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**CASE REPORT****A Patient with Severe Bradycardia Five Years After Copperhead Snake Bite**Farshid Etaee<sup>1</sup>, Aaron B. Hesselson<sup>2</sup><sup>1</sup> Cardiology Department, University of Texas Southwestern Medical Center, Dallas, Texas, USA<sup>2</sup> Division of Cardiovascular Medicine, University of Kentucky, Lexington, Kentucky, USA\* **Corresponding Author:** Aaron B. Hesselson, E-mail: [aaron.hesselson@uky.edu](mailto:aaron.hesselson@uky.edu)

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**ABSTRACT****Introduction:** Copperhead (*Agkistrodon contortrix*) snakes are responsible for approximately 40% of all pit viper envenomations in the US.**Case presentation:** : A 14-year-old girl was bitten by a copperhead snake bite. Electrocardiogram taken approximately one hour after envenomation showed sinus rhythm with no acute ST or T wave changes. She was not administered anti-venom but was monitored, treated with antibiotics and discharged without any significant complications after 2 days time. Approximately 5 years after the incident, she began having issues of refractory constipation. Subsequently, she suffered from numerous episodes of recumbent and ambulatory syncope outside of any acute gastrointestinal distress and occurring without warning. A dual-chamber pacemaker (Medtronic™), programmed for “rate-drop” response, was inserted in the patient.**Conclusion:** Delayed sequelae from a copperhead snakebite appears to be possible given our patient’s presentation. However, the mechanism of delayed autonomic dysfunction and/or possible direct cardiac effect remains unclear.

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**INTRODUCTION**

Snakebite is a neglected public health problem. Copperhead (*Agkistrodon contortrix*) snakes are responsible for approximately 40% of all pit viper envenomations in the United States [1]. In addition, over 14,000 copperhead bites were reported to different poison centers in the United States from 1983 to 2008, and 1809 cases in 2014. Delayed complications after snake bites rarely involve the central nervous system such as delayed cerebellar ataxia, disseminated encephalomyelitis, fatal progressive neuropathy [2], and delayed hypopituitarism [3]. Moreover, cardiac manifestations are uncommon in all snake bite victims as compared to the common acute systemic presentations of renal toxicity, coagulopathy, or neurotoxicity [4]. Herein, we report a rare case of severe bradycardia five years after copperhead snake bite.

**CASE PRESENTATION**

A 14-year-old girl experienced a snake bite on the left-hand 4th digit, which prompted admission to an outside facility followed by subsequent transfer 3 days later to the Universi-

ty of Kentucky Medical Center. On presentation, the patient was fully conscious and alert, complained of pain localized to the extremity, and denied having chest pain, palpitations, dizziness, or dyspnea, with no pallor or jaundice. In addition, no murmurs, gallops, or rubs were heard. The physical examination, including vital signs (Blood Pressure=110/65, Heart Rate=80, Respiratory Rate=14, and temperature=98 degrees Fahrenheit), revealed no abnormalities, save for the hand wound. The patient’s admission electrocardiogram (ECG) taken approximately one hour after envenomation showed her to be in sinus rhythm with no acute ST or T wave changes. Laboratory tests, including complete blood count (white blood cell (WBC)=6200, Hemoglobin=12.3, Platelets=378,000), serum electrolytes (Sodium=140, Potassium=4.3), hepatic and renal function tests (Aspartate Aminotransferase=32, Alanine Aminotransferase=36, Blood urea nitrogen=10, Creatinine=0.9), coagulation profile, and toxicology screen were unremarkable. The urinalysis showed no proteinuria. The snake had been killed and brought into the hospital for identification purposes. It was subsequently identified as a copperhead snake. She was not given anti-venom but was monitored, treated

with antibiotics and discharged without any significant complications after 2 days time. After the snake bite, for almost five years she did not have any issues.

Approximately 5 years after the incident, she gradually began having issues of refractory constipation although she consumed a high fiber diet and led an active lifestyle. For treatment, she was provided a hand-held stimulator to apply to and relax the rectal sphincter. Subsequently, she also had numerous episodes of recumbent and ambulatory syncope outside of any acute GI distress and occurring without warning. The patient denied any childhood or familial history of syncope and autonomic dysregulation. She also denied significant caffeine intake or menorrhagia. An electrophysiologic evaluation, which included a tilt-table study, duplicated her clinical symptoms and was positive for a generous cardio-inhibitory response of asystole of 20 seconds duration and negative for a postural orthostatic tachycardia response. Neurology consultation concurred with the electrophysiologist's diagnosis of cardio-inhibitory neurocardiogenic reflex and gastrointestinal autonomic dysfunction. Despite aggressive fluid/salt intake, midodrine, fludrocortisone and serotonin re-uptake inhibition syncopal episodes persisted. The "rate-drop" response was programmed into a dual-chamber pacemaker (Medtronic™) that was inserted into the patient. Medications were continued. Syncopal episodes ceased with < 256 episodes of activated rate drop response noted during the initial years of follow-up. Afterwards, atrial pacing support was also added due to complaints of fatigue with persistent heart rates in the 50 beat per minute range. Subsequent rheumatologic work-up was non-revealing.

At the age of 25 years, she began experiencing headaches in the setting of systolic hypertension as high as 170 mmHg. Midodrine and florinef were discontinued with blood pressure resolution and without provoking any hypotensive episodes. Between the ages of 25 and 29 years, frequent visits to the clinic were required as she would have periods of hypotension requiring re-insitution of midodrine for 6-12 months at a time, alternating with periods of brief hypertension with sinus tachycardia requiring initiation of a beta blocker and discontinuation of the alpha agonist. Pacemaker function remained normal throughout with the rate drop episodes being < 256 at each visit and the atrial pacing burden being < 34%.

Additionally, she underwent a laparoscopic total colectomy and ileoanal anastomosis with diverting loop ileostomy at the age of 26 years and reversal 2 years later. At age 29 years, she underwent uncomplicated laparoscopic creation of an end ileostomy with Hartman's pouch due to continuing GI difficulties. Her pacemaker reached elective replacement later that same year, and it was successfully performed without complication.

## DISCUSSION

The acute clinical effects of snakebites vary from mild local reactions to severe, life-threatening systemic responses depending on the species and size of the snake; the location of the bite; the amount of venom inoculated; and the age, weight, and well-being of the patient. Children are more likely to experience significant morbidity and mortality because they receive a larger envenomation relative to body size [5]. Snake venom has a very complex, heterogeneous composition, containing enzymes, biogenic amines, lethal peptides, nonenzymatic proteins, carbohydrates, metals, lipids, free amino acids and direct hemolytic factors [6].

Copperhead envenomation is estimated to be less injurious compared to other Viperidae snakes. However, bites from copperhead snakes can have toxic effects, including severe pain, local tissue damage and, infrequently, coagulopathy, rhabdomyolysis, neurotoxicity, and shock. Treatment is usually supportive care and pain control; nevertheless, Crotalinae ovine immune Fab (FabAV), such as CroFab®, may be used for moderate to severe envenomation or airway compromise from local tissue swelling [7].

Acute autonomic dysfunction (AD) can occur from snake bites and manifest as unexplained irregularities in heart rates (tachycardia or bradycardia), hypertension or hypotension, unexplained sweating, salivation, vomiting, lacrimation, pupillary abnormalities, abdominal pain, paralytic ileus, and constipation. The AD, mostly, is not a predominant clinical sign and is overshadowed by other neuromuscular severe events. The pathogenesis of AD may involve decreased parasympathetic activity, blockade of presynaptic alpha-2 receptors by neurotoxins, causing sympathetic nervous system overactivity [8]. Our patient did not experience any acute autonomic effects but rather only developed her issues five years after the snakebite. There were no other subsequent medical events or neurologic/rheumatologic diagnoses to suggest another plausible inciting cause. Any episodes of GI distress were separate in time from her syncopal events. No such cases of delayed sequelae of a snake bite have been previously reported.

To the best of our knowledge, insufficient data are available regarding the cardiotoxic consequences of snake bite. Acute myocardial involvement is observed on occasions and may rarely contribute to morbidity and mortality. T wave irregularities are the most common manifestation of myocardial involvement [9]. Other documented ECG irregularities include sinus tachycardia, bradycardia, "tall T-waves", ST abnormalities suggestive of myocardial ischemia and nonspecific T-wave abnormalities [10-11]. In reports nonspecific to acute Crotalidae or Viperidae envenomation, cases of first-degree atrioventricular block (AVB), bundle branch block, atrial arrhythmias, complete heart block, and sinus tachycardia or bradycardia have been reported.

Electrocardiographic irregularities following snake bite may be due to the direct toxic effect of a venom component against the cardiac myocyte function, hypotension or electrolyte disturbances. Some consequences of cardiotoxin resem-

ble those of digitalis effect [6]. It is considered a direct toxic effect of venom on the atrioventricular node. In addition, snake venom alters the electrophysiological properties of the cardiac cell membrane and can have a profound impact on impulse generation and conduction. However, the exact pathophysiology is not known [12].

## CONCLUSION

Delayed sequelae from a copperhead snakebite appears to be possible as seen in our patient's presentation. The mechanism of delayed autonomic dysfunction and/or possible direct cardiac effect, however, remains unclear.

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## AUTHER CONTRIBUTIONS

All authors equally contributed in this study

## CONFLICT OF INTEREST

NONE

## ETHICAL STANDARDS

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## REFERENCES

1. Brys AK, Gandolfi BM, Levinson H, Gerardo CJ. Copperhead envenomation resulting in a rare case of hand compartment syndrome and subsequent fasciotomy. *Plast Reconstr Surg Global Open*. 2015;3:5.
2. Del Brutto OH, Del Brutto VJ. Neurological complications of venomous snake bites: a review. *Acta Neurol Scand*. 2012 Jun 1;125(6):363-72.
3. Shivaprasad C, Aiswarya Y, Sridevi A, Anupam B, Amit G, Rakesh B, Annie PA, Anish K. Delayed hypopituitarism following Russell's viper envenomation: a case series and literature review. *Pituitary*. 2019 Feb 15;22(1):4-12.
4. Silva A, Pilapitiya S, Siribaddana S. Acute Myocardial Infarction following a possible direct intravenous bite of Russell's viper (*Daboia russelli*). *BMC research notes*. 2012;5:500.
5. Juckett G, Hancox JG. Venomous snakebites in the United States: management review and update. *Am Fam Physician*. 2002;65:1367-78.
6. Gupta P, Mahajan N, Gupta R, Gupta P, Chowdhary I, Singh P, et al. Cardiotoxicity Profile of Snake Bite. *JK Journals*. 2013;15:169-173.
7. Zhang XC, Kearney A, Gibbs FJ, Hack JB. Snakebite! *Crotalinae Envenomation of a Man in Rhode Island*. *R I Med J* (2013). 2016;99:25-7.
8. Vinod K, Dutta T. Snakebite, dysautonomia and central nervous system signs. *QJM: An Int J Med*. 2013;106:865-6.
9. Virmani S. Cardiac involvement in snake bite. *Med J Armed Forces India*. 2002;58:156.
10. Nayak K, Jain A, Sharda D, Mishra S. Profile of cardiac complications of snake bite. *IHJ*. 1990;42:185-8.
11. Quan D, Zurcher K. Reversible atrial fibrillation following *Crotalinae* envenomation. *J Venum Anim Toxins*. 2017;23:16.
12. Vikas L, Ahmed R. Varying AV Block Complicating Snake Bite-A Case Report. *JEMDS*. 2014;3:1713-8.