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.

INTRODUCTION

I f viper bites are well known in France with recent epidemiological studies1–3 and official protocols for the treatment,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.

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 tribial 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 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.

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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 cases7 and Baghat case10 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.

REFERENCES
1. De Haro L, Glaizal M, Tichadou L, et al. M. Asp Viper (Vipera aspis) envenomation: experience of the Marseille Poison Centre from 1996 to 2008. Toxins (Basel). 2009;1:100–112.
2. Boels D, Hamel JF, Deguigne MB, et al. European viper envenomings: assessment of ViperfaTM and other symptomatic treatments. Clin Toxicol (Phila). 2012;50:189–196.
3. Jollivet V, Hamel JF, de Haro L, et al. European viper envenomation recorded by French poison control centers: a clinical assessment and management study. Toxicon. 2015;108:97–103.
4. De Haro L. Management of snakebites in France. Toxicicon. 2012;60:712–718.
5. Mion G, Olive F, Hernandez E, et al. Action of venoms on blood coagulation and diagnosis of bleeding. Bull Soc Pathol Exot. 2002;95:132–138.
6. Chani M, Abouzahir A, Larréché S, et al. Pulmonary embolism in the context of severe envenomation by a Moroccan viper. Bull Société Pathol Exot. 2012;105:162–165.
7. Chani M, L’assimi H, Abouzahir A, et al. À propos de trois observations d’envenimations vipériennes graves au Maroc. Ann Fr Anesth Réanimation avr. 2008;27:330–334.
8. Makis A, Kattamis A, Grammeniatis V, et al. Pulmonary embolism after snake bite in a child with Diamond-Blackfan anemia. J Pediatr Hematol Oncol. 2011;33:68–70.
9. Estrade G, Garnier D, Bernasconi F, et al. Pulmonary embolism and disseminated intravascular coagulation after bitten by a Bothrops lanceolatus snake. À propos d’un cas. Arch Mal Coeur. 1989;92:1903–1905.

Severe hypotheses have been made to explain this late coagulopathy causing localized thromboembolism after snake bites10,11.
10. Bhagat R, Sharma K, Sarode R, et al. Delayed massive pulmonary thromboembolic phenomenon following envenomation by Mojave rattlesnake (*Crotalus scutulatus*). *Thromb Haemost avr.* 2010;104:186–188.

11. Thomas L, Tyburn B, Bucher B, et al. Prevention of thromboses in human patients with *Bothrops lanceolatus* envenoming in Martinique: failure of anticoagulants and efficacy of a monospecific antivenom. Research Group on Snake Bites in Martinique. *Am J Trop Med Hyg mari.* 1995;52:419–426.