Journal of Health and Medical Sciences

Sabirin, Mira Rellytania, Sudjud, Reza Widianto, Suwarman, and Pradian, Erwin. (2020), Case Report: Management of Respiratory Failure Following Snake Bite. In: *Journal of Health and Medical Sciences*, Vol.3, No.3, 338-349.

ISSN 2622-7258

DOI: 10.31014/aior.1994.03.03.129

The online version of this article can be found at:
https://www.asianinstituteofresearch.org/

Published by:
The Asian Institute of Research

The Asian Institute of Research *Journal of Health and Medical Sciences* is a peer-reviewed International Journal. The journal covers scholarly articles in the fields of Medicine and Public Health, including medicine, surgery, ophthalmology, gynecology and obstetrics, psychiatry, anesthesia, pediatrics, orthopedics, microbiology, pathology and laboratory medicine, medical education, research methodology, forensic medicine, medical ethics, community medicine, public health, community health, behavioral health, health policy, health service, health education, health economics, medical ethics, health protection, environmental health, and equity in health. As the journal is Open Access, it ensures high visibility and the increase of citations for all research articles published. The *Journal of Health and Medical Sciences* aims to facilitate scholarly work on recent theoretical and practical aspects of Health and Medical Sciences.

Asian Institute of Research
Connecting Scholars Worldwide

ASIAN INSTITUTE OF RESEARCH
Connecting Scholars Worldwide

The Asian Institute of Research
Journal of Health and Medical Sciences
Vol.3, No.3, 2020: 338-349
ISSN 2622-7258

DOI: 10.31014/aior.1994.03.03.129

Case Report: Management of Respiratory Failure Following Snake Bite

Mira Rellytania Sabirin[1], Reza Widianto Sudjud[2], Suwarman[3], Erwin Pradian[4]

[1] Soreang General Hospital
[2] Department of Anesthesiology and Intensive Therapy, Faculty of Medicine Universitas Padjajaran, Hasan Sadikin General Hospital Bandung

Abstract
Venomous snakebite cases are life-threatening medical emergencies. Most deaths were caused by respiratory failure due to acute neuromuscular paralysis. In this case, a man, 17 years old, was treated for snakebite on his upper arm one-hour prior hospital admission. Snakes was identified as cobras. Patient experienced symptoms of vomiting, seizures, headaches, weakness in the extremities and decreased consciousness. Local examination revealed two deep teeth marks. No hemorrhagic and myotonic manifestations were found. He then experienced respiratory failure, intubated and treated in the intensive care unit. Management of respiratory failure due to neurotoxic snake bites, namely administration of snake antivenom to bind poison, anti-cholinesterase and atrophine sulfate to release toxins from neuromuscular. Supportive therapy included ventilators, fluids, nutrition, tetanus toxoid, antibiotics. Fasciotomy was done on the bite wound because compartement syndrome was found. This patient did not show other abnormal manifestations because patient was promptly taken to the hospital. On day 3 hospital stay, he showed improvement, on day 6, he was moved to the ward. To achieve optimal results in cases of venomous snake bites, early diagnosis, early transportation to hospital and adequate management of snakebite were needed.

Keywords: Anti Snake Venom, Neurotoxic, Respiratory Failure, Snake Bite

INTRODUCTION

Snake bites were classified by WHO as neglected tropical disease. Kasturiratne et. Al (2008) estimated 1.2 million snake bites occurred annually, 421,000 venomous snake bites and mortality rate up to 20,000 snake bites worldwide. Most deaths were due to respiratory failure following the bite of neurotoxic snakes. Neurotoxicity were caused by snake species of Elapidae (family elapidae) such as Kraits (Bungarus spp), Cobras (Naja spp), Taipan (Oxyuranus spp), and Tiger Snake (Notechis spp). Snake venom had different enzymatic and non-enzymatic components. Snakes were classified based on their toxicity; hematotoxic, myotoxic and neurotoxic. In the neurotoxic type, manifestations of respiratory failure caused by acute neuromuscular paralysis were the main

causes of morbidity and mortality (Kasturirane, et al., 2008; Ranakawa, Lalloo, & de Silva, 2013).

Respiratory failure, a syndrome where the respiratory system cannot perform the function of gas exchange, both oxygenation and or elimination of carbon dioxide (CO_2). There were two types of respiratory failure, namely type I respiratory failure (hypoxemia), in which oxygenation disturbance occurred and type II respiratory failure (hypercapni) where ventilation was disrupted to eliminate CO_2. In the case of this neurotoxic snake bite, hyperpapni breath failure occurred. This was due to the effect of the snake's toxin that attacked neuromuscular junction, triggering acute neuromuscular paralysis and difficult ventilation (Kasturirane, et al., 2008; Ranakawa, Lalloo, & de Silva, 2013)

Management of acute respiratory failure in patients with snake bites required multidisciplinary involvement. Causative therapy aimed to eliminate the effects of snake venom from neuromuscular junction. This type of therapy used snake antivenom (SAV) based on its type. Supportive therapy was given to promote the primary life functions by providing mechanical ventilation to support adequate respiration, nutrition and fluids. Additional therapy was done by treating wound area with wound care, antibiotics for the prevention of infection and fasciotomy if needed (Ranakawa, Lalloo, & de Silva, 2013; Warrell, 2010; Kakaria, Narkhede, Agrawal, Bhavsar, & Nukte, 2014).

CASE REPORT

Patient's identity

Name	: An. S
Age	: 17 years
Ethnicity	: Sundanese
Occupation	: Student
Medical record	: 688368
Hospital admission	: 23/01/2020
ICU admission	: 23/01/2020
ICU discharge	: 28/01/2020

Subjective

Chief complain: Bitten by cobra snake

A-17-year man weighed 60 kg came to Emergency Department in Soreang District Hospital with decreased consciousness following snake bite one hour prior hospital admission. He was alert at first but on the way to the hospital, his consciousness was declining. He also experienced two times of vomiting, headache and difficulties in moving both upper and lower extremities. After arrival, he showed three times seizure with five minutes duration each. He was known to pet a Cobra snake since one month ago.

Objective

General condition: severely ill
- Consciousness : Comatus E1M1V1
- Vital signs :
  BP : 100/70 mmHg HR :109x/'
  RR : 30x/mnt T : 36,8 °C
- BW: 60 kg BH: 170 cm BMI: 21
- Predicted Body Weight (male) : 50+[2,3x(67-60)] = 66,1 kg

Primary survey :
- A: clear airway
- B: Retraction +/+ nasal flares + RR: 35 x/min, ronchi +/+, slem +/+
  Wheezing -/- SpO2: 92% with SMNR 10 liter/min

- C: BP 100/70 mmHg; regular adequate pulse 100-120 x/m, murmur -.
- D: comatus, GCS 3 (E1M1V1), motoric 0/0/0/0 ptosis eyelids, pupil isocor
- E: venomous snake bite trauma at right forearm

Secondary survey :
- Head: ptosis right and left eyelids, red eyes (-)
- Neck: JVP does not increase
- Thorax: basic vesicular sounds, ronchi +/ + slem ++ / +
- Abdomen: flat, not distended, bowel sound (+) N, melena (-), hematuria (-), brownish urine (-)
- Extremities: petechie (-), ecchymosis (-)
- Local status: visible snake bite marks on the right forearm, edema, erythema, bull and necrotic tissue was found.

ECG result: sinus tachycardia

Emergency Department laboratory results:
- Routine blood count: Hb : 17,4 gr/dl Ht: 51% Leuko: 29.400 /uL Trombo: 381.000 /uL
- Coagulation function : PT 15,6s aPTT: 38,3s INR: 1,57
- GDP: 196,1 mg/dl Ureum: 12,0 Creatinine: 0,88 mg/dl
- Electrolyte: Natrium: 136 meq/L Kalium: 4,10 meq/L Calcium: 8,42 mg/dL Magnesium: 1.35 mg/dl
- Xray was not done

Assessment : Decreased consciousness and acute respiratory failure due to neurotoxic snake bite grade IV

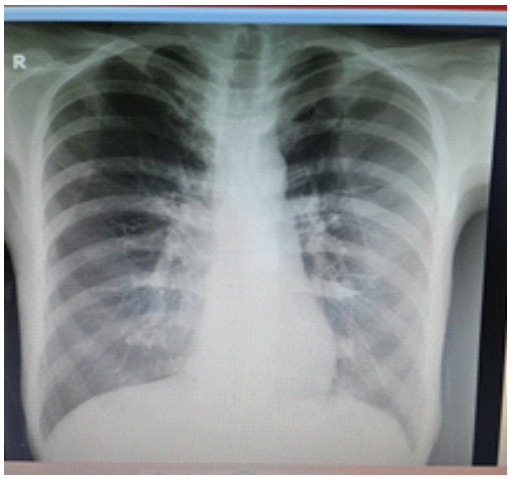
Therapy plan:
- ICU care with ventilator
- Injection five vials of serum antivenin (SAV) in D5% 500 cc for 30-60 minutes
- Cetriaxon 1x2 gram iv injection
- ATS 1500 iv
- Wound toilet with chlorhexidine and wound immobilization with elastic bandage
- Dexametason 3x5 mg iv injection
- Intubation
- Consult to Surgery Department

ICU CARE

Day 1: 23 January 2020

Subjective : -
Objective :
On 16.00, arrival at ICU, patient was intubated with ETT no.7
- GCS 3 (E1M1Vt)
- APACHE score: 23
- Airway was installed ETT no 7 depth of 22 cm
- Breathing : on ventilator
  Mode SIMV RR: 12 x/' TV: 400 ml PEEP: 5 FiO2: 50% gradually reduced until 45% SpO2 92-98%
- Circulation :
  - NIBP : 110/80 mmHg without vasopressor
  - HR : sinus tachycardia, 120 x/'
  - Temperature : 36,5-37,5 °C
- Pain : CPOT 0
- Laboratory result :
  - Albumin : 3,6 Lactate 1,2 SGOT: 27 SGPT: 25
  - BGA : pH: 7,34 pCO2: 37,4 pO2: 158 HCO3: 19,5 BE: -5 SpO2 99% Pf 264,5

- Fluid balance :
  - Intake : 1466 cc
  - Output : 1627 cc
  - Cummulative balance : -161 cc, clear urine
- Thorax x-ray : Bronchopneumonia bilateral



Assessment : Decreased consciousness and acute respiratory failure due to neurotoxic snake bite grade IV

Therapy plan:
- Fasciotomy by surgical department
- Injection five SAV vials in D5% 500 cc within 6 hours
- Ceftriaxon 1x2 gram iv (D1) injection
- Dexamethason 3x5 mg iv injection
- Prostigmin: SA = 10 ampul: 5 ampul iv continue in 24 hour
- Blood glucose test every one hour.
- Feeding (F) : fasting
- Analgetic (A) : fentanyl 25 mcgr/hour
- Sedation (S) : -
- Tromboprophylaxis (T) : -
- Head of bed elevation ((H); +
- Ulcer gastric prevention (U): Omeprazol 2x40 mg iv
- Glucose control (G) : -

Day-2: 24 January 2020

Subjective : -
Objective :
- Consciousness E1M1Vt
- Breathing : on ventilator
  Mode Ventilator SIMV PS RR: 12-15 x/' TV: 375-420 ml PEEP: 5 PS 6-8 FiO2: 45% SpO2 97-99%
- Circulation :
  - BP : 118/75 mmHg without vasopresor
  - HR : sinus tachycardia, 109-110 x/'
  - Temperature : 36,4-36,8 °C
- Abdomen : bowel sound+, NGT murky 50 cc
- Pain : CPOT 1
- Laboratory result :
  - BGA : pH: 7,48 pCO2: 30,5 pO2: 109,4 HCO3: 23,6 BE: -3 SpO2 98,1% Pf 260,5

  - Hb: 12,8 Ht: 37,1 Leu: 15.080 Trombo: 205.000 Na: 135 K: 4,0 Cl: 98 Ca: 4,49 Mg: 2,5
- Fluid balance :
  - Intake : 2040 cc
  - Output : 2248 cc
  - Cummulative balance : +208 cc

Assesment : Decreased consciousness and acute respiratory failure due to neurotoxic snake bite grade IV

Therapy plan:

- Ceftriaxon 1 x 2 gram iv (D2) injection
- Dexamethasone 3 x 5 mg iv injection
- Prostigmin: SA = 10 ampul: 5 ampul iv continue in 24 hours
- Ca gluconas 2 gr
- Feeding (F) : formula RS 1000 kcal diet
- Analgetics (A) : fentanyl 25 mcg/hour iv continue
- Sedation (S) : midazolam 3 mg/hour iv continue
- Tromboprophylaxis (T) : -
- Head of bed elevation ((H); +
- Ulcer gastric prevention (U): Omeprazol 2x40 mg iv
- Glucose control (G) : blood glucose test within normal limit

During the patient's treatment, an muscle strength with hand grasping, ability to open eyes, moving limbs were evaluated.

Fasciotomy was done, wound care was done every day.

Day 2 : 24 January 2020

The patient condition hasn't changed. Hemodynamics and therapy in intensive care remain the same

Day-3: 25 January 2020

Subjective : -

Objective : began to open the eyes slowly, fingers and toes can be moved

- Consciousness: E2M2Vt
- Breathing : on ventilator
  Mode SIMV PS RR: 14-20 x/' TV: 360-425 ml PS: 6-8 PEEP: 5 FiO2: 45% SpO2 98-100%
- Circulation:
  - BP : 128/70 mmHg
  - HR : sinus tachycardia, 100-109 x/'
  - Temperature: 36,4-36,8 °C
- Pain : CPOT 2
- Laboratory result :
  AGD : pH: 7,49 pCO2: 29,3 pO2: 116,2 HCO3: 22,7 BE: 0,9 SpO2 98,2% Pf 258,2
- Fluid balance :
  - Intake : 2040 cc
  - Output : 2248 cc
  - Cummulative balance : +208 cc

Assessment : Decreased consciousness and acute respiratory failure due to neurotoxic snake bite grade IV

Therapy plan:

- Ceftriaxon 1 x 2 gram iv (D3) injection
- Dexamethasone 3 x 5 mg iv injection
- Prostigmin: SA = 10 ampul: 5 ampul iv continue in 24 hours
- Feeding (F) : liquid diet 500 kcal
- Analgetics (A) : fentanyl 25 mcgr iv

- Sedation (S) : midazolam 3 mg/hour iv continue
- Tromboprophylaxis (T) : -
- Head of bed elevation ((H); +
- Ulcer gastric prevention (U): Omeprazol 2x40 mg iv
- Glucose control (G) : blood glucose test within normal limit

Day-4: 26 January 2020

Subjective :gaining muscle strength, dyspnea improved
Objective : begin to open eyes, able to grasp hands, increase strength of limbs
- Consciousness E3M5Vt
- Breathing : on ventilator
  Spontaneous mode RR: 18-22 x/' TV: 360-420 ml PEEP: 5 PS 6 FiO2: 45% SpO2 98-100%
- Circulation :
  - BP : 130/85 mmHg
  - HR : sinus rhythm, 84 x/'
  - Temperature : 36,5-37,5 ℃
- Pain : CPOT 2
- Laboratory result:
  - Hb: 12,0 Ht: 35,5 Leu: 6.090 Trombo: 204.000
  - BGA: pH: 7,514 pCO2: 28 pO2:191 HCO3:23,4 BE: 0,3 SpO2 99,1% Pf 424,4
- Fluid balance :
  - Intake : 2699 cc
  - Output : 2461 cc
  - Cummulative balance : +238 cc

Assessment : Decrease consciousness and type II respiratory failure (hypercapnia) due to neurotoxic snake bite grade IV

Therapy plan:
- Ceftriaxon 1 x 2 gram iv (D4) injection
- Mestinon 4x1
- Dexamethasone 3x5 mg iv injection
- Feeding (F) : liquid diet 1500 kcal
- Analgetics (A) : paracetamol 4x1 gr iv
- Sedation (S) : midazolam 3 mg/hour iv continue
- Tromboprophylaxis (T) : -
- Head of bed elevation ((H); +
- Ulcer gastric prevention (U): Omeprazol 2x40 mg iv
- Glucose control (G) : blood glucose test within normal limmit

Day-5: 27 January 2020

Subjective: muscle strength gaining, decreasing dyspneu
Objective : ptosis (-), hand grip (+)
- Consciousness E4M6Vt
- Breathing : on ventilator
  Spontaneous mode RR: 18-20 x/' TV: 350-430 ml PEEP: 4 PS: 4 FiO2: 40% SpO2 98-100%
- Circulation :
  - NIBP : 130/85 mmHg
  - HR : sinus rhythm, 84 x/'
  - Temperature: 36,5-37,5 ℃
- Pain : CPOT 2
- Laboratory result :
  - Hb: 12,1 Ht: 36,5 Leu: 8.230 Trombo: 287.000

- Na: 136 K: 4,2 Cl: 100 Ca: 4,37 Mg: 2,2
- BGA : pH: 7,415 pCO2: 34 pO2:148,8 HCO3:23 BE:-1,3 SpO2 99% Pf 328

- Fluid balance :
  - Intake : 2322 cc
  - Output : 2650 cc
  - Cummulative balance : -320 cc

Assesmen : Type II respiratory failure (hypercapnia) due to neurotoxic snake bite grade IV

Plan therapy:
- Ceftriaxon 1 x 2 gram iv (D6) injection
- Mestinon 4x1
- Feeding (F) : liquid diet 1500 kcal
- Analgetics (A) : paracetamol 4x1 gr iv
- Sedation (S) :
- Tromboprophylaxis (T) : -
- Head of bed elevation ((H); +
- Ulcer gastric prevention (U): -
- Glucose control (G) : blood glucose test within normal limit
- Plan: extubation

Day-6: 28 January2020

Subjective : dyspnea (-)
Objective : ptosis (-), hand grip (+), extremity muscle strength (+)

- Breathing : binasal canul 3l/' satuaration 98-100% RR 15-18x/'
- Circulation:
  - NIBP : 120/75 mmHg
  - HR : sinus rhythm, 80 x/'
  - Temperature : 36,5-37,2 ℃
- Pain : NRS 2

- Fluid balance :
  - Intake : 1745 cc
  - Output : 2470 cc
  - Cummulative balance : -725 cc

Assesmen : Type II respiratory failure (hypercapnia) due to neurotoxic snake bite grade IV (improved)

Therapy plan:
- Mestinon 4x1 tablet per oral
- Feeding (F) : formula RS 1500 kcal
- Move to ward

Tabel 1. Ventilator mode per day

Date	**23/1/20**	**24/1/20**	**25/1/20**	**26/1/20**	**27/1/20**	**28/1/20**
	D1	**D2**	**D3**	**D4**	**D5**	**D6**
Mode	SIMV	SIMV PS	SIMV PS	Spontaneous	Spontaneous	NC
RR	12	12-15	14-20	18-20	18-20	15
PS	-	8	6	6	4	-
PEEP	5	5	5	5	4	-
VT	400	375-420	360-425	360-420	350-430	-

FiO2	50%	45%	45%	45%	40%	-
SaO2	98%	99%	98%	100%	98%	99%
P/F ratio	264	260	258	424	328	-

DISCUSSION

In many countries in the Southeast Asian region, snakebite was classified as a notable medical emergency and accounted hospital admission. This condition resulted in death or chronic disability in patients of childbearing age (Kasturirane, et al., 2008; Ranakawa, Lalloo, & de Silva, 2013). The characteristics of snake species in each country differed depending on the local geographical conditions. This made each country develop snake antivenom (SAV) in accordance with the type of poisonous snake in that country. For example, the type found in England was viper, so British government made a monovalent SAV (one type) for viper snakes venom. There were numerous and variant type of snakes. Indonesian government combined for 3 types of SAV in 1 (polyvalent) for the snake species Bungarus spp, Naja spp, Ankilostrodon spp (Warrell, 2010; Kakaria, Narkhede, Agrawal, Bhavsar, & Nukte, 2014). Patients suffering from snake bites should be taken to the hospital immediately to get primary clinical assessment and rapid resuscitation. Cardiopulmonary resuscitation might be needed, including oxygenation and intravenous access (Kasturirane, et al., 2008; Warrell, 2010). In emergency settings, patients were assessed from airway (airway patency), breathing (breathing movement), circulation, disability (disability of the nervous system), and exposure.

Differential diagnosis

In the case of snake bites, consider the possibility of cardiotoxic, renotoxic, myotoxic, neurotoxic and hematotoxic snakebites. Careful history taking, physical examination and complete supporting examination is needed to rule out other toxic diagnoses (Ranakawa, Lalloo, & de Silva, 2013; Kakaria, Narkhede, Agrawal, Bhavsar, & Nukte, 2014). Examination of hemostasis profile, ECG, urinalysis, and neurological status were needed. In general assessment, detection of hypovolemia and shock must be carried out with its bleeding signs (petechiae, purpura, ecchymosis and conjunctival bleeding), or bleeding in the gums and nose. Abdominal pain might indicate gastrointestinal bleeding. Lower back pain and tenderness might refer to acute renal ischemia. Intracranial bleeding was characterized by lateralization of neurological signs, seizures or disturbance of consciousness (in the absence of respiratory or circulatory failure). Rhabdomyolisis, myoglobinuria can be found clearly three hours after the bite (Ranakawa, Lalloo, & de Silva, 2013; Warrell, 2010; Kakaria, Narkhede, Agrawal, Bhavsar, & Nukte, 2014). In this case, no myoglobinuria was detected and no signs of bleeding were found. This could be due to the varied signs and symptoms of bleeding based snake species. In this case neurotoxic manifestations such as dizziness, nausea, vomiting, ptosis, headaches, convulsions and acute respiratory failure were found. Pysical examination revealed that snake venom was neurotoxic, but not hematotoxic, cardiotoxic, myotoxic or renotoxic. Therefore, it is important to identify the type of snake for diagnostic and therapeutic purposes.

Pathophysiology of Respiratory Failure

Decreased consciousness, seizures with history of vomiting in this patient was due to neurotoxic manifestation of cobra (Naja spp) venom which attacked the neuromuscular junction (Ranakawa, Lalloo, & de Silva, 2013; Warrell, 2010; Kakaria, Narkhede, Agrawal, Bhavsar, & Nukte, 2014). Immediate management in this patient was possible because he was directly sent to the hospital. Cobra toxin effects could be irreversible if patient's arrival was delayed. The results of blood gas analysis shortly after the patient was intubated didn't show a significant increase in their CO_2 pressure. Respiratory failure in snake bite cases occurs because neurotoxins of snakes spread to neuromuscular junction and damage the nerves both in pre-synapses, post synapses and in the central. This resulted in paralysis of the skeletal muscles including respiratory muscles, palate, palpebral and extremities.

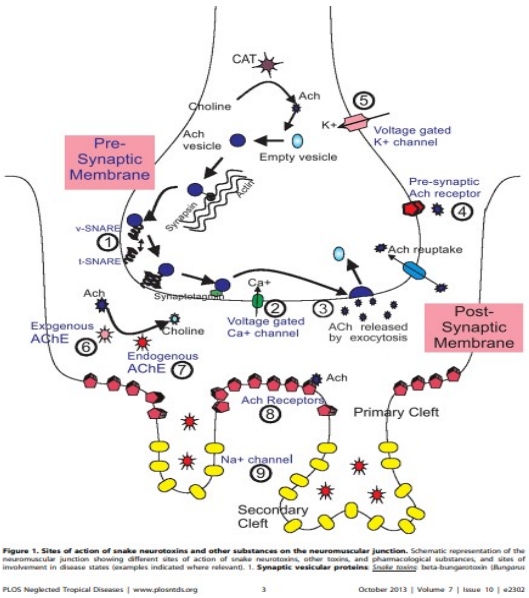


Figure 1. Neurotoxic mechanism in snakebite

Under certain conditions, snake bites might cause hypotension leading to severe shock due to cardiovascular effect from poisons or secondary effects such as hypovolemia, release of inflammatory vasoactive mediators, hemorrhagic shock, or rarely primary anaphylaxis induced by the poison itself (Ranakawa, Lalloo, & de Silva, 2013). In this case, the patient didn't experience shock, his vital signs were normal. This might be caused by the neurotoxic type of Naja spp poison while shock cases mostly found in cardiotoxic snake bites (Hifumi, et al., 2015; Djunaedi, 2009; Anil, et al., 2010). Snake bites might lead to cardiac arrest following hyperkalemia due to rhabdomyolysis after bites of certain krait, and Russell vipers. In this case, the patient did not experience cardiac arrest. But it was necessary to monitor electrolytes, especially hyperkalemia and kidney function. Another emergency clinical situation was the possibility of kidney failure and septicemia, which was triggered by necrosis of bite wound. This might happen if hospital admission was delayed. In this case, fortunately, the patient was taken to hospital one hour after being bitten. Kidney function was found normal, shown by ureum and creatinine within normal limits.

Management of Respiratory Failure due to Snake Bite

Respiratory failure was a complication of acute neuromuscular paralysis due to inhibition of snake toxins in the neuromuscular junction. This inhibition can occur in pre-synapses, post synapses or autonomic ganglia. Patient in this case experienced a type II (hypercapni) respiratory failure (Sanmuganathan, 1998; WHO, 2010; Agrawal, et al., 2001). In general, lungs was in good condition, without infection and no other abnormalities found in its parenchyma. Management of respiratory failure by intubation and ventilators was needed to support ventilation functions while protecting the lungs from pneumonia aspiration. Meanwhile, to restore respiratory function and other organs due to paralysis, it was necessary to do causative treatment (Anil, et al., 2010).

Causative therapy

Antivenin therapy were first described by Albert Calmette in the Institute of Pasteur, Saigon in 1890. Antivenin was an immunoglobulin purified from horse plasma, donkeys or sheep that were immune with one or more species of snake toxin. Monovalent antivenin (monospecific) neutralized toxins from one snake species. Polyvalent antivenin neutralized toxins from several species of different snakes, usually the main ones that had adverse medical effect, in certain geographical area. Antibodies that were raised against poisons from one species may have cross neutralization activity against other poisons, usually from closely related species. This is known as paraspecific activity. Antivenin is indicated when there is one or more of the following: hemostatic abnormalities, neurotoxic signs, cardiovascular abnormalities, acute kidney injury, hemoglobinuria and rapid expansion of

swelling. In Indonesia, government supplied polyvalent antivenin and it was derived from antibodies against the poison Ankystrodon, Bungarus, and Naja sputarix (Warrell, 2010) (Kakaria, Narkhede, Agrawal, Bhavsar, & Nukte, 2014) (Hifumi, et al., 2015).

Table 2. Guideline for antivenin therapy according to Luck (Djunaedi, 2009).

Grade	Envenom severity	Teeth	Edema/ erythema (cm)	Systemic symptoms	Number of vial
0	none	+	<2	-	0
I	Minimal	+	2-15	-	5
II	Moderat	+	15-20	+	10
III	Severe	+	>30	++	15
IV	Severe	+	<2	+++	15

In this case, patient received 15 vials of SAV in total administered in Dextrose 5% infusion. He experienced severe systemic symptoms including respiratory failure and classified as Grade IV.

Classification

Grading of snakebite severity cases were divided into four grades, generally symptoms appear in 2-6 hours after the bite (Niasari & Latief, 2003).

Table 3 Classification of venomous snakebite (Niasari & Latief, 2003).

***Crotalidae* famili**			***Elapidae* famili**		
Grading	**Severity**	**Signs and symptoms**	**Grading**	**Severity**	**Signs and symptoms**
1	Minor	Bite marks, no edema, no pain, no systemic symptoms, no coagulopathy	0	None	History of snakebite, local edema with strokes, no neurological disorder
2	Moderate	Bite marks, local edema, no systemic symptoms, no coagulopathy	1	Moderate	Grade 0 with neurological signs or with euphoria, vomiting, nausea, paresthesia, ptosis, paralysis, dyspnea
3	Severe	Bite marks, regional edema (2 segments from extremity), pain not resolved with analgetics, no systemic symptoms, with coagulopathy	2	Severe	Grade 1 symptoms with repiratory muscle paralysis in the first 36 hours
4	Major	Bite marks, extensive edema, systemic symptoms (vomiting, headache, abdominal and chest pain, shock), systemic trombosis			

Anti-cholinesterase

Snake venom contains complex enzymes, polypeptides, non-enzymatic proteins, nucleotides and other substances. Cobra snake poison (Naja spp) as in this case, neurotoxins that act on post synapses (α-neurotoxin) were bound to nicotinic type acetylcholine receptors in the muscles, also called thee-finger toxin (Agrawal, et al., 2001) (Niasari & Latief, 2003). Provision of anti-cholinesterase must be accompanied with administration of atropine sulfas.

Atropine was given to prevent undesirable muscarinic side effects of anti-cholinesterase, such as bradycardia, hypersalivation and sweating. This snake poison was nerve-damaging and could be irreversible if it is delayed. Research showed time over 210 minutes since snakebite as an irreversible time limit of damage (Anil, et al., 2010). Administration of anti-cholinesterase in patients with neurotoxics might overcome post synapse neurotoxic blocks, but did not play a role in overcoming pre-synapse or central blocks. The types of drugs used include neostigmine and prostigmine, which were given together with atropine sulfate, to avoid respiratory muscle paralysis, respiratory failure, and death. Neostigmine dose given 0.01-0.04 mg / kg every 1-3 hours or continuous intravenous with a maximum dose of 10 mg / 24 hours. An anticholinesterase trial: atrophine sulfate 0.6 mg followed by prostigmine 0.02 mg / kg im or endrophonium 10 mg iv for cobra bite were recommended by WHO (Anil, et al., 2010) (Sanmuganathan, 1998). Patient was given 10: 5 ampoules of athropine sulphate and neostigmine within 24 hours (Sanmuganathan, 1998). Substitution of intravenous preparations for oral mestinon was carried out on day 5.

Supportive therapy

Tabel 4. Indications of Mechanical Ventilators in Breath Failure due to Snake Bites (Agrawal, et al., 2001).

Respiratory rate	Apneu, no breath in 10 seconds, or RR>25-30/’
Respiratory pattern	Apneu, irregular respiration, agonal, gasping
Clinical signs and symptoms	Cough reflex (-), gag reflex (-), RR <10x/’, salivary retention, broken neck sign
Blood Gas Analysis result	pH <7,30, paCO2 >50 mmHg, severe hypoxemia, PaO2 <60 mmHg in FiO2>50% or PaO2 <40 mmHg in any FiO2
Ventilatory Support Profilaxis	To reduce pulmonary complication Severe cyanosis Coma

In this case the patient had not shown signs of severe acute hypercapni, PH was still 7.34 with PaCO2 37.4 and PO2 158, blood gas analysis was done after the patient was intubated, and may interfere with the results. In addition the patient was also immediately resuscitated, hindering severe acidosis. Ventilator support was given according to the patient's respiratory conditions, while administering causative therapy in the form of snake antivenin and anti-cholin esterase. Patients remained in comatus state, could breathe spontaneously, but clinical signs of muscle paralysis was found such as ptosis, limb weakness and shortness of breath. Extubation was carried out on the fifth day after clinical improvement of ptosis, limb muscle strength, respiratory muscle strength, based on improvement criteria for blood gas analysis. The FASTHUG bundle was undertaken, but preventative thromboprophylaxis was not performed. This patient should still be given thromboprophylaxis considering the risk of thrombus. Giving 2x5000 heparin subcutan units could be an option.

Additional therapy

Additional therapy included management of bite site from infection, including the use of broad-spectrum antibiotics immediately (amoxicillin, cephalosporin, gentamicin plus metronidazole) and tetanus prophylaxis (Sanmuganathan, 1998). In this patient, an increase in the number of leukocytes at entry (29,400) was found and might be due to the inflammatory reaction caused by snake venom that the body responded. According to WHO guidelines, it was necessary to administer broadspectrum antibiotics, as an option one of which was Ceftriaxone 1x2 gram iv. Ceftriaxone administration showed a good response, with a significant decrease in the number of leukocytes the following day. Ceftriaxon was given until signs of infection improve. In addition, monitoring of vigilance against the occurrence of compartement syndrome in the bite area was needed. Fasciotomy was performed because there was a clear tension (intra-compartment pressure> 40 mmHg in adults), weakness, hypoaesthesia, pain in passive stretching of compartments on palpation (WHO, 2010). However, before fasciotomy, normal hemostatic function must be confirmed. In this case, fasciotomy was done because the bitten limb showed compartment syndrome.

CONCLUSION

Management of snake bites is very dependent on the type of snake venom. Snake venom can be neurotoxic, cardiotoxic, myotoxic, renotoxic or hematotoxic. Careful history, physical and laboratory examination are needed to determine the type of snake venom. Respiratory failure in cases of neurotoxic snake bites in this case was diagnosed based on clinical symptoms of acute neuromuscular paralysis and laboratory results.

Gold standards of treatment given to patients include antivenom and anti-acetylcholine esterase (causative therapy), ventilator support (supportive therapy) and prophylactic infections of the bitten limb (additional therapy). Early diagnosis, early transportation to the hospital and also adequate management of neurotoxin snake bites are very important to achieve optimal results

References

Agrawal, P. N., Aggarwal, A. N., Gupta, D., Behera, D., Prabhakar, S., & Jindal , S. K. (2001). Management of Respiratory Failure in Severe Neuroparalytic Snake Envenomation. *Neurology India, 49*(1), 25-8.

Anil, A., Singh, S., Bhalla, A., Sharma, N., Agarwal, R., & Simpson, I. (2010). Role of Neostigmine and Polyvalent Antivenom in Indian Common Krait (Bungarus Caeruleus) bite. *Journal of Infection and Publich Health, 3*, 83 -87.

Djunaedi, D. (2009). Penatalaksanaan Gigitan Ular Berbisa. In A. W. Sudoyo, B. Setiohadi, I. Alwi, M. K. Simdibrata, & S. Setiadi, *Buku Ajar Ilmu Penyakit Dalam* (5 ed., p. 280). Jakarta: Interna Publishing.

Hifumi, T., Sakai, A., Kondo, Y., Morine, N., Ato, M., Shibayama, K., . . . Kuroda, Y. (2015). Venomous Snake Bites: Clinical Diagnosis and Treatment. *Journal of Intensive Care, 3*(16).

Kakaria, A., Narkhede, M., Agrawal, S., Bhavsar, A., & Nukte, V. (2014). A Study of Outcome of Neuroparalytic Snake Bite Patients Treated with FIxed Dose Antisnake Venom. *International Jounal Research in Medial Science (IJRMS), 4*(2), 1676-82.

Kasturirane, A., Wickermasinghe, A., de Silva, N., Gunawardena, N., Pathmeswara, A., Premaratna, R., . . . de Silva, H. (2008). The Global Burden of Snakebita: A Literature Analysis and Modelling Based on Regional Estimates of Envenoming and Deaths. *PLoS Medicine, 5*(11), e218.

kasturiratne, A., Wickremasinghe, A. R., de Silva, N., Premaratna, R., Savioli, L., Lalloo, D., . . . Pathmeswaran, A. (2008, 11). The Global Burden of Snake Bite: A Literautre Analysis and Modelling Based on Regional Estomates of Envenoming and Deaths. *PLoS Medicine, 5*(11), e218.

Niasari, N., & Latief, A. (2003). Gigitan Ular Berbisa. *Sari Pediatri, 5*(3), 92-93.

Ranakawa, U., Lalloo, D., & de Silva, H. (2013). Neurotoxicity in Snakebite: The Limits of Our Knowledge. *PLoS Neglected Tropial DIsease, 7*(10), e2302.

Sanmuganathan, P. S. (1998). Myasthenic Syndrome of Snake Envenomation: A Clinical and Neurophysiological Study. *Postgrade Med J, 74*, 596 - 599.

Warrell, D. (2010). *Guidelines for the Clinical Management of Snake Bites in the South-East Asian Region.* Thailand: World Health Organization. Regional Center for Tropical MEdicine, Faculty of Tropical Medicine, Mahidol University.

WHO. (2010). *Guidelines for The Production Control adn Regulation of Snake Antivenom Immunglobulin.* Geneva: World Health Organization. Retrieved from https://www.who.int/bloodproducts/snake_antivenoms/en/