<sup>th</sup> day, treatment with cefepim and clindamycin was initiated (Figure 3).

Oedema and erythema resolved on the 12<sup>th</sup> day, a necrotic area 2×6 cm remained at the site of the bite. Haemorrhage with a decrease in red blood cells (RBC) occurred during surgical treatment, RBC were gradually replaced (Figure 2).

Persisting thrombocytopenia, coagulation disorder and anaemia were corrected with FFP, AT and RBC replacement during hospitalization. In total, 17 TU of thrombocyte concentrate, 24 TU of RBC, 26 TU FFP and 9000 IU of AT was administered to the patient.

The patient was extubated on the 13<sup>th</sup> day of hospitalization with subsequent spontaneous ventilation on oxygenotherapy and with good respiratory parameters.

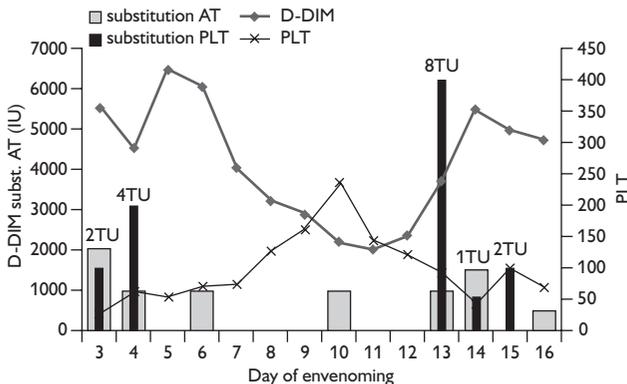


Figure 2 – Haemocoagulation laboratory disorder and substitution of AT and PLT.

Day of envenoming							
9	10	11	12	13	14	15	16
1.3	1.3	1.3	1.2	1.1	1.1	1.1	1.2
52.7	57.2	61	39.5	40.7	48.1	42.5	42.3
16.1	13.8	19.5	15.4	15.4	29.9	18.5	16.4
4.9	4.9	4.7	4.5	4.5	4.4	4.5	4.5
87	78	92	105	93	109	102	83
2862	2185	2015	2344	3659	5476	4972	4722
158	234	141	121	95	37	100	69
n/a	n/a	n/a	n/a	8	1	2	n/a
n/a	1000	n/a	n/a	1000	1500	n/a	500
3.87	2.79	3.66	4.37	4.74	3.46	3.06	2.26

Over the second week of hospitalization the coagulation tests (PT, APTT) returned to normal values, thrombocytopenia and high D-dimer level persisted (Table 1). CVVHDF was continued because of persisting renal failure. The pancreatitis improved remarkably as well as local findings in the extremity. Respiratory functions normalized. On the 18<sup>th</sup> day after envenoming the patient was transferred back to the district hospital. Renal function returned to normal and the signs of pancreatitis had resolved by the beginning of the 2<sup>nd</sup> month after the bite. Minor postnecrotic defects remained at the site of the snakebite.



Figure 3 – Phlegmon and erythema of the arm, incisions with drainage on the 10<sup>th</sup> day.

## Discussion

Envenoming by the *Cerastes cerastes* viper is quite common both in the area of its occurrence and among snake-keepers because of the high popularity and availability of this species.

The clinical course of intoxication is usually not severe, presenting with mild discomfort, elevated temperature, nausea, sometimes vertigo, vomiting accompanied by laboratory evidence of coagulation disorder without major clinical presentation, and minor local lesion.

Some afflicted persons do not even seek medical consultation. For these reasons, publications on envenoming by the *Cerastes* viper are quite rare and mostly depict a typical course with coagulation disorder and renal failure (Lifshitz et al., 1995, 2000, 2002; Schneemann et al., 2004).

The reported case represents a more exceptional serious course of intoxication with coagulopathy, profound thrombocytopenia, bleeding, anaemia and renal failure. In addition, the case was unexpectedly complicated with early onset exudative pancreatitis and transient respiratory insufficiency.

The venom contains, among others, thrombin-like enzymes and other components activating factor X. This leads to the activation of plasmatic coagulation cascade with consumption type of coagulopathy characterized by high D-dimer level detected in serum. Moreover, components of venom cause degradation of fibrinogen (FBG). The drop in fibrinogen level was not observed in the reported case; on the contrary, the FBG level was elevated due to systemic inflammation during pancreatitis. Consumption and degradation of FBG was not profound enough to decrease its level. However, according to the D-dimer level it was sufficient to cause marked formation of fibrin polymers and microthrombi. Another effect of venom constituents is the activation of platelets which aggregate increasingly and are either destroyed or consumed and thus participate in (micro)thrombi formation. In our patient, reactivation of the hemocoagulation system occurred after replacement therapy withdrawal over the 11<sup>th</sup> to 14<sup>th</sup> day after envenoming (Figure 2), probably as the effect of persisting venom components.

Renal failure can be expected after envenoming by vipers including *Cerastes cerastes* with a serious course of intoxication. The underlying mechanisms are, besides glomerular hypofiltration by bleeding, decrease of intravascular volume by extravasation, microthrombi formation within consumption coagulopathy and vasoconstriction and direct nephrotoxicity of venom constituents: enzymatic destruction of renal marrow and renal tubules (Warrell, 1995).

Pancreatitis associated with snakebite is an exceptional complication, though enzymatic components of both snake venom phospholipase A2 (PLA2) and human pancreatic PLA2 are used for cell destruction *in vitro* (Martikainen et al., 1993) and one case of acute pancreatitis following snakebite was reported (Kjellström, 1989). We assume that the pancreatitis was induced by enzymatic destruction of tissue, in

particular by activity of venom PLA2. Capillary obstruction and organ hypoperfusion could also contribute to the pathogenesis as well in the case of renal failure. Taking into account the CT scan findings of our patient, we cannot exclude the underlying chronic cholecystitis with pancreatic irritation in the history. However, the further course and relatively rapid resolving of pancreatitis support the hypothesis that other than typical hemorrhagic pancreatitis was encountered in this case. We suppose that damage to the pancreas (exudative pancreatitis) was caused by venom components analogously to common involvement of the kidneys and less frequent damage of lung tissue with symptoms of respiratory insufficiency of lung failure type or liver damage with elevation of liver enzymes (*Echis* envenoming – author’s experience).

Intoxication was treated only with symptomatic and replacement therapy, without antivenom administration. The antivenom was available only by urgent import from abroad at the time of treatment and the patient was admitted to a specialized ward when organ complications in the kidneys and pancreas had already developed; generally early administration of antivenom is recommended (Schneemann et al., 2004). It remains a question whether the delayed antivenom administration would have mitigated the course and reduced the time of morbidity in this case.

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