



## COMPLICATED VIPERINE ENVENOMATION WITH A PULMONARY EMBOLISM

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Article Received on 19/03/2018

Article Revised on 09/04/2018

Article Accepted on 30/04/2018

### SUMMARY

Ophidian envenomation is a major public health issue in the world due to its seriousness and the complications that it can lead to. We report the case of a viper bite envenomation in southern Morocco that has been complicated by pulmonary embolism. The composition of venom secreted by vipers is very rich in enzymes and toxins, they act on platelets, plasma coagulation and fibrinolysis, and they are responsible for clinical signs: edema, coagulation disorders and hemostasis. The antivenom immunotherapy remains the only specific treatment for a serious envenomation; its preparation must be based on venoms used to obtain antibodies able to neutralize the main activities of the venoms of the species living in the region.

**KEYWORDS:** Envenomation, snake venom, pulmonary embolism, antivenom immunotherapy.

### INTRODUCTION

Snake bites pose a serious public health problem around the world, with around 5 million people being killed, 48% of them envenomed and over 94,000 deaths a year.<sup>[1]</sup> In Morocco, the number of cases recorded at the anti-poison center and pharmaco-vigilance center of Morocco between 1980 and 2008 was 1761 snake bites, 70% of these cases were in rural areas, the mortality rate was 7.2% per year.<sup>[2]</sup> The only treatment for envenomation is the parenteral administration of antivenom sera of animal origin. The availability of these products is very limited and the difficulty of access to care in rural areas remains a major problem for this population.

### CASE REPORT

A 48-year-old patient from the Esmara region of southern Morocco was received at the emergency department of the 3rd Military Hospital, Laayoune 6 hours after being bit by a viper at the left index finger (estimated bite time: 22h10).

At admission, the patient was afebrile, conscious, the forearm was edematous and painful, and his blood pressure was 120/70 mmHg. Graduation in grade 2 indicated the type of the immunotherapy which rapidly allowed administering 20 ml of FAVAFrique<sup>®</sup> serum in 20 min. The hematologic assessment made at admission revealed the following results: 70% PR, 30 second APTT, thrombocytopenia (70,000 platelets / mm<sup>3</sup>), 12.6 g / dl hemoglobin. On day 2, PR was 43%, APTT was 33

seconds, and platelets were 60,000 / mm<sup>3</sup> and hemoglobin 15.4 g / dl. The treatment consisted of hydration, analgesic treatment (paracetamol IV infusion 1g / 8h and nefopam 20mg / 8h for 4 days), antibiotic therapy (amoxicillin + clavulanic acid inj 1g / 6h), an anti H2 (ranitidine inj 50mg / 8h ) for 4 days.

On the 10<sup>th</sup> day, the patient was in a respiratory distress chart, a polypnea at 25c / min, a tachycardia at 128 beats / min, lower limbs examination was normal, thoracic CT scan revealed pulmonary embolism. The treatment consisted of an antithrombotic (enoxaparin sodium 0.6 ml / 12h for 4 days and acenocoumarol 4mg / d), a platelet anti-aggregating agent (DL-Lysine acetylsalicylate 250mg / day) for 4 days, an analgesic treatment (nefopam 20 mg / 8h), and antibiotic therapy (ceftriaxone 2g / 12h for 10 days and gentamicin 160mg / day for 7 days). Six sessions of right pleural physiotherapy have been programmed. The evolution was favorable and the patient was put on acenocoumarol at a rate of 2 mg / day.

### DISCUSSION

The evaluation of the envenomation severity was made using the clinical grade.<sup>[3]</sup> Viperin syndrome was grade 2 associating local pain, extensive edema and hemostasis disorders. In Morocco, two families of snakes are involved: Seven species of the viperidae family that are found throughout the country (*Daboia mauritanica*, *Bis arietans*, *Cerastes cerastes*, *Cerastes vipera*, *Echis leucogaster*, *Vipera latastei* and *Vipera monticola*);

whereas the family of Elapidae is represented by a single species *Naja haje*.<sup>[4]</sup> The snake in question, described by our patient, is a *Cerastes cerastes* "horned viper"; it has a complex venomous apparatus with canaliculated solenoglyphic hooks.

The biochemical structure of the venom secreted by the venomous gland of vipers is variable; it is composed of several enzymes, toxins, and the proportion of different proteins depends on the geographical sub-population.<sup>[5]</sup> These proteins are generally nucleotidases, disintegrins, phospholipases A2, metalloproteinases, type-C lectins or serine proteinases. They act on platelets, plasma coagulation and on fibrinolysis.<sup>[6]</sup> More than 30% of the composition of the venoms is constituted by the metalloproteinases<sup>[7]</sup>; they are responsible for edema and haemorrhages.<sup>[8]</sup> Their function is to degrade the proteins of the extracellular matrix, and they activate certain factors of the coagulation, in particular FX and FII, thus causing systemic haemorrhages.<sup>[9]</sup> Other enzymes such as cerastocytin result in platelet activation responsible for thrombocytopenia<sup>[10]</sup>, a nanomolar concentration of isolated cerastocytin can induce platelet aggregation.<sup>[11]</sup> The mechanism to activate platelet is similar to that of thrombin.<sup>[12]</sup> The systemic complications are therefore explained by the richness of venom procoagulant enzymes that primarily target the hemostatic process by excessive release of tissue factors causing disseminated intravascular coagulation that could explain the occurrence of pulmonary embolism. This complication has already been reported in the literature for the species *Crotalus scutulatus*<sup>[13]</sup> native to Central America, *Bothrops lanceolatus*<sup>[14]</sup> endemic to Martinique and a triangular-headed viper in Morocco.<sup>[15]</sup> Makis *et al.* described the occurrence of pulmonary embolism following a viper bite. However, the patient was treated for a form of congenital anemia (Diamond-Blackfan's Anemia)<sup>[16]</sup>

Antivenom immunotherapy remains the only specific treatment for severe ophidian envenomation. The antivenom that was available in Morocco at this time was FAVAFrique<sup>®</sup>. Its production was abandoned by the manufacturer Sanofi Pasteur in 2014. It is a serum that has a neutralizing activity of the venom of certain species found in Morocco namely: *Bitis gabonica*, *Bitis arietans*, *Echis leucogaster*, *Naja haje*. There is no information regarding its ability to neutralize the main toxic activities induced by the venom of *Cerastes*, the snake involved in the poisoning of our case. The preparation of an appropriate antivenom must therefore be based on the selection of the venoms used for immunization in order to obtain appropriate antibodies against the venom of the species present in this region. Today, we have another serum, Inoserp<sup>®</sup> MENA (MIDDLE EAST AND NORTH AFRICA) manufactured by Inosan Biopharma; a one that is more adapted to the most venomous species in Morocco: *Bitis arietans*, *Cerastes cerastes*, *Cerastes vipera*, *Echis leucogaster*, *Maprovipera mauritanica*, *Macrovipera deserti*, *Naja haje* and *Vipera latastei*.

According to a recent study in Benin and Guinea, involving a total of 209 patients treated with Inoserp<sup>®</sup>, it has been shown to be effective against severe envenomations in the two epidemiological contexts explored.<sup>[17]</sup>

## CONCLUSION

An Ophidian envenomation is an absolute emergency. Complications in pulmonary embolism are rare. Antivenom immunotherapy is the key to care and to improve the efficacy of antivenom serum and to reduce acquisition costs, it is essential to carry out epidemiological studies to determine causal relationships.

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