LETTER TO EDITOR

LETHAL CASE OF VIPERA BERSUS BITE

NICHOLAS G KOUNIS, IOANNA KONIARI, GEORGE HAHALIS

Department of Cardiology, University of Patras Medical School, Patras, Greece

To the Editor,

Snake bites constitute environmental hazards, particularly in rural areas, causing significant morbidity and mortality that need meticulous approach and careful prevention and treatment. While snake bites are responsible for as many as 94,000 deaths worldwide every year [1], in underdeveloped countries such as in Sub-Saharan Africa, it is estimated that the annual deaths are over 7,300 [2]. In Europe, snake bites are rare but can cause both local and/or systemic symptoms with occasionally fatal complications due to cardiovascular, hemostatic and nervous system involvement [3].

In the very important report published in *Clujul Medical* [4], a 56-year-old male patient, weighing 90 kg, was found mydriatic with warm and wet skin, oral cyanosis, shortness of breath and two bitten lesions on his right thigh suggesting a snake bite. Despite intubation, volume expansion with crystalloids, Ringer and gelofusine, antiallergic treatment with nor-adrenaline, dexamethasone, antihistamines and Zagreb viper antivenom serum administration in the emergency and intensive care unit he finally succumbed from multi-organ failure. Purplish petechia with vesicles had appeared on his thorax and abdomen. Postmortem examination revealed necrosis in several organs.

Unfortunately, electrocardiogram was not given and on autopsy the coronary arteries were not examined for presence or absence of plaque formation and histology was not performed for presence of eosinophils and/or mast cells. While signs of pre-existing myocardial ischemia were not described, myocardial fibrosis with epicardial and interstitial hemorrhages were present in the heart.

This report, therefore, raises important questions concerning the patho-physiology and mechanism of death as well as laboratory and histological procedures necessary to elucidate the cause of death and especially the manner of death. This could enable physicians to reach to the correct diagnosis and provide timely prediction, prevention and treatment.

Manuscript received: 21.10.2016
Accepted: 31.01.2017
Address for correspondence: ngkounis@otenet.gr

Pathophysiology and mechanism of snake bite-induced sudden death

Snake venom contains a plethora of proteins with enzymatic, toxic and allergic activity. These include peptide hydrolases, proteolytic enzymes, phospholipase A2, phosphodiesterase, metalloproteases, cysteine-rich secretory proteins and L-amino acid oxidase. Their action facilitates the release of endogenous histamine, bradykinin, prostaglandins and serotonin. Neuromuscular toxicity, acute kidney injury, venom consumption coagulopathy and inhibition of platelet aggregation and agglutination are the results of venomus snake bites. Although, the most common symptoms of snake biting are local swelling, local necrosis, hemorrhage, abdominal pain, vomiting, diarrhea, hypotension, or edema [5], anaphylactic reactions including urticaria, asthma, angioedema and cardiac anaphylaxis are sometimes observed. Anaphylactic reactions would be expected to occur predominately in individuals with previous expose to snake venom. Indeed, in a report of 10 patients who were bitten by snakes, and developed systemic snake bite reactions suggestive of an allergic reaction, 7 had both positive skin tests and IgE antibodies to snake venoms [6].

The authors of this report correctly anticipated anaphylactic reaction and administered nor-adrenaline, dexamethasone and antihistamines.

Snake bites and Kounis allergy-associated acute coronary syndrome

Myocardial infarction following snake envenomation can be the result of several mechanisms including extensive myocardial necrosis from toxic myocarditis, focal myocardial hemorrhage, fibrin deposition inside the coronary arteries, toxic vasculitis, coagulation abnormalities, and vasoconstricting substances such as hemorrhagins, endothelins or sarafotoxins [7]. On the other hand, Kounis syndrome combines allergic reactions with acute coronary syndromes including coronary spasm (type I), acute coronary thrombosis (type II) and stents thrombosis (type III) and is the result of action of inflammatory mediators such as histamine tryptase and arachidonic acid products released from mast cells and other interacting and interrelated inflammatory cells [8]. Severe fatal coronary artery spasm [9], fatal acute myocardial infarction [10], and stent thrombosis [11] following snake bites, have been reported on some occasions.

Despite that the cause of myocardial infarction following snake bites may involve more than one mechanism, the Kounis-like syndrome reaction leading to death is one of the causes that could not be excluded in the described case.

Coronary artery histology

The authors of this report wisely performed histological examination of epidermal, dermal, lung, heart, liver and larynx sections for eosinophils and other inflammatory cell infiltration that was proved to be negative. Since the heart and especially the coronary arteries are

regarded as main organs and primary target of anaphylaxis [12] serving as a primary door through which life crosses to death, these organs should be scrutinized histologically in any postmortem examination.

Therefore, in order to diagnose or exclude anaphylactic death, the myocardium and especially the coronary arteries that are usually infiltrated by inflammatory cells such as mast cells and eosinophils should be always examined.

Physicians and pathologists should have in mind all above pathologies in cases of fatal snake bite events and, when pathologic examination is regarded necessary, they should always look for myocardial and especially coronary artery infiltration by inflammatory cells such as mast cells and eosinophils. This, together with postmortem serum tryptase estimation, would help in elucidating the cause of sudden death and the manner of death. Furthermore, it will enable practicing physicians to apply predicting, preventing and appropriate therapeutic measures in cases of snake envenomation.

References

1. Pałgan K, Kuźmiński A, Janik A, Gotz-Żbikowska M, Bartuzi Z. Snake (Vipera berus) bite: The cause of severe anaphylactic shock and hepatocellular injury. Int J Immunopathol Pharmacol. 2015;28:119-121.

2. Chippaux JP. Estimate of the burden of snakebites in sub-Saharan Africa: a meta-analytic approach. Toxicon. 2011;57:586–599.

3. Plate A, Kupferschmidt H, Schneemann M. Bites of venomous snakes in Switzerland. Praxis (Bern 1994). 2016;105:679-685 (article in German).

4. Tranca S, Cocis M, Antal O. Lethal case of Vipera bersus bite. Clujul Med. 2016;89:435-437.

5. Frangides CY, Koulouras V, Kouni SN, Tzortzatos GV, Nikolaou A, Pneumaticos J, et al. Snake venom poisoning in Greece. Experiences with 147 cases. Eur J Intern Med. 2006;17:24-27.

6. Reimers AR, Weber M, Müller UR. Are anaphylactic reactions to snake bites immunoglobulin E-mediated? Clin Exp Allergy. 2000;30:276-282.

7. Saadeh AM. Case report: Acute myocardial infarction complicating a viper bite. Am J Trop Med Hyg. 2001; 64:280-282.

8. Kounis NG. Kounis syndrome: an update on epidemiology, pathogenesis, diagnosis and therapeutic management. Clin Chem Lab Med. 2016;54:1545-1559.

9. Abd-Elsalam MA. Bosentan, a selective and more potent antagonist for Atractaspis envenomation than the specific antivenom. Toxicon. 2011;57:861-870.

10. Silva A, Pilapitiya S, Siribaddana S. Acute myocardial infarction following a possible direct intravenous bite of Russell's viper (Daboia russelli). BMC Res Notes. 2012 Sept 12;5:500. doi: 10.1186/1756-0500-5-500.

11. Satish R, Kanchan R, Yashawant R, Ashish D, Kedar R. Acute MI in a stented patient following snake bite-possibility of stent thrombosis - a case report. Indian Heart J. 2013;65:327-330.

12. Kounis NG, Kounis GN, Soufras GD, Lianas D, Patsouras N. Postmortem diagnosis of drug-induced anaphylactic death: Kounis syndrome and hypersensitivity myocarditis are the likely culprit in death of severe anaphylactic reactions. J Forensic Leg Med. 2016;40:40-41.