STM JOURNALS

International Journal of
Toxins and Toxics

Volume 1, Issue 2, 2024
July—December
DOI (Journal): 10.37591/IJTT

https://journals.stmjournals.com/ijtt

Case Study IJTT

ADR Caused Byanti-snake Venom A Case Report Highlighting the Pathophysiology, Prevention, and It's Management

Shivani Chandrashekhar Bedarkar[1,*], Avishkar Hanamantrao Agarkhed[2]

Abstract

Even in situations where it wasn't necessary, antivenom research was applied to snake bite cases. In order to improve their level of understanding, primary practitioners should receive training on handling envenomation situations as well as current recommendations and references. In cases of snake bites, antivenom must be delivered according to applicable systemic and original indications.More than ten percent of cases with admitted ASV experience some sort of reaction, ranging from a minor urticarial rash to a serious anaphylactic reaction. While antivenoms are the first line of treatment in situations of life-threatening envenomation, especially snake sucks, they also result in serious adverse medication reactions. Asia is home to many different species of snakes, and one of the biggest health risks is hemotoxic snake envenomation. Because of resource limitations, the standard diagnostic procedure calls for a 20-minute whole blood clotting time (20WBCT). Antisnake venom (ASV) must be administered in cases of systemic envenomation, which is characterized by bleeding problems or an extended clotting time. This case report describes a patient who needed two doses of ASV at first, but whose clotting time eventually recovered to normal. The case report that is being presented highlights even more the variation in the way that patients react to antivenom, illuminating the complexities of treatment and the need for close observation. The goal of this all-inclusive strategy is to improve practitioners' proficiency in handling cases of snake envenomation, reducing risks, and improving patient outcomes.

Keywords: Snakebite; Envenoming; Antivenom; Elixir responses; Anaphylaxis.

INTRODUCTION

A whole blood clotting time of 20 minutes is the most widely used diagnostic method for hemotoxic snakebite. In cases of prolonged CT or bleeding disorders, antisnake venom must be administered until CT returns to normal in order to treat hemotoxic snakebite. The clotting time returned to normal in the case report that we present [1] (Figure 1).

***Author for Correspondence**
Shivani Chandrashekhar Bedarkar
E-mail: shivanibedarkar22@gmail.com

[1]Research Scholar, Department of Pharmacology, Student of ASPM's KT Patil College of Pharmacy, Siddharth Nagar, Barshi Road, Osmanabad, Maharashtra, India
[2]Research Scholar, Department of Pharmacology, Student of ASPM's KT Patil College of Pharmacy, Siddharth Nagar, Barshi Road, Osmanabad, Maharashtra, India

Received Date: February 09, 2024
Accepted Date: February 21, 2024
Published Date: March 4, 2024

Citation: Shivani Chandrashekhar Bedarkar, Avishkar Hanamantrao Agarkhed. ADR Caused Byanti-snake Venom A Case Report Highlighting the Pathophysiology, Prevention, and It's Management. International Journal of Toxins and Toxics. 2024; 1(2): 40–46p.

Around 300 different species of snakes are thought to exist in Asia, including at least 67 different Elapidae (cobras and kraits) and Viperidae (pit vipers, Russel vipers, and green pit vipers) species. Original indications, including as pain, swelling, and blisters at the bite site, might appear in either group. Nevertheless, pulmonary edema, hemorrhage, renal failure, and ecchymosis are the symptoms of Viperidae. The neurological symptoms of envenomation by the Elapidae family and the Russell Serpent resemble altered internal

status, involvement of cranial nerves, and further motor weakness to palsy. Individual viper bites cause clotting issues after snakebite in South-East Asia [2].

Clinical diagnosis is the standard method used to diagnose toxic snakebite. Poisonous snakebite diagnosis can be aided by coagulation investigations such as prothrombin time and renal and hepatic function testing. Nonetheless, the 20-minute whole blood clotting time (20WBCT) at the bed site is typically used to diagnose envenomation in the majority of developing nations with limited resources. For this test, two milliliters (mL) of blood are drawn into a sterile glass vial and allowed to stand at room temperature for twenty minutes. To check for coagulation, the vessel is tipped. It is possible that the snakebite was poisonous if there is no clot [3].

Currently, patients suspected of having been bitten by a snake and exhibiting symptoms of systemic envenomation (such as spontaneous bleeding, extended clotting time, neurotoxic indications, and acute kidney injury) or initial edema involving more than half of the limbs are given anti-snake venom. These demand that patients be thoroughly examined prior to receiving ASV in snake-suck instances. Additionally, unsatisfactory surgeries may result in a lack of this rare and somewhat costly antidote. Next, we describe a case in which the patient received two doses of anti-snake venom. Nevertheless, despite the patient's high 20WBCT, ASV was stopped because there was no bleeding diathesis and the patient was clinically normal. After many days, the 20WBCT resumed its normal range [4].

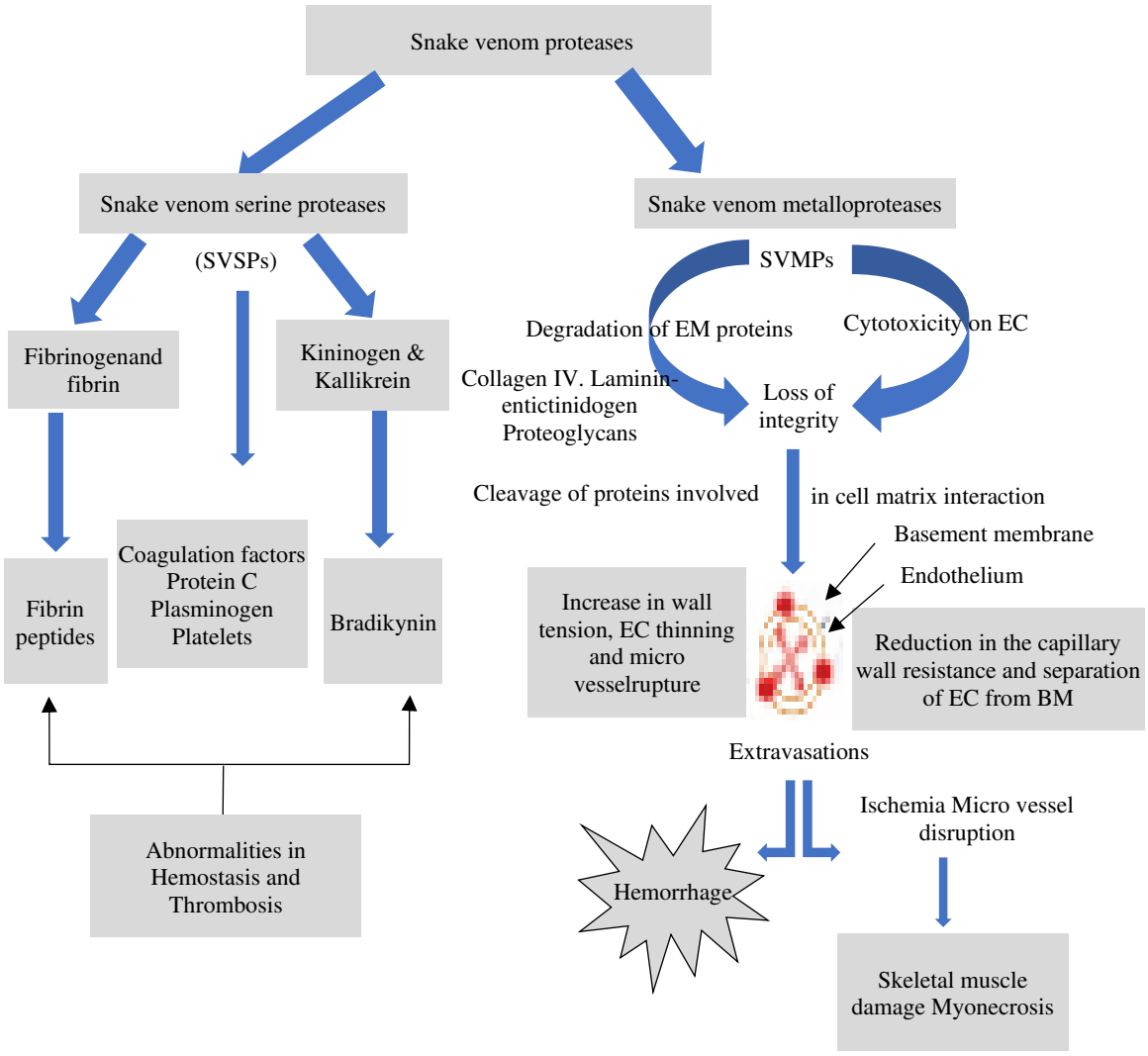

Figure 1. Pathophysiology of snake envenomation.

PATHOPHYSIOLOGY

Components

The main components of snake venom are secreted proteins, which are decoded by poly-adenylated mRNA from the poisonous glands (12S and 20S). These proteins have a variety of natural purposes; some are hydrolytic enzymes that aid in the digestive process for the snake, while others have the ability to cause metabolic problems in their prey or even cause death. A portion of these enzymes might be involved in the venoms' harmful properties. Snake venom, particularly that of the Viperidae family, contains chemicals that also create inflammatory mediators on the four interconnected blood systems: (i) coagulation system, (ii) fibrinolysis, (iii) complement, and (iv) kinin system [5].

Proteinases

In particular, proteolytic enzymes play a role in the pathophysiology of bleeding disorders, hemorrhage, and tissue necrosis. Proteinases are a diverse set of enzymatic proteins ranging in size from 15 to 100 kDa that are extracted from the venoms of vipers. Certain proteinases function by affecting blood coagulation factors and have the potential to operate as coagulant anticoagulants by either stimulating or suppressing the effects of plasma factors. They also possess plasmin, thrombin, and fibrino (geno) lytic activity [6].

Snake Venom Serine proteases (SVSPs)

Serine proteases are widely found in snake venoms; they are primarily associated with venoms from the following families: Viperinae (Cerastes cerastes, Cerastes vipera, and Bitis gabonica), Crotalinae (Agkistrodon, Crotalus, Lachesis, and Trimeresurus), and Colubrinae (Dipholidus typus). They can be categorized as fibrinogenases or kallikrein-like, which causes the release of bradykinin, based on how they affect the hemostatic system. The majority of these proteases impact many targets related to the fibrinolytic system, platelets, plasma coagulation, and hemostasis. We refer to them as "Snake Venom Thrombin-like Enzymes" (SVTLEs) or "Thrombinic Enzymes from Snake Venom". Aspartic acid (Asp 102), histidine (His 57), and serine (Ser 195; hence the term "serine protease") comprise the catalytic triad that makes up the conserved common domain of SVSPs (20 to 100 kDa). These amino acids are all necessary for the catalytic process. SVSPs primarily target the coagulation cascade and function as exogenous plasma factors or as strong platelet amplification molecules [7].

Snake Venom Metalloproteinases (SVMPs)

A number of SVMPs (ranging in size from 22 to 100 kDa) that were extracted from snake toxins have been identified as Zn2-metalloproteinases, with their primary targets being elements of endothelial cell basement membranes. The most researched biological impact supported by SVMPs is hemostatic system abnormalities. Along with their procoagulant and anticoagulant properties, SVMPs have a role in the pathophysiology of skin injury, inflammation, myonecrosis, edema, and the onset of cardiovascular shock. In order to convert significant blood extravasation, SVMPs are also effective in breaking down the extracellular matrix components (fibronectin, collagen, proteoglycans, and laminin). These metalloproteinases are known as hemorrhage because they cause the convincing initial and systemic bleeding following bites, which affects multiple organs including the heart, liver, lungs, intestines, and brain. They may also result in necrosis, blisters, and edema [8].

ADVERSE ANTI-SNAKE VENOM REACTIONS

Treatment for snakebite has suffered greatly by the idea of unfavorable reactions to ASV, far more than from the real danger. Even with proper management, these reactions can be treated in even the most basic medical settings, therefore efforts to raise the quality of ASVs must be weighed against the associated expenses.

(a) Preemptive anaphylactic reactions occur between 10 and 180 minutes after the medication is started and are typified by fever, tachycardia, diarrhea, urticaria, dry cough, nausea, and vomiting, as well as abdominal pain. A severe, potentially fatal form of anaphylaxis that manifests as bronchospasm, angioedema, and hypotension can occur in certain circumstances.

After beginning the ASV in drip, any new symptom or sign, such as vomiting, feeling hot or chilly, abrupt dry coughing, new abdominal discomfort, dyspnea, low blood pressure, shock, swelling of the face, conjunctiva, and tongue protrusion from angioedema, may be suspected as a reaction to the ASV [9].

(b) Pyogenic reactions usually appear one to two hours following therapy. Fever, hypotension, chills, and rigors are among the symptoms. Pyrogen contamination of the ASV during the production process is the cause of these reactions.

(c) After therapy, late (serum sickness-type) responses appear 1–12 (mean 7) days later. Clinical manifestations include arthralgia, myalgia, lymphadenopathy, fever, nausea, vomiting, diarrhea, itching, recurrent urticaria, and, rarely, encephalopathy.

Mechanism of the Response

It is unclear which particular mechanism causes negative reactions.

1. Directly support the ASV proteins' activity. There is some proof that ASV can in vitro activate complement.
2. Vulnerable complexes mediate complement activation.

Prediction of Adverse Reactions

Attempting to predict ASV responses through the use of a test dosage is a frequently employed approach. The victim receives an intradermal test dose; after around 30 twinkles are allowed to stop, the sufferer is examined to see whether any wheals that would indicate sensitivity are present. Testing for Type I hypersensitivity allergy responses frequently involves skin tests. They show elevated IgE levels when a particular allergen is present

1. They are nonpredictive – ASV responses are complement actuated and not intermediated by IgG, they are also de novo responses.
2. They waste time when the patient needs ASV.
3. They might increase the likelihood of a severe reaction and sensitize the patient to the principal dose of ASV.

IgE-intermediate Type I hypersensitivity to steed or lamb proteins can be detected by skin and conjunctival "hypersensitivity" tests. However, these tests are not predictive because most early (anaphylactic) or late (serum illness type) elixir responses are caused by direct complement activation rather than by IgE-intermediated hypersensitivity. These tests shouldn't be employed because they could cause therapy delays and sensitization in and of themselves (position of evidence T).

Preventing Adverse Reactions

Preventive medication is frequently used to assist prevent adverse reactions to ASV. Reaction rates of 25 or above are reported when employing developed nation ASVs, despite the fact that these products are usually considered superior.The preventive method, which is mostly based on two trials conducted in Sri Lanka, seemed to indicate that preemptive dosages of hydrocortisone or adrenaline as well as antihistamines prevented reactions. Due to statistical underpowering, one trial was stopped midway through because the results were considered good at that point [10].

These medications should not be taken, with the exception of high-risk individuals, as no preventive treatment regimen has been shown to be useful in lowering the incidence or severity of early antivenom responses. Following the antivenom administration, all patients should be closely monitored for two hours, and at the first indication of a reaction, epinephrine or adrenaline should be administered.

Handling of Adverse Events

Managing ASV reactions is simple if:

1. They are detected early.
2. They receive prompt treatment.

3. The preferred medication is used to treat them.
4. The proper time for reevaluation is utilized.
5. The medication is administered according to the recommended method.

Step 1 Linked Early

Since the clinician isn't actively searching for ASV reactions, many go missed. An average time to reaction onset will most likely be established by local experience with ASV. For instance, the typical onset time of reactions with Indian ASV is 20 minutes. This is an important time to closely review the case, especially across the trunk, as this is when the answers become apparent for the first time. Shining a torch across the trunk is a helpful technique since it creates shadows for the urticaria.

Step 2 Treated Immediately

Stop administering the ASV as soon as a reaction appears. Any itching or a single spot of urticaria are among the initial symptoms. Frequently, the patient will become agitated right before these symptoms appear. Additional symptoms that have been noted include dyspnea, sudden dry cough, new abdominal pain, conjunctiva swelling, vomiting, heat or cold feelings, shock, and angioedema-related facial and tongue protrusions.

Step 3 Drug of Choice

Adrenaline (epinephrine) is administered intramuscularly to adults (0.5 mg/ml; 1 in 1,000 results) over deltoid or ham (0.01 mg/kg body weight in children) for the treatment of early allergic and pyrogenic ASV reactions. If the ASV is known to cause frequent reactions, it is ideal to have two syringes prepared. intravenous delivery of chlorpheniramine maleate (10 mg for adults, 0.2 mg/kg for children).

Step 4 Correct Mode of Administration

Speed is a key component in controlling ASV responses. More venom will be allowed to attach to the target cells and the longer the reaction lasts, the longer the victim is free of ASV. As a result, how quickly adrenaline takes affect is crucial. Thus, intramuscular (IM) injection is the method of action. Adrenaline takes 8 minutes to take effect intramuscularly and 34 minutes to take effect subcutaneously. IM is the initial line of treatment, even though the majority of physicians would prefer to choose the subcutaneous method. An intravenous dose of 0.5 mg of 110,000 adrenaline can be administered in incredibly unusual and life-threatening situations.

Step 5 Correct Reassessment Period

After IM administers the initial dosage of adrenaline, the case is almost resolved. The patient's pulse rate should start to rise at about three twinkles, indicating that the medication was correctly injected intramuscularly. The patient is examined for evidence of improvement for five to seven minutes after the adrenaline reaches its peak, which occurs at eight minutes.If, however, none are visible or the patient's illness has gotten worse, a further dose is given intramuscularly. Very rarely, a third dose can be required. Most individuals will respond to one dose, however some patients will respond to a different dosage. Given that a single subcutaneous dose of adrenaline is required for maximum impact, two doses of adrenaline can be administered simultaneously via the IM route. Promethazine hydrochloride (25 mg IV) or, if available, 10 mg chlorpheniramine maleate can be given intravenously together with 100 mg of hydrocortisone. Pediatric patients should get 0.5 mg/kg/day IV of Phenimarine maleate, 0.3–0.5 mg/kg IV of Promethazine HCl, 0.2 mg/kg IV of Chlorpheniramine maleate, and 2 mg/kg IV of Hydrocortisone.

The ASV can be gradually restarted for ten to fifteen minutes while the patient is closely monitored after they have recovered. It's also time to get back to the regular drip pace. (National Guidelines Draft)

Late serum sickness reactions are easily managed with oral steroids, such as prednisolone (5 mg 6 hourly for adults and 0.7 mg/kg/day for children). H1 antihistamines used orally provide substantial symptom alleviation.

CASE REPORT

The case of a 28-year-old farmer from Washi, Osmanabad, is being presented. He was brought to the hospital after half an hour of snakebite to the right foot with signs of severe pain at the site, swelling, and bleeding. The physician advised to take first-line treatment of Anti-Snake Venom (ASV). The report of the test (CT = 5' 28" min normal, BT = 1' 04" min abnormal, PT = 16 sec abnormal, INR = 1.28 sec).

The patient is shifted to the government hospital of osmanabad by physician advice due to its worst condition. The case reached to hospital after three hours of first-line treatment and was shifted to Male Medicine Ward (MMW). The symptoms after arriving at the hospital are dizziness, and hypotension (BP = 108/63, PR = 89).

The treatment is given as:

Inj. ASV 10 ml through the intravenous route,

Inj. Avil 2 cc through the intravenous route,

Inj. Dexa 2 cc through the intravenous route,

Inj. Amox1.2 through the intravenous route,

Inj. Metro 100 mg through the intravenous route,

Inj. Diclo 75 mg through the intramuscular route.

At 830 pm case was shifted immediately to the emergency ward under the advice of the clinical pharmacist by observing his symptoms as – chills, hypotension, and angiooedema (red spots with itching & burning sensation around the eyes). The clinical pharmacist concludes that it's an ADR case of ASV.

In the emergency ward, the doctors suggested giving treatment of steroids with Anti-histamine to recover ADR.

Drugs

1. Corticosteroids
    a. Inj. Dexamethasone 8 mg through intravenous route,
    b. Inj. Hydrocortisone 100 mg through the intravenous route,
2. Anti-histamine
    a. Inj. Avil 2 ml through the intravenous route.

The ASV is tested on the patient to confirm that it should show a positive response to AVS without any adverse medical reaction. Also, the patient is shifted again to its MMW after 12 hr; also its AVS dose was continued with the prescription.

CONCLUSION

Antivenom's high incidence of acute adverse reactions is one illustration of how inadequate production and quality control by antivenom manufacturers lead to issues for both patients and their physicians. This emphasizes how important it is to deal with problems pertaining to subpar and maybe dangerous elixir. In the end, the elixir's quality will be the primary factor in preventing responses. The results of this investigation demonstrated the ineffectiveness of pre-hydrocortisone on its own. However, it is impossible to rule out the significant positive impact of hydrocortisone combinations with injectable antihistamines or adrenaline as premedications used to treat ADRs. As a result, using

hydrocortisone in conjunction with injectable antihistamines or adrenaline as a preventative measure may lessen adverse drug reactions to antivenom. Physicians will have to rely on pharmaceutical prophylaxis and close monitoring of patients starting antivenom in order to promptly handle both acute and delayed responses when they occur until these improvements occur.

REFERENCES

1. Habib AG. Effect of pre-medication on early adverse reactions following antivenom use in snakebite: a systematic review and meta-analysis. Drug safety. 2011 Oct;34:869–80.
2. Moran NF, Newman WJ, Theakston RD, Warrell DA, Wilkinson D. High incidence of early anaphylactoid reaction to SAIMR polyvalent snake antivenom. Transactions of the Royal Society of Tropical Medicine and Hygiene. 1998 Jan 1;92(1):69–70.
3. Malasit P, Warrell DA, Chanthavanich P, Viravan C, Mongkolsapaya J, Singhthong B, Supich C. Prediction, prevention, and mechanism of early (anaphylactic) antivenom reactions in victims of snake bites. British medical journal (Clinical research ed.). 1986 Jan 1;292(6512):17.
4. de Silva HA, Pathmeswaran A, Ranasinha CD, Jayamanne S, Samarakoon SB, Hittharage A, Kalupahana R, Ratnatilaka GA, Uluwatthage W, Aronson JK, Armitage JM. Low-dose adrenaline, promethazine, and hydrocortisone in the prevention of acute adverse reactions to antivenom following snakebite: a randomised, double-blind, placebo-controlled trial. PLoS medicine. 2011 May 10;8(5):e1000435.
5. León G, Herrera M, Segura Á, Villalta M, Vargas M, Gutiérrez JM. Pathogenic mechanisms underlying adverse reactions induced by intravenous administration of snake antivenoms. Toxicon. 2013 Dec 15;76:63–76.
6. Warrell DA. Epidemiology of snake-bite in South-East Asia region. Guidelines for the management of snakebite. New Delhi: WHO regional office for Southeast Asia. 2010:35–45.
7. Gawarammana IB, Kularatne SA, Kumarasiri RP, Senanayake N, Dissanayake WP, Ariyasena H. Parallel infusion of hydrocortisone±chlorpheniramine bolus injection to prevent acute adverse reactions to antivenom for snakebites. Medical Journal of Australia. 2004 Jan;180(1):20–3.
8. Simons FE, Gu X, Simons KJ. Epinephrine absorption in adults: intramuscular versus subcutaneous injection. Journal of allergy and clinical immunology. 2001 Nov 1;108(5):871–3.
9. Rawas-Qalaji MM, Simons FE, Simons KJ. Sublingual epinephrine tablets versus intramuscular injection of epinephrine: dose equivalence for potential treatment of anaphylaxis. Journal of allergy and clinical immunology. 2006 Feb 1;117(2):398–403.
10. Lieberman P. Use of epinephrine in the treatment of anaphylaxis. Current opinion in allergy and clinical immunology. 2003 Aug 1;3(4):313–8.

