

Case Report

Acute myocardial infarction with no chest pain following a *Trimeresurus stejnegeri* snakebite: a case report

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Abstract: A 74-year-old female was bitten by a *Trimeresurus stejnegeri*, which is an unusual but dangerous type of snakebite. After the snakebite, the patient developed oedema, pain and numbness in the injured limb, and acute myocardial infarction, but no chest pain. The patient received base treatment, including anti-venom serum, statins and wound cleaning. After treatment, the pain in the injured limb disappeared and the swelling decreased. The patient underwent a coronary angiogram the next day, and severe stenosis of the anterior descending branch of the left coronary artery was found. She was given coronary stent implantation. After surgery, she was treated with anti-coagulants, and antiplatelet medication and was discharged from the hospital on the sixth day after the condition improved. This case report of myocardial infarction-related snake envenomation aims to increase the awareness that snakebites may cause AMI and therefore, multidisciplinary management particularly from emergency physicians and cardiologists may be necessary.

Keywords: Acute myocardial infarction, snakebite, *Trimeresurus stejnegeri*

Introduction

Snakebites are common medical emergencies in many parts of the world, especially in rural areas [1]. Every year, about 5.4 million snakebites occur worldwide, which cause up to 2.7 million envenomings, with almost 138,000 deaths and 400,000 cases of sequelae or disability. Snakebite diagnosis is often based on a combination of patient history and a syndromic approach, supported by national guidelines and assays assessment serum biochemistry, coagulopathy (for example by measuring clotting time), and renal function etc. [2]. The high variability in snake venom composition is responsible for the various clinical manifestations, ranging from local tissue damage to potentially life-threatening systemic effects. Intravenous administration of antivenom is the only specific treatment to counteract envenoming. Analgesics, ventilator support, fluid therapy, haemodialysis and antibiotic therapy are also used. Novel recombinant antibody-based therapeutics and new toxin inhibitors are being

explored [3]. For the patients with severe and critical conditions after being bitten a by *Trimeresurus stejnegeri*, treatment with injection of antivenom serum, internal administration and external application of Jidesheng snake tablet, and wound incision and detoxification, early application of low molecular weight heparin sodium anticoagulation and other comprehensive therapy is helpful to improve limb swelling and inflammation, reduce blood transfusion, promote the recovery of coagulation function, and shorten the length of hospitalization [4]. Although a variety of clinical manifestations have been recorded in snakebite victims, acute myocardial infarction (AMI) is rare to see. What's more, there was no report of myocardial infarction caused by a *Trimeresurus stejnegeri*. Thus, patient with AMI and no chest pain following being bitten by a snake was described in this study. Physicians must consider AMI in the differential diagnosis of snakebite. Verbal informed consent was obtained from the patient via telephone for participation in this review.



Figure 1. A *Trimeresurus stejnegeri*.



Figure 2. Two fang marks with swelling of the fourth toe in the left foot.

Case report

A 74-year-old female with no history of cardiac disease was bitten by a snake on the fourth toe in her left foot. She lives in Guangxi Zhuang Nationality Autonomous Region, Southern China. She was bitten at 10:30 p.m. on September 13th, 2021, when she was pacing at home. The patient soon developed oedema, pain, and numbness in the left foot, along with wound bleeding. She tied the proximal end of the injured limb with a cloth strip as first aid treatment, and later she was taken to the emergency department of the hospital by her family, registered at 01:52 a.m. on September 14th. The dead snake, identified as a *Trimeresurus stejnegeri*, was also brought to the hospital (**Figure 1**).

Her initial vital signs at the hospital were recorded as temperature of 36.2°C, pulse of 78 beats/min, respiratory rate of 20 breaths/min, and blood pressure of 155/70 mmHg. Physical examination showed she was in moderate pain and conscious. Examination of the heart, lungs, abdomen and central nervous system revealed no remarkable abnormality. There were two fang marks with swelling and blood crust on the fourth toe in the left foot (**Figure 2**). In the left foot, oedema was noted to extend to 10 cm above the ankle joint. Immediately, the patient received basic initial treatment including injecting anti-venom serum and wound cleaning.

At 03:12 a.m. on September 14th, the patient was examined again, revealing a full blood count with white cell count of 12,170/mm³ (normal, 4000 to 10000/mm³), haemoglobin of 15 g/dL (normal, 11 to 15 g/dL) and platelets of 262,000 mm³ (normal, 100,000 to 300,000 mm³); blood clotting function, including normal prothrombin time/international normalized ratio (PT/INR) and activated partial thromboplastin time (APTT), thrombin time (TT) of 21.4 s (normal, 14 to 21 s), and D-dimer of 0.76 mg/L (normal, <0.55 mg/L). Besides, high-sensitivity troponin of T 325.7 ng/L (normal, <14 ng/L), myoglobin of 95.48 ng/mL (normal, 25 to 58 ng/mL), and creatine kinase isoenzyme of 12.37 ng/mL (normal, <2.88 ng/mL) were also recorded (**Table 1**).

The electrocardiogram (ECG) (**Figure 3**) showed sinus rhythm, occasional atrial premature beats, ST-segment elevation in lead II, III and AVF, and T-wave inversion. A myocardial injury was indicated by examination and ECG results. However, the patient had neither previous history of coronary disease nor typical symptoms of myocardial infarction such as chest pain. Direct damage from the snake venom to the heart was taken into consideration. Therefore, no coronary angiogram was performed, and statins were given for plaque regression.

On September 15th, the symptom of pain in the left lower limb was relieved, and the swelling decreased. There was no chest pain. A recheckup showed an increase in myocardial enzymes. ECG revealed a more elevated ST segment in the inferior leads and an abnormal Q wave. Cardiac ultrasound findings revealed aortic sclerosis, cardiac ejection fraction (EF)

Table 1. Changes in routine blood, myocardial enzyme and blood clotting results during treatment

Test	Day 1	Day 1 (6 H later)	Day 2	Day 4
White cell count (normal, 4,000-10,000/mm ³)	12,170	-	-	7,440
Haemoglobin (normal, 11.0-15.0 g/dL)	15	-	-	12.9
Platelets (normal, 100,000-300,000 mm ³)	262,000	-	-	220,000
Myoglobin (normal, 25.00-58.00 ng/mL)	95.48	93.88	137.40	21.00
Creatine kinase isoenzyme (normal, <2.88 ng/mL)	12.37	34.30	9.63	1.51
High-sensitivity troponin of T (normal, <14.0 ng/L)	325.7	638.1	940.9	335.9
Prothrombin time (normal, 9.8-13.5 s)	11.4	10.9	-	10.5
International normalized ratio (normal, 0.85-1.18)	0.99	0.94	-	0.91
Thrombin time (normal, 14.0-21.0 s)	21.4	20.5	-	21.9
Activated partial thromboplastin time (normal, 21.5-36.5 s)	32.0	28.9	-	30.5
Fibrinogen (normal, 1.80-3.50 g/L)	3.23	3.91	-	3.74
D-dimer (normal, 0-0.55 mg/L)	0.76	1.45	-	0.51

Note: - indicates no data available.

of 62% (normal, >50%). Considering the possibility of AMI, the patient was transferred to the CCU on the same day for further treatment. A coronary angiogram was performed at 22:45 p.m. on the same night. The coronary angiogram (**Figure 4**) showed that the right coronary artery was dominantly distributed, and the circumflex branch was opened to the right coronary artery. There was 80% stenosis of the left anterior descending branch, and 90% stenosis of the first diagonal branch. No abnormality in the right coronary artery or circumflex branch was found. Given the serious lesions of the anterior descending branch of the patient, percutaneous coronary balloon dilatation and coronary stent implantation were performed, with the consent of the patient's family members. After surgery, enoxaparin anticoagulation, aspirin enteric-coated tablets, ticagrelor antiplatelet, statins and other treatments were given.

On September 18th, the ST-segment of ECG II, III and AVF leads returned to normal. On September 19th, the patient was discharged.

Discussion

In China, there are several poisonous snakes fatal to humans, such as *Naja naja*, *Ophiophagus hannah*, *Bungarus fasciatus*, *Bungarus multicinctus*, *Vipera russelli siamensis* (*Daboia russelli siamensis*), *Agkistrodon halys*, *Deinagkistrodon acutus*, *Trimeresurus stejnegeri*, *Trimeresurus mucrosguamatus* and *Calliophis maclellandii* [5]. The diagnosis of snakebite envenoming is commonly based on a combina-

tion of the patient record and a syndromic approach. Specific signs of envenoming in the patient include local signs such as swelling, blistering, and local necrosis. Systemic signs like haemorrhage, incoagulable blood, and hypovolemic shock, are common in viper bites. Neurotoxic signs occur primarily in elapid bites, whilst rhabdomyolysis (muscle damage) in sea snake bites. Based on the changes in the blood of envenomed victims, laboratory diagnosis of snakebite includes the detection of abnormal changes in blood parameters, dramatic fall in the platelet counts, changes in red and white blood cell counts, changes in certain enzyme levels (such as creatine phosphokinase) and specific venom antigens in the victims' blood [6]. In this case, the snakebite displayed typical symptoms of limb oedema, pain and numbness. In addition, laboratory diagnosis revealed abnormal changes in white blood cell counts, TT, and D-dimer.

In China, hemotoxic envenomation is mainly found in *Daboia russelli siamensis*, *Agkistrodon halys*, *Deinagkistrodon acutus*, *Trimeresurus stejnegeri* and *Trimeresurus mucrosguamatus* [5]. Ischemic cardiac and ischemic stroke rarely occur after hemotoxic snakebite. However, myocardial infarction following hemotoxic snakebite has been previously reported in Sri Lanka, whilst acute cerebral infarction following a *Trimeresurus stejnegeri* snakebite has been reported in China [7, 8]. Overall, there are about 10 reports of myocardial infarction and 1 report of cerebral infarction due to hemotoxic snakebites (**Table 2**) [7-17]. However, there are

AMI following a snakebite

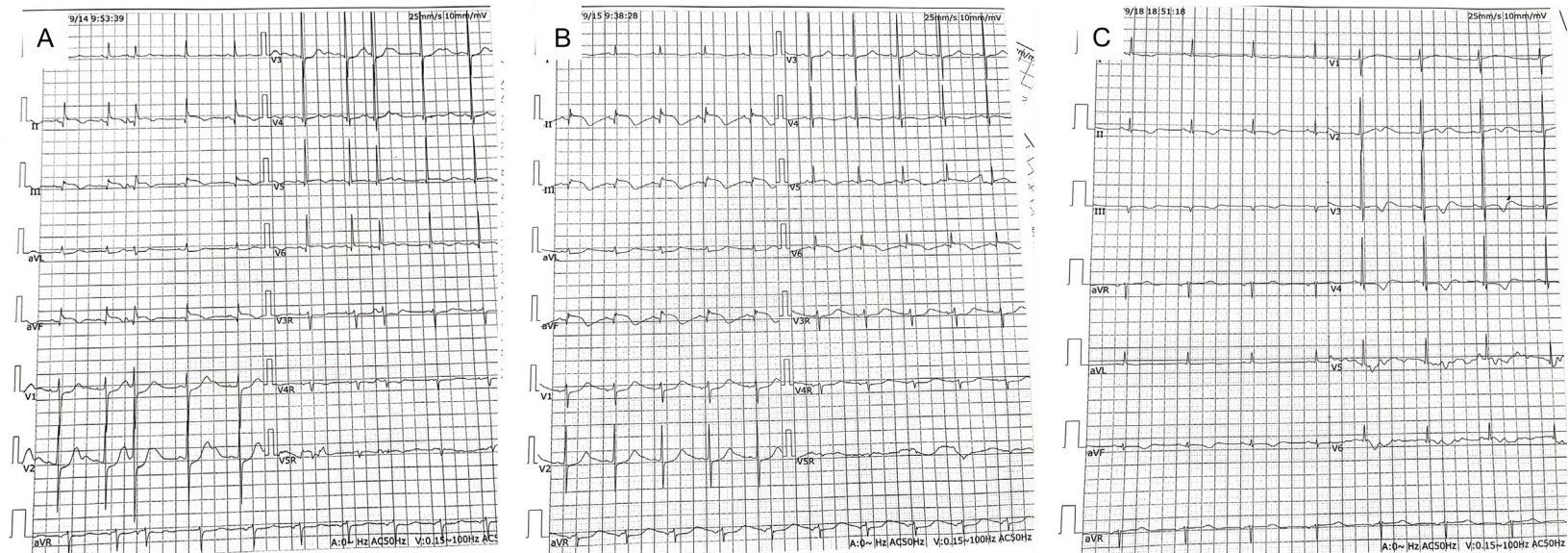


Figure 3. Results from electrocardiogram (ECG). A: Sinus rhythm, occasional atrial premature beats, ST-segment elevation in lead II, III and AVF, and T-wave inversion on day 1; B: Sinus rhythm, ST-segment elevation in lead II, III and AVF, and T-wave inversion on day 2; C: Sinus rhythm, the ST-segment of ECG II, III and AVF leads returned to normal, and T-wave inversion on day 4.

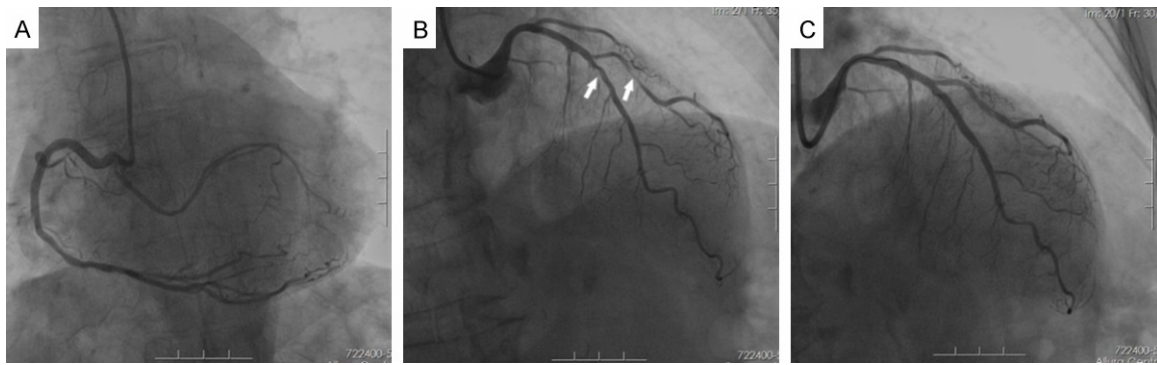


Figure 4. Coronary angiogram. A: Right coronary artery was dominantly distributed, and the circumflex branch was opened to the right coronary artery; B: The left arrow indicated 80% stenosis of left anterior descending branch, and the right arrow indicated 90% stenosis of first diagonal branch; C: Left coronary artery (after stenting).

Table 2. Ischemic cardiac or ischemic stroke following a hemotoxic snakebite

Author	Characteristics	Snake	Ischemic event	References
Silva	38-year-old male	Russell's viper	Inferior myocardial infarction	[7]
Aravanis	17-year-old female	viper	Inferior myocardial infarction	[9]
Blondheim	28-year-old male	viper	Myocardial infarction	[10]
Tony	45-year-old male	viper	Inferior myocardial infarction	[11]
Niraj	37-year-old female	Russell's viper	Inferior myocardial infarction	[12]
Saadeh	40-year-old male	viper	Inferior myocardial infarction	[13]
Brown	22-year-old male	Adder (<i>Vipera</i>)	Myocardial infarction	[14]
Maheshwari	47-year-old male	viper	Inferior myocardial infarction	[15]
Gaballa	28-year-old male	viper	Myocardial infarction	[16]
Satish	60-year-old male	viper	Anterior myocardial infarction	[17]
Zeng	49-year-old female	<i>Trimeresurus stejnegeri</i>	Acute cerebral infarction	[8]

no reports of AMI caused by snakebites in China, and only a few in other countries. The mechanism of this myocardial infarction has not yet been elucidated. Researchers have proposed some possible mechanisms, which are mainly about the effects of snake venom, coronary spasm, and indirect mechanism of cardiogenic shock, coronary thrombosis and anaphylactic shock [9-11, 18].

In this case, there is little possibility of myocarditis directly caused by snake venom because the direct cardiotoxic effect of snake venom usually results in myocarditis and extensive myocardial necrosis [19]. In acute myocarditis, the ECG may show sinus tachycardia with nonspecific ST-segment elevation, ST-segment depression and T-wave abnormalities [20]. In this case, upon ECG analysis, inferior STEMI displayed ST-elevation in leads and there was no obvious abnormality in echocardiography. Coronary angiogram showed stenosis of the

left anterior descending artery, without imaging changes of thromboembolism. Similarly, a plaque rupture is unlikely to cause myocardial infarction. However, coronary spasms cannot be completely excluded from being the cause of AMI.

D-dimer might serve as a marker of thrombogenesis and a hypercoagulable state following plaque rupture, while a high level of D-dimer was found to be independent, long-term predictors of all-cause mortality in chest pain patients with a suspected ACS [21]. D-dimer level of the patient increased at first and then decreased after treatment, suggesting coronary thrombosis was an important possible etiological factor for AMI. Failing to perform coronary angiogram on the first day, the absence of arterial occlusion and the infarction in the patient's coronary angiogram does not eliminate the possibility of thrombosis that may have resolved after anti-venom serum

treatment. The level of D-dimer may predict prognosis in patients with AMI caused by Snakebite.

Chest pain is one of the hallmark symptoms of AMI, but the patient in this study had no chest pain. A literature review of symptom presentation in AMI found that 1/3 women did not experience chest pain [22]. Other studies have reported similar findings [23, 24]. Early myocardial enzyme and ECG examination for snakebite patients, especially elderly women, may be diagnosed by ST-segment elevation myocardial infarction in an early stage, and intervention may improve the prognosis of patients.

In summary, this unique case may provide evidence for effective treatment of AMI caused by snakebite with antivenom serum. Physicians must consider AMI in their differential diagnosis of snakebite. The medical team may consider that a patient may be exhibiting probable AMI in the setting of a presumed systemic envenoming, and thus take prompt percutaneous cardiac catheterization if there is no sufficient evidence of active, serious coagulopathy in snakebite patients.

Disclosure of conflict of interest

None.

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