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Case report

Compartment syndrome after viper-bite in toddler: case report and review of literature

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Abstract. Snakebites in Italy are a rare source of severe medical condition, except in case of venomous snakes. The venom causes both local and/or systemic complication which may determine death in 6-60 hours, particularly in children and the elderly. In fact, the same amount of venom affects children more severely than adults because of the reduced total dilution volume in children. The only specific and conflicting therapy for venomous snakebite is to administer the appropriate anti-venom; the remaining therapy is symptomatic and supportive. We describe the case of a 22 months old child who, despite appropriate symptomatic treatment, developed severe signs and an acute compartment syndrome of the right upper limb, a rare complication of venom snakebite. Administration of antivenom and fasciotomy were needed to resolve the acute episode permitting a positive outcome. On the basis of literature review and our experience we hypothesize an algorithm for the treatment of these patients. (www.actabiomedica.it)

Key words: viper-bite, children, envenomation, antivenom, compartment syndrome

Introduction

A recent review on snakebites in Europe, estimates the annual incidence of snakebite as 1.6 per 100000 inhabitants, with a total number of bites of 7992 and only 4 deaths. However it is important to say that a maximum variability which raises the question of coherence and representativeness of the results is observed (1). It is presumable that most snakebites in Italy are caused by non-venomous snakes, even if no national epidemiological data have been published related to the incidence of snakebite in our country (2).

In Europe the *Viperidae* are the only venomous snake, and four different types may be found in Italy (*V. berus, V. aspis, V. ammodytes, and V. ursinii*).

All the types of venom of the European vipers are similar and contain neurotoxins, cardiotoxins, proteolytic and haemolyzing enzymes, and cytochrome oxidase inhibitors (3); they mainly cause hematotoxic effects[2].

Snakebites frequently occur in the extremities with approximately two thirds occurring in the upper extremities, as in our patient. In this site, especially the hand, almost no subcutaneous fat tissue is present, the skin of the dorsum is very thin, and there are many superficial veins. The palmar surface of the hand includes a rich vascular network, which makes snakebites of the hand more susceptible to systemic spreading of the venom. Moreover, vital tissue such us joints, nerves, and tendons are very superficial in the upper hand. Therefore, snakebite on the hand is more urgent than snakebite elsewhere, so it must be treated at a very early stage (4). Compartment syndrome after viper snakebite is rare.

We describe the case of a 22 months old child who, despite appropriate symptomatic treatment, developed severe signs and an acute compartment syndrome of the right upper limb.

Case report

A 22 months old child had snakebite at the proximal phalanx of the second finger of right hand where there was a bleeding open wound.

Immediately transported at local hospital the pediatrician found typical fang marks, hard swelling of the finger and edema until the arm with beginning lymphangitis. General conditions rapidly worsened with pallor, drowsiness, tachycardia, hypotension and he required respiratory support with high-flow oxygen (8 L/min) in mask with reservoir. Laboratory data showed neutrophil leukocytosis (WBC 20.100/ml, N 67.2%) and decreasing aPTT (22 sec) so he was admitted to our Intensive Care Unit 4 hours after the bite. The main symptoms were edema and cyanosis of the second finger, significant swelling of the right hand, forearm and upper arm with lymphangitis up to the axilla, and strong spontaneous pain (Fig. 1). To reduce edema and counteract the systemic effects of the venom the patient was treated with intravenous hydrocortisone (9 mg/kg) and saline 0.9% (40 cc/kg/day). Then the following therapy was set: antibiotics (clindamycin: 15 mg/kg each 8 hours; ceftriaxone: 50 mg/kg/die), mannitol (0.25 g/kg each 6 hours) to avoid renal failure, morphine (0.05 cc/kg/h) as painkiller, heparin (2000 U first day and then 1000 U) and dexamethasone (0.2 mg/kg each 6 hours). Laboratory tests confirmed leukocytosis and decreasing aPTT; an incoming severe acidosis (pH 7.04, BE -9.2) was also observed so that bicarbonates was administered (20 mEq). No ECG abnormalities were observed.

The antivenom (Viper venom antiserum, European), with $F(ab)_2$ fragments of immunoglobulin (equine) for specific neutralization of different viper venom (V. *ammodytes*, *V. aspis*, *V. berus, V. lebetina, V. xanthina*, and *V. ursinii*), was available after 6 hours and administered to the patient without any adverse reaction.

Despite the supportive treatment, the patient rapidly developed an acute compartment syndrome. It pushed us to urgently submit the child to the surgical fasciotomy (Fig. 2).

A significant improvement of both general conditions and compartment syndrome was shown after 12 hours. Two days after the bite the child was transferred to the General Pediatric Ward; after 4 days, he started a rehabilitation program to prevent adherence and retraction due to the intervention. He was discharged at day 11. The defect coverage was corrected with secondary wound closure (Fig. 3). The follow up showed complete *restitutio ad integrum*.

Figure 1. Swelling of the right hand, forearm and upper arm with edema and ecchymosis

Figure 2. Fasciotomy of the forearm

Figure 3.The hand and the forearm after the surgery: healed wound

Discussion

Clinical findings of venomous snakebite may vary according to the species and the size of the snake, the depth and the location of the bite, the volume of the injected venom, the age, size and general health status of the victim, and the effectiveness of the initial therapy (2, 4-6).

As an emergency medical condition venomous snakebite importance is more marked in childhood[2].

The critical period for a victim is usually thought to be the first 12 hours, but may last for several days. The most commonly signs and symptoms are pain, edema, weakness, numbness, tingling, tachycardia, ecchymosis, and muscle fasciculation, metallic taste in the mouth, vomiting, confusion and hemorrhagic diathesis (2, 7-9).

It is a general agreement that, immediately after snakebite, the bite site should be immobilized to delay the spread of venom and the reassurance of the victim is important (8, 10-12). It is also important to remove tight clothing and jewelry (watches, bracelets, etc.) from the bitten extremity to avoid tightening due to swelling (12). Instead, the bite area should not be manipulated or incised, as this may increase the rate of venom absorption and worse local damage to the skin and underlying tissues. Similarly, potassium permanganate and ice packs (cryotherapy) should not be used, as these may promote local necrosis. Moreover, the use of light bandaging or a ligature/tourniquet above the bite site and assay to remove poison from inoculation's place through suction or squeezing are not recommended.

The effects of poisoning are unpredictable and therefore any snakebite victim should be referred to hospital for monitoring for at least 2-4 hours (12, 13). Asymptomatic cases may then be discharged, while all victims showing any evidence of poisoning should continue to be observed and monitored for at least 24 hours (Fig. 4) with measurement of vital signs (blood pressure, heart and respiratory rate) as well as lab tests including white blood cell and platelet count, coagulation parameters (PT, aPTT, fibrinogen, FDP), serum creatine kinase and electrolytes, LDH, bicarbonate and urinalysis. This is especially important in case of children and the elderly, who are at particular risk (2, 12-14). It is recommended that victims also should have an ECG twice daily if hypotension persists (14).

In order to obtain an indicator for the specific anti-venomous treatment, as well as for a prognostic estimation (13), it has been proposed to classify the signs and symptoms of poisoning into 5 grades (from 0 to IV; Table 1) (15). Our patient with rapidly progressive edema, gastrointestinal symptoms and hypotension was ranked in grade IV.

In case of severe poisoning, treatment has 2 components: symptomatic and supportive (correction of the systemic hemodynamic, respiratory and hematological disturbances), and administration of specific antivenom (13, 16). However, conflicting data emerge from literature about the appropriate treatment.

Corticosteroids are generally used to reduce the edema and to counteract the systemic effects of the venom[3], but it seems that early corticosteroids administration has no real effect on the symptoms of snakebite (9, 10-12).

Since hypotension is quite a common symptom of snakebite, establishing an intravenous line and starting parental fluid therapy at an early stage is justified (9, 12), but a too large infusion could diffuse the venom and worse the symptoms.

Although the use of heparin is recommended for the treatment of coagulopathies, in some studies no significant benefit is achieved with heparin treatment (2, 17, 18). Moreover injection of low molecular weight heparin may promote spreading of venom.

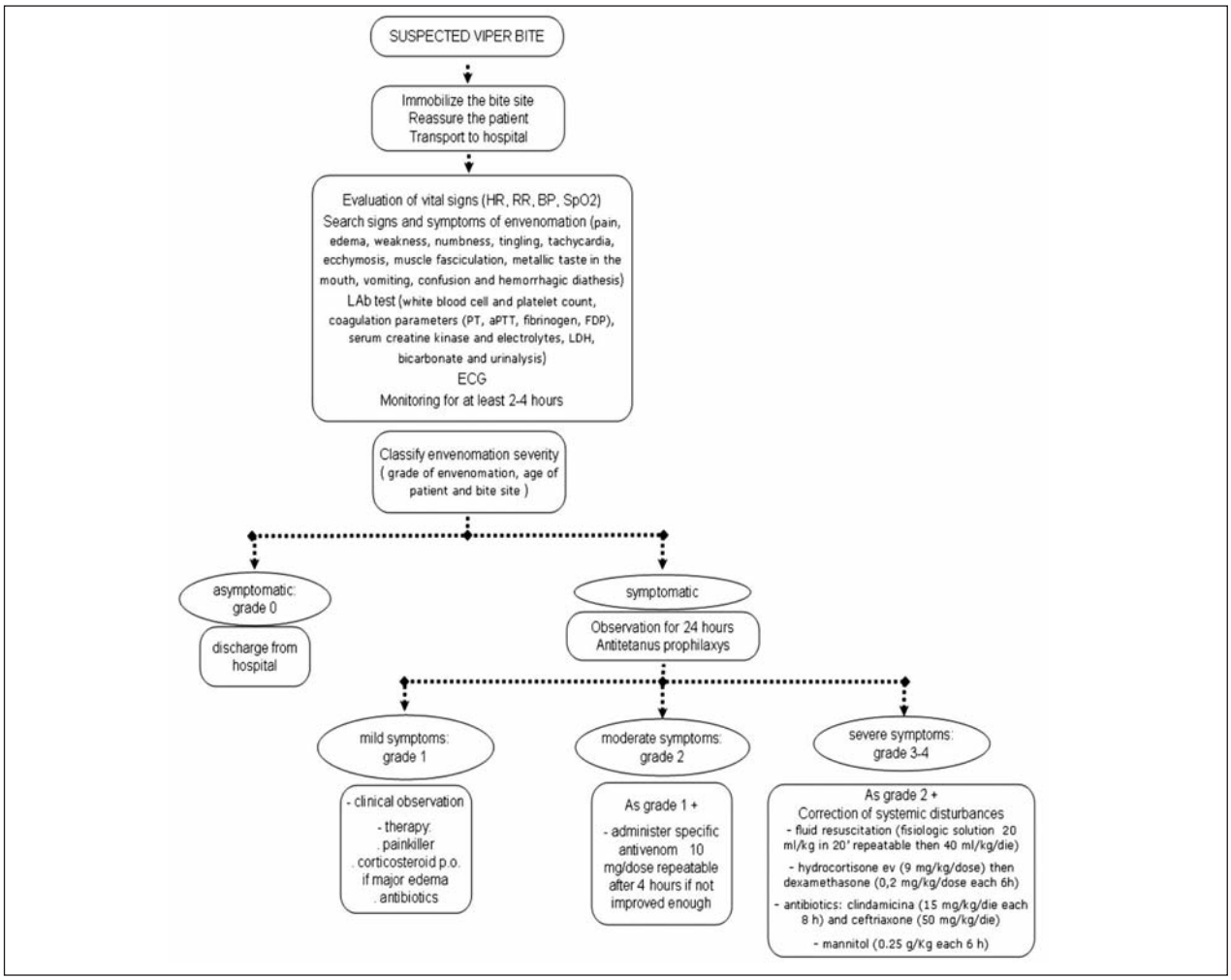

Figure 4. Practical algorithm for treatment of venomous snakebite

Therefore this treatment may be useful in only two cases: to prevent possible venous thrombosis in patient presenting snakebites located on the lower extremity which require prolonged immobilization and in patients that develop disseminate intravascular coagulation (DIC) (12). We used it for the presence of a central venous access (CVC).

Antibiotics are widely used as prophylaxis although their efficiency has never been documented (9, 11). Considering that the leukocytosis might be the response against toxins or acute stress, antibiotics should not be started because of the elevated leukocyte counts alone in patients having no findings of infections (2, 9, 12).

The antivenom should be given in case of systemic poisoning or when local symptoms are severe (from grade II to IV) (1, 12, 13). It has to be preferably administered within 4 hours of the snakebite, but it is effective within the first 24 hours (4, 19). The antivenom administration may cause 2 main adverse reactions: anaphylaxis and serum sickness. An anaphylactic reaction is immediate, while serum sickness may occur 7-12 days after the first injection of antiserum, or 3-5 days after the second injection following the first one by 4-5 months. The risk of reactions with currently available antivenoms for use in bites by European vipers is reported as very low (20, 21). However, victims with allergy are at increased risk of devel-

Table 1. Severity grading (revised by Norris) (15)

Severity:	Dry Bite (non venomous) Grade 0	Mild Grade I	Moderate Grade II	Severe/Very severe Grade III/IV
Fang Marks	+/-	+	+	+
Pain	None	Moderate	Severe	Severe
Edema	None	Minimal 0 to 15 cm	Moderate 15 to 30 cm	Severe > 30 cm
Erythema	None	+	+	+
Ecchymosis	None	+/-	+	+
Systemic signs and symptoms	None	None	Mild	Early, severe
Coagulation Tests	None	Normal	Abnormal, without bleeding	Abnormal, with bleeding

oping severe antivenom anaphylactic reactions (22). They should therefore only be given antivenom if definite signs of severe systemic envenoming are present. A Sheep-fab-fragment antivenom, which is less allergenic than other antivenoms, should be employed in case of severe symptoms.

On laboratory evaluation, thrombocytopenia, elongation of PT and aPTT, DIC, and markers of hemolysis and rhabdomyolysis may be seen (2, 23-27). Although the classically characteristic finding of DIC prolongs clotting times (PT, aPTT), paradoxically, acute phase response may lead to shortening of the aPTT. For this reason the International Society of Thrombosis and Haemostasis's guidance on identifying non-overt DIC takes not only the abnormal coagulation test results into consideration but abnormal trends in these test results (2, 28). The short aPTT of our patient may be the result of acute phase response. Serum fibrinogen concentration may be decreased due to the thrombin-like activity of snake venom and fibrin degradation products may be increased due to the secondary activation of fibrinolytic system; however, AT III may be normal or increased (2, 28, 29). Early leukocytosis, as that found in our patient, may serve as a warning signal for higher probability of severe reactions. Cortisone increases the amount of leucocytes in peripheral blood by releasing granulocytes from leucocyte reserves, for example, bone marrow and spleen. Therefore only early leukocytosis is notable while estimating the severity of the poisoning (9).

In the Intensive Care Unit our patient did all these things and neutrophil leukocytosis, aPTT decreasing, important acidosis, CPK increasing and hypotension were found.

Compartment syndrome (CS) is a limb-threatening and life-threatening condition which occurs when the tissue pressure exceeds the venous pressure and impairs blood outflow in a closed anatomic space. Early manifestations include pain, because of lack of oxygenated blood and accumulation of waste products and decreased peripheral sensation secondary to nerve irritation; in a secondary time absence of a distal pulse, hypoesthesia and extremity paresis appear, because the elevating tissue pressure eventually compromises arterial blood flow. If left untreated or if inadequately treated, the muscles and nerves within the compartment undergo ischemic necrosis and a limb contracture, called a Volkmann contracture, results. Severe cases may lead to renal failure and death. CS may affect any compartment, including hand, forearm, upper arm, abdomen, buttock, and entire lower extremity. Almost any injury may cause this syndrome. The definitive surgical therapy is emergent fasciotomy (compartment release). The goal of decompression is restoration of muscle perfusion within 6 hours.

CS after a venomous snakebite is extremely rare (3, 13, 30) even in grade IV, as in our patient. It develops as a result of increased pressure due to the edema limiting blood circulation (2). Without prompt surgical treatment, it may lead to irremediable nerve

Table 2. Results of the studies about treatment for venomous snakebite

Authors	Year	Patients n.	Severity of poisoning	Corticosteroids	Antibiotics	Antivenom
De Haro L et al.	2009	174	0 = 0 I = 52 II = 90 III/IV = 32	No	No	106/174 Yes
Bozkurt M et al.	2008	12	n.a.	n.a.	12/12	9/12
Ozay G et al.	2005	77	0 = 0 I = 23 II = 44 III/IV = 10	44/77	72/77 No *	57/77 Yes
Grönlund J et al.	2003	68	0 = 24 I = 23 II = 14 III/IV = 7	64/68 **	47/68 No *	8/68 Yes
Reading CJ	1996	n.a.	n.a.	n.a.**	No	Yes
Persson H et al.	1981	136	0 = 37 I = 62 II = 21 III/IV = 16	123/136 **	80/136 No	Yes
Reid HA	1976	95	n.a.	No	No	Yes

In the table "Yes" mean that in the study the use of the drug is advised while "No" means that it is not recommended. In some studies authors don't give any opinion about treatment.
* Despite the large use in their patients authors say that antibiotic should not be started for elevated leukocyte counts alone in patients having no findings of infections, even because infections are not frequent in adder bites.
** In the discussion authors say that the value of corticosteroid therapy is questionable.

damage and muscle death (3, 13). Current experience has demonstrated that antivenom, reducing edema, avoids peripheral ischemia due to compression, thus fasciotomy may be considered as unnecessary for viper envenomation and used only in rare cases (12). Our patient developed compartment syndrome since few hours from the bite and fasciotomy was urgently needed to avoid irreparable damage to the neuromuscular and vascular structure of the arm because the baby had absence of a distal pulse, hypoesthesia and extremity paresis and antivenom was not yet accessible. Severe acute tubular necrosis and bilateral renal cortical necrosis after *Viperidae* bites have been reported in the literature (2, 7). Since compartment syndrome, with CPK increasing, may affect renal function too, in our case, in order to prevent renal failure, a diuretic therapy with mannitol was started and no renal injury was registered.

Conclusions

The analysis of the literature does not allow obtaining an evidence based conclusion on the appropriate treatment for venomous snakebite. In fact the studies about the treatment of venomous snakebite are mainly retrospective and, at the best of our knowledge, we do not know randomized clinical trial in these patients (Tab. 2). However we think that is possible to hypothesize an algorithm for the treatment of these patients even if some concerns yet exist especially about the appropriate use of antibiotic and corticosteroids.

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