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CLINICAL CASE REPORT

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Bilateral Pulmonary Embolism Following a Viper Envenomation in France

A Case Report and Review

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Abstract: Complications following snake bites are not common in France. We report the case of a bilateral pulmonary embolism following a viper envenomation in France.

A healthy 72-year-old female presented with a lower limb hematoma following a viper bite. She was admitted at the hospital 2 days later and received low-molecular-weight heparin because of bed rest. Seven days later, she complained of thoracic pain and respiratory failure, and a bilateral pulmonary was diagnosed, without biological sign of neither disseminated intravascular coagulation nor coagulation trouble. Repeated lower limbs Doppler ultrasound were normal.

This case is particularly interesting because it is only the 7th reported case of pulmonary embolism following a snake envenomation; moreover, it happened in France where poisonous snakes are very rare.

Several hypotheses have been made to explain this late localized coagulopathy: an increased level of unstable fibrin produced by thrombin-like glycoproteins from the venom is one of them.

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Abbreviations: aPTT = activated partial thromboplastin time, CPK = creatine phosphokinase, DIC = disseminated intravascular coagulation, INR = international normalized ratio, US = ultrasound.

INTRODUCTION

If viper bites are well known in France with recent epidemiological studies[1–3] and official protocols for the treatement,[4] pulmonary embolism is an exceptional complication of human envenomations induced by European vipers.

We report the interesting case of a bilateral pulmonary embolism following a viper bite in French Western Coast.

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CASE

A 72-year-old female was admitted to the emergency department with a swollen leg, after a snake bite on her right foot while walking in the countryside, on the French western coast. The scar with 2 points confirmed it was the fang marks of a viper.

The leg swill immediately and she came to the Emergency Department 48 hours after, because of an extensive hematoma on her calf and thigh. She had no other signs of hemorrhage, no fever. Hemodynamic and respiratory parameters were normal. She had no prior significant medical and gynecological troubles, and no history of neoplasia or thrombosis. She was not taking any medication nor hormonal replacement therapy. Tourniquet to the lower limb was never used on this patient before hospitalization.

She did not receive antivenom drug (Viperfav). Complete bilateral Doppler powered ultrasound (US) at admission did not show any lower limbs thrombosis. It was performed from vena cava to distal tibial veins. Blood tests showed no disseminated intravascular coagulation (DIC) (Table 1); she had no clinical or biological signs of rhabdomyolysis or renal failure. She had no clinical sign of compartment syndrome. She received daily preventive low-molecular-weight heparin injections (enoxaparin 4000 IU/day) and lower limb compression device was prescribed.

Seven days after admission, the hematoma started to heal although she presented acute thoracic pain and dyspnea; computed tomography angiogram showed a bilateral pulmonary embolism. Blood test (troponin and coagulation factors) and second complete bilateral lower limbs Doppler US were still normal.

A complete examination and a computed tomography scan eliminated other causes of thrombosis.

She healed rapidly with low-molecular-weight heparin (enoxaparin with a weight-related dosage of 12,000 IU/day) and oxygen therapy (2–3 L/min).

Then she received warfarin and compression stockings for 6 months.

During the 18-month follow-up, she did not present any other hemorrhagic or thrombotic episode. At the end of follow-up, lower limb Doppler US, coagulation blood tests, and pulmonary function were strictly normal. She came back to normal life activities.

Ethical approval was not necessary because all data were collected anonymously, and the patient gave her consent for publication.

RESULTS AND DISCUSSION

Usually, snake envenomations lead to pain, swelling, and moderate hemorrhagic symptoms. In many countries (in Africa, Australia, and South America), snakes can cause death because of neurotoxicity, rhabdomyolysis, or severe coagulopathy causing necrosis or disseminated hemorrhage.

TABLE 1. Initial Biological Findings of Our Patient

Blood Test	Value	Normal Range
Platelet counts	195×10^9	$150–400 \times 10^9$
Prothrombin time	99%	70–120
INR	1.1	—
aPTT	0.72	0.80–1.20
Fibrinogen	4.4	2.0–4.0
Serum creatinine	70 μmol/L	44–80
CPK	1.41 μKat/L	0–2.85

aPTT = activated partial thromboplastin time, CPK = creatine phosphokinase, INR = international normalized ratio.

Several species (Viperidae, Crotalidae, Elapidae, and Colubridae) can also be responsible for haemostatic troubles.[5]

Toxicity Due to the ''Old World'' Vipers on Coagulation (Europe and North Africa)

In French western coast only 2 species of Viper can be seen: *Vipera aspis,* which is more common and *Vipera berus*. Venom from Viperidae has an effect on coagulation, that is why hemorrhagic complications are common and heparin treatment is not recommended during the acute phase of envenomation. In contrast, thromboembolic complications are very rare but can be seen during the later phase of envenomation. To our knowledge, only 4 others cases of pulmonary embolism following viper envenomation have been described so far.[6–8]

Three happened in Morocco, caused by different Moroccan vipers.[6,7] In these cases,[7] pulmonary embolism also occurred exactly 1 week after the bite, without associated phlebitis and after a previous subcutaneous hematoma. However, DIC syndrome was described in all 3 cases, with decreased fibrinogen and elevated activated partial thromboplastin time (aPTT) ratio.

One more envenomation case was caused by Greek viper on a child who suffered from Diamond–Blackfan anemia.[8] This disease is characterized by a congenital erythroid aplasia but usually no coagulopathy symptoms.

Toxicity Due to Other Snakes (America and Australia)

Other snake species can be responsible for thrombosis symptoms. We found out 2 other cases in the literature: the first one occurred in Martinique[9] (French West Indies) was because of *Bothrops lanceolatus,* whose venom is responsible for acute thromboembolic complications in 30% cases. In this case, pulmonary embolism happened a few hours after the bite, suggesting a different way of hypercoagulation activation.

The second one[10] was because of *Crotalus scutulatus,* an American snake. In this case, Baghat et al described an interesting case of DIC syndrome with decreased levels of fibrinogen.

Hypothesis

Several hypotheses have been made to explain this late coagulopathy causing localized thromboembolism after snake bites.[10,11]

First, hypercoagulability could be caused by an increased systemic inflammation starting a few days after the bite, biologically showed by increased prothrombotic factors (fibrinogen and thrombocytosis). All published cases of pulmonary embolism following envenomation had no associated lower limb thrombosis, which suppose a complex localized hypercoagulability. It is also important to note that thrombosis usually occurs at some distance from the site of bites.

Other hypotheses are more complex: venoms contain molecules directed against several targets of a coagulation pathway. For example, thrombin-like protease with initial fibrinolytic activity could cleave fibrinopeptide A or B from fibrinogen and activate coagulation factors, resulting in a cross-linked fibrin clot. This could create a ''DIC-like syndrome,'' without real biologic DIC: coagulation factors, D-dimer levels, and antithrombin 3 are usually normal. A ''localized coagulopathy'' appears because of increased levels of unstable fibrin produced by thrombin-like glycoproteins from the venom.

In conclusion, we reported an extremely rare case of envenomation following viper bite in France, responsible for a late bilateral pulmonary embolism. Our case is atypical because the patient had normal levels of fibrinogen, aPTT, INR, and platelet counts, whereas in Chani cases[7] and Baghat case[10] patients had DIC-like syndrome with low levels of fibrinogen. However, delay between the bite and happening of pulmonary embolism was similar between our case and all described cases.

So far, heparin is not recommended in the acute phase of envenomation because of initial hypocoagulability, but could be useful once hemorrhagic symptoms improve.

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