

# Favorable Course after a Second Infusion of Antivenin Using Premedication

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**Abstract** An 80-year-old woman had suffered a mamushi bite to the left hand 3 days ago and visited a local hospital. She was admitted for observation but received only tetanus toxoid, antibiotic and cepharanthine. Physicians hesitated to administer antivenin due to the risk of severe side effects, as she had previously received antivenin for mamushi bite at 50 years old. On the third day, the swelling had reached her left chest (grade V), so she was transferred to our hospital via ambulance. She had two bite wounds from a mamushi on her left hand and showed swelling with subcutaneous hemorrhaging from the finger to her chest and upper back. Chest computed tomography showed left pleural effusion. She underwent infusion of mamushi antivenin after premedication using a subcutaneous injection of 0.3 mg of adrenaline and drip infusion of 10 mg of chlorpheniramine, 20 mg of famotidine and 100 mg of hydrocortisone. She was not complicated with an anaphylactic reaction. After the infusion of the antivenin, her swelling and pleural infusion gradually improved, so she discharged on the seventh hospital day. Even after discharge, she showed no complication with serum sickness. This case showed a favorable course after a second infusion of antivenin using premedication. As there have been few reports of multiple infusions of antivenin for the same patient, a further analysis with the accumulation of similar cases is necessary.

**Keywords:** *mamushi, antivenin, adrenaline, steroid*

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## 1. Introduction

The mamushi (*Gloydius blomhoffii*) is a pit viper responsible for 1.67 bites per 100,000 persons every 6 months and 10 deaths every year in Japan. [1] The mamushi venom mainly consists of multiple enzymes that work as hemolytic toxins, including phospholipase A2; neurotoxins, an alpha-toxin/beta-toxin; increased vascular permeability, arginine ester dehydrogenase; rhabdomyolysis, endopeptidase/bleeding factor (HR1 or HR2); platelet aggregation, L-amino acid oxidase. [2]

Severe cases of mamushi bites usually require the administration of a horse-derived antivenin. [1] Basically, 6000 units of antivenin is administered immediately after the mamushi bite, and if symptoms improve, an additional 3000-6000 units is administered within a few hours. However, the antivenin has the potential to cause anaphylaxis (3.2%) and serum diseases (11%-12%); therefore, physicians tend to hesitate to apply this treatment in mild cases. [2,3,4,5,6] Multiple exposure to antivenin might result in severe anaphylaxis. [7,8] However, there have been few reports of the treatment of such cases [8,9,10].

We herein report a case of a patient who received infusion of mamushi antivenin twice and obtained a favorable outcome with premedication.

## 2. Case Presentation

An 80-year-old woman had suffered a mamushi bite to the left hand 3 days ago and visited a local hospital. She was admitted for observation but received only tetanus toxoid, antibiotic and cepharanthine. Physicians hesitated to administer antivenin due to the risk of severe side effects, as she had previously received antivenin for mamushi bite at 50 years old. On the third day, the swelling had reached her left chest (grade V), so she was transferred to our hospital via ambulance 12. She had history of hypertension and dyslipidemia.

Upon arrival, she showed clear consciousness. Her vital signs were as follows: blood pressure, 135/82 mmHg; heart rate, 90 beats per minute; respiratory rate, 20 breaths per minute; percutaneous saturation, 97% under room air; and temperature, 36.8 °C. She had two bite wounds from a mamushi on her left hand (Figure 1) and showed swelling with subcutaneous hemorrhaging from the finger to her chest and upper back.

The findings of chest roentgen, an electrocardiogram and cardiac echography were negative. Chest computed tomography showed left pleural effusion, in addition to subcutaneous swelling at left chest and upper back (Figure 2).



**Figure 1.** Appearance of the patient's fingers on arrival. She had two bite wounds from a mamushi on her left hand.



**Figure 2.** Chest computed tomography (CT) findings on arrival. CT showed left pleural effusion in addition to subcutaneous swelling at the left chest and upper back.

The results of biochemical analyses of the venous blood on arrival were as follows: white blood cells, 11,000/ $\mu$ L; hemoglobin, 11.2 g/dL; platelets,  $41.3 \times 10^4$ / $\mu$ L; total protein, 5.5 g/dL; albumin, 2.7 g/dL; glucose, 120 mg/dL; HbA1c, 6.1%; total bilirubin, 0.3 mg/dL; aspartate aminotransferase, 91 IU/L; alanine aminotransferase, 20 IU/L; amylase, 68 IU/L; blood urea nitrogen, 26.3 mg/dL; creatinine, 0.73 mg/dL; creatine phosphokinase, 2020 IU/L; sodium, 139 mEq/L; potassium, 5.0 mEq/L; chloride, 107 mEq/L; prothrombin time 11.1 (11.3) sec; activated partial thromboplastin time, 23.0 (26.7) sec; fibrinogen, 295 mg/dL; fibrin degradation product 17.5  $\mu$ g/ml and CRP, 0.72 mg/dL.

She underwent infusion of mamushi antivenin after premedication with a subcutaneous injection of 0.3 mg of adrenaline and drip infusion of 10 mg of chlorpheniramine, 20 mg of famotidine and 100 mg of hydrocortisone. She was not complicated with an anaphylactic reaction. She also received 10 mg of cephazolin and 3 g of cefazolin per day for 2 days. After the infusion of the antivenin, her swelling and pleural effusion gradually improved, so she was discharged on the seventh hospital day. Even after discharge, she showed no complication with serum sickness.

### 3. Discussion

This case showed a favorable course after a second infusion of antivenin using premedication. Among severe

cases of mamushi bite, there has been one report of a patient who underwent repeated infusion of antivenin within a few hours. [12] However, we were unable to find a report describing repeated infusion of mamushi antivenin across 30 years. Tateno et al. reported a study of 64 cases of mamushi bite. [8] Among them, three cases underwent repeated infusion of the antivenin without any premedication. The interval between the first and second bite was 1, 2, 5 years respectively. All three cases showed serum sickness after the second infusion of antivenin. While, 5 out of 61 cases showed serum sickness and 1 out of 61 cases showed anaphylactic reaction after the first infusion of antivenin. Makino et al. reported a study of 114 cases of mamushi bite. [9] Among them, only one case underwent repeated infusion of the antivenin without any premedication. The interval between the first and second bite was unknown, but the case showed hypotension, loss of consciousness and urticaria within eight days after the second infusion of antivenin. In addition, Zeng et al. reported a case of allergic reaction to antivenin in a 75-year-old man who had been bitten twice by the same snake within a month. While the patient did not show any allergic disorder after the first bite, [10] after the second infusion of antivenin, he had a pale face with a large erythematous area, rashes on the chest and swelling on the back with unstable circulation. Following the intramuscular injection of promethazine and intravenous injection of methylprednisolone, he achieved relief.

Most adverse reactions to the antivenin can be divided into two general categories: type I (immediate hypersensitivity), which are life-threatening reactions, and the more common type III (immune complex) reaction, which is characterized by serum sickness. [13,14] The administration of epinephrine and antihistamines can be lifesaving in cases of type I reactions, while steroids and antihistamines can ameliorate type III reactions. [14] de Silva et al. reported the results of 1,007 patients from a randomized, double-blind, placebo-controlled trial of adrenaline, promethazine and hydrocortisone administered immediately before infusion of antivenin for snake bite. [15] Patients were monitored for adverse reactions for at least 96 h. They concluded that pretreatment with low-dose adrenaline was safe and reduced the risk of acute severe reactions to snake antivenin. They did not treat serum sickness. However, oral corticosteroids are given prophylactically after some uses of snake antivenin to prevent serum sickness in Australia, and there have been a few immediate or delayed reactions. [16] Prophylactic oral corticosteroids after antivenin administration may be responsible for this low reaction rate. [11] Accordingly, the combined use of adrenaline and steroids may have resulted in a favorable outcome without immediate or delayed adverse reactions in the present case.

### 4. Conclusion

This case showed a favorable course after a second infusion of antivenin using premedication. As there have been few reports of multiple infusions of antivenin for the same patient, a further analysis with the accumulation of similar cases is necessary.

## Conflict of Interest

The authors declare no conflicts of interest in association with the present study.

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