Case Report

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Fatality Following Gila Monster Envenomation

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Abstract

Helodermatid lizard envenomations are rarely reported in the literature, and symptoms are usually mild to moderate, primarily causing pain and localized effects. However, severe toxicity can occur with systemic effects, such as angioedema, hemodynamic instability, and myocardial infarction. Although there are reports of *Heloderma* bites that are reputedly fatal, the data are inconclusive at best. We report a fatal case following a Gila monster (*Heloderma suspectum*) bite likely resulting from cascading events initiated at the time of envenomation. This case reinforces the importance of recognizing that envenomated patients may have complex and occasionally idiosyncratic responses to venom and that treatment should be tailored accordingly.

Keywords

Heloderma suspectum, venomous lizards, venomics, critical care, Kounis syndrome

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Introduction

Helodermatid lizards comprise several species of venomous lizards that are native to the southwestern United States, Mexico, and Central America. They are slow-moving, nonaggressive lizards that infrequently bite humans.[1] Their venom is produced in modified multilobed salivary glands located in the anterolateral aspect of the mandible, and venom flows through ducts associated with each lobe. Movement and pressure during strong jaw closure force venom along the base of grooved teeth, and capillary action carries the venom into the wound.[2] Helodermatid lizards generally have a tenacious bite, and prolonged contact can increase venom delivery.

Although *Heloderma* bites primarily result in local effects and prolonged convalescence, there are reports of severe systemic effects (eg, angioedema, hemodynamic instability, and myocardial infarction), especially from tenacious and deep bites.[3–6] Even with more severe envenomations, most patients recover with minimal long-term sequelae.[7] There are reports of *Heloderma* bites that are reputedly fatal, but the best-referenced case is inconclusive at best.[2,8] We present a case of a fatality associated with *H suspectum* bite.

Case Report

A 34-y-old male developed vomiting and loss of consciousness following a bite on his right thenar eminence by 1 of his 2 pet Gila monsters (*H suspectum*). The bite time was 4 to 5 min. The lizard released its grip only after the patient's partner sprayed it in the face with hand sanitizer. Despite our patient reporting that he was okay, he became progressively less responsive and lost consciousness, prompting his partner to call Emergency Medical Services (EMS) 13 min after the bite.

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Table 1. Laboratory Progression 24 Hours After the Bite.

	Time after the bite (h)							
Selected laboratory tests	Units (reference range)	1	3	6	12	16	20	24
WBC	10^3/μL (3.7–11)	23.2				20.2	23.7	16.7
Hemoglobin	g/dL (13.4–18)	17.6				17.8	14	13
Platelets	10^3/μL (150–400)	387		171		207	175	124
Sodium	mmoL/L (136–145)	140		143		145	151	
Potassium	mmol/L (3.5–5.1)	2.6		3.6		4.9	3.2	
Bicarbonate	mmol/L (20–30)	18		16		17	13	
Creatinine	mg/dL (0.65–1.36)	1.74		1.64		1.96	2.36	
pH	(7.35–7.45)	7.21				7.48	7.26	7.19
PCO_2	mm Hg (35–45)	49				24	28	20
HCO_3	mmol/L (22–26)	20				18	13	8
Lactate	mmol/L (0.4–2)	8.4			5.8	5	13.2	13.4
CK	U/L (39–308)	97						
High-sensitivity troponin	ng/L (≤41)	117	511		26,136		53,167	
PT	s (9.3–11.7)			17.3				
PTT	s (22–34)			>139				
INR	(0.9–1.1)	1.2		1.6				
Fibrinogen	mg/dL (174–425)			52				
D-dimer	mg/L (<0.49)			>30				
AST	U/L (7–37)	23					682	
ALT	U/L (12–78)	59					564	

Note. WBC, white blood cell count; CK, creatine kinase; PT, prothrombin time; PTT, partial thromboplastin time; INR, international normalized ratio; AST, aspartate aminotransferase; ALT, Alanine aminotransferase.

When EMS arrived, the patient was tachycardic, hypotensive, and minimally responsive. EMS personnel suspected anaphylaxis, and epinephrine was administered with no clinical improvement. On arrival to the Emergency Department, 30 min after the bite, the patient's vital signs were a heart rate of 138 beats/min, respiratory rate of 28 breaths/min, blood pressure of 158/102 mm Hg, pulse oximetry of 95% on room air, and temperature of 36°C. Physical examination was remarkable for an ill-appearing male with mottled skin, cool extremities, dilated pupils with roving, unfocused eye movements, tensing and contracting of the bilateral hands, and a bite wound with abrasions to the right hand and dorsal aspect over the base of the thumb.

The patient's medical history included obsessive-compulsive disorder, attention-deficit hyperactivity disorder, and chronic back pain, for which he was prescribed fluoxetine, lisdexamfetamine, and methocarbamol. His substance-use history was notable for alcohol use, infrequent fentanyl use, and previous cocaine and nicotine use. He did not use over-the-counter drugs or supplements. He had a rash associated with penicillin but no known environmental allergies, previous animal bites, or recent travel. There was no known personal or family history of cardiac disease.

Forty minutes after the bite, the patient developed convulsions and was treated with 6 mg lorazepam, 1500 mg fosphenytoin, and 1000 mg levetiracetam. Subsequently, he developed hemodynamic instability and was intubated, sedated with propofol 8 micrograms·kg^{-1}·min^{-1}, started on a norepinephrine infusion at 6 micrograms·min^{-1}, received 2000 mg cefepime, and was admitted to the intensive care unit. One-hour after the bite, laboratory investigations demonstrated respiratory and metabolic acidosis, hyperlactatemia, acute kidney injury, and troponin elevation (Table 1).

Two hours after the bite, an electrocardiogram (ECG) demonstrated sinus tachycardia at 130 beats/min with 2 to 3 mm ST segment elevations in leads II, III, and aVF (Figure 1). A noncontrast head computed tomography study demonstrated no acute findings. Chest x-ray demonstrated appropriate endotracheal tube placement, bibasilar atelectasis, and borderline enlarged heart size. Six hours after the bite, an echocardiogram demonstrated normal left ventricular size with mild concentric hypertrophy and an ejection fraction of 25 to 30%, normal right ventricular size with reduced systolic function, no valvular abnormalities, and a noncollapsible inferior vena cava.

The patient was weaned off norepinephrine 12 h after the bite, when his mean arterial pressure remained >60 mm Hg. Fifteen hours after the bite, cardiac catheterization was performed due to rapidly rising serum troponin concentrations. This showed normal coronary arteries and normal ventricular filling pressures, cardiac output, and cardiac index.

Twenty hours after the bite, the patient again became hypotensive (55/29 mm Hg) and tachycardic (heart rate 140 beats/min). An epinephrine infusion was initiated, followed by administration of diphenhydramine and dexamethasone due to concerns for biphasic anaphylaxis. This clinical change prompted a repeat right-sided cardiac

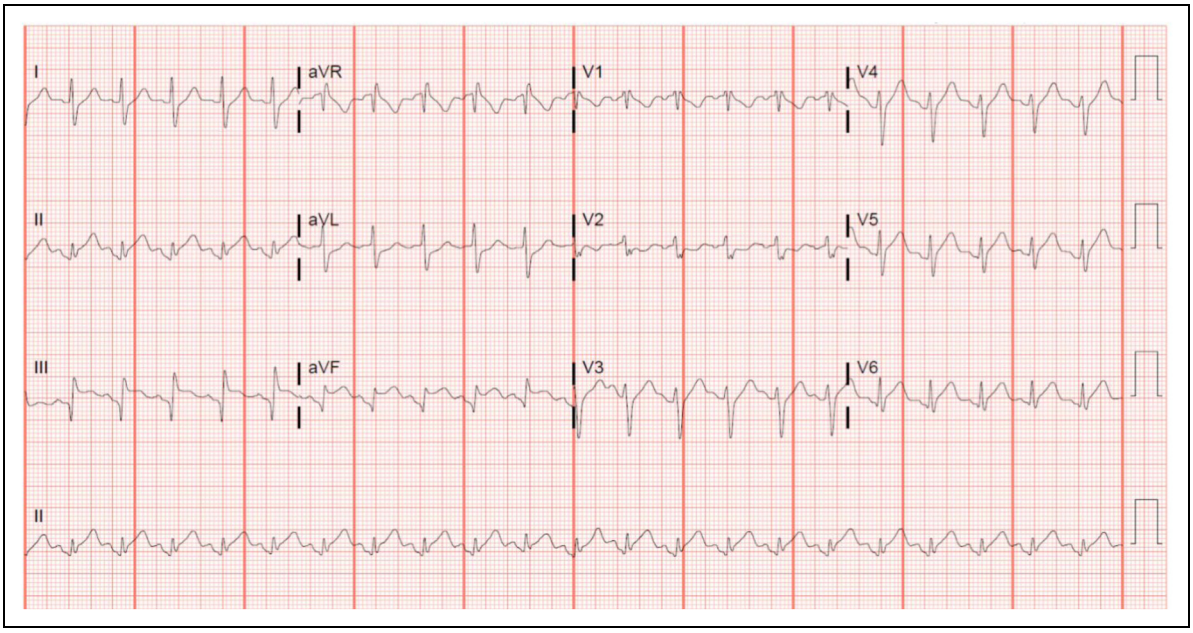

Figure 1. Electrocardiogram demonstrating sinus tachycardia with 2- to 3-mm ST segment elevations in leads II, III, and aVF.

catheterization 22 h after the bite that demonstrated similar right-sided filling pressures as reported earlier. Laboratory findings showed persistent metabolic acidosis, hyperlactatemia, acute kidney injury, troponin elevations, liver injury, and coagulopathy, as demonstrated by rotational thromboelastometry (Table 2).

Due to worsening hemodynamics and the development of central diabetes insipidus, a noncontrast head computed tomography was repeated 26 h after the bite, demonstrating global ischemia, cerebral edema, and midline shift. A magnetic resonance imaging study of the brain performed 39 h after the bite showed acute infarcts involving the left middle cerebral artery territory and right cerebral hemisphere and upper left cerebellum swelling with transtentorial and uncal herniation.

A formal brain death exam was unable to be performed due to hypernatremia and acidemia. Following a clinical consideration of brain death, the patient was transitioned to comfort care per family preference. The patient was deemed not a candidate for organ donation due to limitations in the literature surrounding organ donation after death following envenomation. He was compassionately extubated 83 h after the bite and died 20 min later.

Table 2. Rotational Thromboelastometry Analysis.

Component	Value	Reference range
EXTEM CT clotting time	72 s	43–80 s
EXTEM CFT clot-formation time	139 s	48–127 s
EXTEM alpha angle	63°	65–80°
EXTEM A10 amplitude	44 mm	46–67 mm
EXTEM A20 amplitude	50 mm	50–70 mm
EXTEM MCF maximum clot firmness	50 mm	52–70 mm
EXTEM ML maximum lysis	8%	<15%

Note. EXTEM is a screening test for the (extrinsic) hemostasis system.

Postmortem Findings

An autopsy was performed. Serum toxicology testing via enzyme-linked immunosorbent assay and high-performance liquid chromatography/time of flight mass spectrometry was positive for caffeine, lorazepam, fluoxetine, and norfluoxetine. No testing for ethanol was performed on pre- or postmortem samples.

There was a 2.8×1.9 cm ecchymotic and crusted lesion on the right thenar eminence consistent with a bite wound. Internal examination revealed a moderate dilated cardiomyopathy, a globoid appearance, and no injury to the myocardium. Coronary arteries were normal. There were histologic changes consistent with severe macro- and microvesicular steatosis in the liver. There were minimal to mild chronic inflammatory changes in the portal tracts. The brain showed evidence of severe cerebral edema. The epiglottis and larynx showed scattered and increased submucosal positive mast cell tryptase-staining cells.

Venom Analysis

The offending *H suspectum* was obtained from authorities for venom extraction and analysis at a venomics lab. The lizard was noted to be unusually defensive, often displaying defensive posturing toward staff who were standing

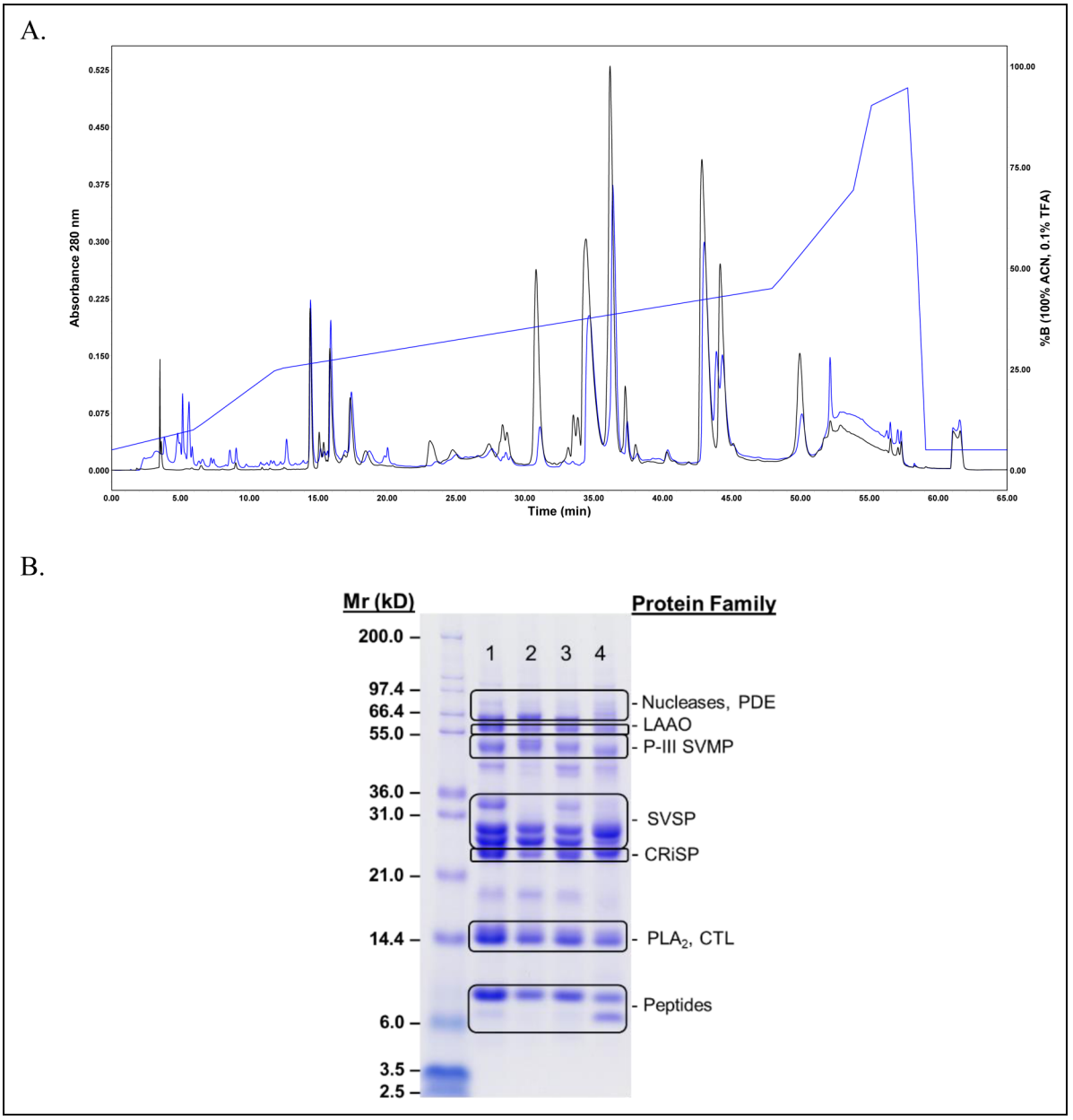

Figure 2. Venom analysis of patient's Gila monster compared with unrelated Gila monsters. A, High-performance liquid chromatography demonstrating similar venom composition of patient's Gila monster (black line) compared with unrelated Gila monster (blue line). B, Sodium dodecyl sulfate–polyacrylamide gel electrophoresis analysis of patient's Gila monster (1) and 3 unrelated Gila monsters (2–4). Note the similarities in all 4 venoms. CRiSP, cysteine-rich secretory protein; CTL, C-type lectin; LAAO, L-amino acid oxidase; M_r, molecular mass; PDE, phosphodiesterase; PLA_2, phospholipase A_2; SVMP, snake venom serine proteinase; SVSP, snake venom serine proteinase.

several yards away. The lizard was extracted over a 4- to 5-min period to replicate the timeframe of this case scenario. Other *H suspectum* specimens in the lab, 1 significantly larger, also were extracted under the same conditions. The lizard responsible for the envenomation produced 55 mg of dry-weight venom; the other lizards produced 5 to 10 mg of dry-weight venom, which is more typical for this species.

Venom analysis was performed, including gel electrophoresis, reversed-phase high-performance liquid chromatography, mass spectrometry, and quantitative enzyme assays. Venom from the responsible lizard was compared with venom from other captive and wild specimens whose venom was available for analysis. The reversed-phase high-performance liquid chromatography and gel electrophoresis analyses are shown in Figure 2.

Overall, there were no truly unique features among the analyzed venoms, including on mass spectrometry.

Discussion

This case describes an exceptionally rare fatality associated with a *H suspectum* envenomation. The exact cause of death in our patient is unclear. Factors such as direct venom effects, coagulopathy, Kounis syndrome, and biphasic anaphylaxis may have contributed to our patient's death.

Direct Venom Effect

H suspectum envenomation in humans has resulted in mild to severe effects, with severe envenomations resulting in angioedema, hemodynamic instability, myocardial infarction, and coagulopathy.[3–6,9]

Helodermatid venom shares similarities with the venoms of other venomous reptiles, containing constituents such as phospholipase A_2, hyaluronidase, and kallikrein- and thrombin-like serine proteases. Specific to *Heloderma* spp, gilatoxin, horridum toxin, and helodermatin all have kallikrein-like effects.[10,11] Kallikrein and kallikrein-like proteases are responsible for the cleavage of kininogen to bradykinin, which then leads to downstream effects of vasodilation and vascular permeability responsible for hypotension, angioedema, pain, and bronchoconstriction. Venom thrombin-like toxins typically produce hypofibrinogenemia, disrupting the final stage of clot production.[12]

Although the venom components of our patient's *H suspectum* were not unique, it was noted to be more defensive than typical specimens. During the extraction, to replicate the time of alleged exposure to the patient, the Gila monster produced 55 mg of dry-weight venom protein in 4 min, ~5 to 10 times the amount of venom typically produced. The potentially large venom load may have contributed to a dose-dependent effect in our patient.

Coagulopathy

Our patient developed a coagulopathy, as evidenced by his laboratory parameters and thromboembolic events. *Heloderma* venom effects on coagulation are poorly understood and are contradictory in the literature, with reports of both anticoagulant and procoagulant effects.[13,14] Furthermore, case reports of *Heloderma* envenomations associated with coagulopathy are rare.[5,9]

Venom-induced consumptive coagulopathy is a well-described phenomenon following snake envenomations. Although it is often likened to disseminated intravascular coagulation, the pathophysiology is distinct.[15] Venom-induced consumptive coagulopathy has not been reported following *Heloderma* envenomations. However, considering the temporal relation between our patient's envenomation and the abnormal coagulation labs shortly after presentation, these abnormalities are likely due to direct venom effect.

Kounis Syndrome

Kounis syndrome is an acute coronary syndrome associated with allergic or anaphylactic reactions, triggered by both IgE- and non-IgE-mediated mast cell and platelet activation. This phenomenon has been described after exposure to venoms and animal proteins (eg, Hymenoptera, *Hypnale* vipers, and antivenom) as well as other nonproteinaceous pharmaceuticals (eg, antibiotics and analgesics).[16]

Although infrequently diagnosed, the presentations of Kounis syndrome are characterized by the development of cardiac symptoms such as chest pain, shortness of breath, nausea, and vomiting, often accompanied by other cardiac presentations, such as laboratory, electrocardiographic, or echocardiographic changes. While the syndrome is further divided into subtypes based on the presence/absence of any plaque or stent, most cases have no underlying cardiovascular disease.[17]

Our patient's ECG demonstrated an ST elevation myocardial infarction, minimal to no risk factors for cardiovascular disease, and cardiac catheterization without evidence of stenosis following exposure to an allergenic compound (ie, *H suspectum* venom), making Kounis syndrome a potential contributor to our patient's presentation. However, this is unlikely to be the sole cause because most patients have a favorable outcome with supportive care.

Biphasic Anaphylaxis

Biphasic anaphylaxis is the recurrence of anaphylactic symptoms following resolution of initial signs and symptoms without re-exposure to the purported allergen. This phenomenon occurs in fewer than 5% of anaphylaxis cases, with the primary risk factor being severely affected patients with multiorgan involvement.[18] The patient was initially treated for potential anaphylaxis by EMS personnel per their protocols. During his hospital course, his recurrence of hypotension was considered by treating physicians to be possible recurrent anaphylaxis. He was subsequently treated with epinephrine, dexamethasone, methylprednisolone, and diphenhydramine. Additionally, his coagulopathy may have been a complication of severe anaphylaxis.[19] Lastly, anaphylaxis has been associated with cerebral infarction and vasospasm, which may have contributed to our patient's cerebral injuries.[20]

Our patient's autopsy demonstrated positive mast cell tryptase staining in his epiglottis and larynx; however, mast cell tryptase staining of the coronary arteries was not reported. Furthermore, serum and postmortem tryptase concentrations were not determined. The positive mast cell

tryptase staining findings are likely representative of a Type I hypersensitivity reaction but must be interpreted with caution because several etiologies, such as multiple intubations, prolonged hypoxia, and other pathophysiologic pathways, are less likely but can yield positive test results.

Limitations

Some of the authors (DM, KM, AL, LY, and NB) served as consulting clinicians by phone via the regional poison center on this case, not as the primary treating clinicians. Clinical information was obtained via phone consultation, interview of the patient's fiancé, and chart review.

Conclusion

Our patient's clinical course and outcome are likely the sum of cascading events initiated at the time of envenomation. When managing envenomated patients, it is critical to recognize that patients may have complex and occasionally idiosyncratic responses to venom and that treatment should be tailored accordingly.

Ethical Considerations

Our institution does not require ethical approval for reporting individual cases.

Consent to Participate

Written informed consent for the case report was provided by next of kin.

Consent for Publication

Written informed consent for publication was provided by next of kin.

Author Contribution(s)

Danae Massengill: Conceptualization; Investigation; Writing – original draft; Writing – review & editing.
Karen Muschler: Conceptualization; Investigation; Writing – original draft; Writing – review & editing.
Andrea Lielkoks: Conceptualization; Investigation; Writing – review & editing.
Cara F. Smith: Investigation; Writing – review & editing.
Anthony J. Saviola: Investigation; Writing – review & editing.
Samuel Kerwin: Investigation; Writing – review & editing.
Farshad Shirazi: Conceptualization; Writing – review & editing.
Stephen P. Mackessy: Conceptualization; Investigation; Writing – original draft; Writing – review & editing.
Nicklaus Brandehoff: Conceptualization; Investigation; Supervision; Writing – original draft; Writing – review & editing.

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Declaration of Conflicting Interest

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References

1. French R, Brooks D, Ruha AM, Shirazi F, Chase P, Boesen K, et al. Gila monster (*Heloderma suspectum*) envenomation: descriptive analysis of calls to United States Poison Centers with focus on Arizona cases. *Clin Toxicol (Phila)*. 2015;53(1):60–70.
2. Bogert CM, Martin Del Campo R. The Gila monster and its allies. The relationships, habits, and behavior of the lizards of the family Helodermatidae. *Bull Am Mus Nat Hist*. 1956;109:1.
3. Piacentine J, Curry SC, Ryan PJ. Life-threatening anaphylaxis following Gila monster bite. *Ann Emerg Med*. 1986;15(8):959–961.
4. Bou-Abboud CF, Kardassakis DG. Acute myocardial infarction following a Gila monster (*Heloderma suspectum cinctum*) bite. *West J Med*. 1988;148(5):577–579.
5. Preston CA. Hypotension, myocardial infarction, and coagulopathy following Gila monster bite. *J Emerg Med*. 1989;7(1):37–40.
6. French RN, Ash J, Brooks DE. Gila monster bite. *Clin Toxicol (Phila)*. 2012;50(2):151–152.
7. Chippaux JP, Amri K. Severe *Heloderma* spp envenomation: a review of the literature. *Clin Toxicol (Phila)*. 2021;59(3):179–184.
8. Grant ML, Henderson LJ. A case of Gila monster poisoning with a summary of some previous accounts. *Proc Iowa Acad Sci*. 1957;64(1):686–697.
9. Amri K, Chippaux JP. Report of a severe *Heloderma suspectum* envenomation. *Clin Toxicol (Phila)*. 2021;59(4):343–346.
10. Utaisincharoen P, Mackessy SP, Miller RA, Tu AT. Complete primary structure and biochemical properties of gilatoxin, a serine protease with kallikrein-like and angiotensin-degrading activities. *J Biol Chem*. 1993;268(29):21975–21983.
11. Sanggaard KW, Dyrlund TF, Thomsen LR, Nielsen TA, Brondum L, Wang T, et al. Characterization of the Gila monster (*Heloderma suspectum suspectum*) venom proteome. *Data Brief*. 2015;3:137–142.
12. Mackessy SP. Thrombin-like enzymes in snake venoms. In: RM Kini, MA McLane, K Clemetson, FS Markland, T Morita, Eds. *Toxins and Hemostasis: From Bench to Bedside*. Springer-Verlag; 2010:519–557.
13. Patterson RA, Lee IS. Effects of *Heloderma suspectum* venom on blood coagulation. *Toxicon*. 1969;7(4):321–324.
14. Dobson J, Chowdhury A, Tai-A-Pin J, van der Ploeg H, Gillett A, Fry BG. The clot thickens: differential

coagulotoxic and cardiotoxic activities of Anguimorpha lizard venoms. *Toxins (Basel)*. 2024;16(6):283.
15. Isbister GK. Snakebite doesn't cause disseminated intravascular coagulation: coagulopathy and thrombotic microangiopathy in snake envenoming. *Semin Thromb Hemost*. 2010;36(4):444–451.
16. Soufras GD, Lianas D, Patsouras N, Tsigkas G, Kounis NG. Kounis syndrome: aspects on pathophysiology and management. *Eur J Intern Med*. 2016;32:e30–e31.
17. Kounis NG. Kounis syndrome: an update on epidemiology, pathogenesis, diagnosis and therapeutic management. *Clin Chem Lab Med*. 2016;54(10):1545–1559.
18. Kraft M, Scherer Hofmeier K, Ruëff F, Pfohler C, Renaudin JM, Bilo MB, et al. Risk factors and characteristics of biphasic anaphylaxis. *J Allergy Clin Immunol Pract*. 2020;8(10): 3388–3395.e6.
19. Nguyen SMT, Rupprecht CP, Haque A, Pattanaik D, Yusin J, Krishnaswamy G. Mechanisms governing anaphylaxis: inflammatory cells, mediators, endothelial gap junctions and beyond. *Int J Mol Sci*. 2021; 22(15):7785.
20. Watanabe T, Yamana H, Ishigami K, Tsutsumi Y, Kato N. Anaphylaxis-associated cerebral infarction: a case report. *Cureus*. 2025;17(3):e80887.