

## Rapid Progressive Course of *Naja Naja Oxiana*-bitten Patient

Maliheh Rajabi<sup>1,2</sup>, Bita Dadpour<sup>3</sup>, Parastoo Rahimi<sup>4</sup>, Mohammad Moshiri<sup>3\*</sup>

1. Department of Chemistry, Faculty of Science, Payame Noor University, Mashhad, Iran
2. School of Nursing and Midwifery, Mashhad University of Medical Sciences, Mashhad, Iran
3. Medical Toxicology Research Center, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
4. Veterinary Faculty of Islamic Azad University, Science and Research Branch, Tehran, Iran



### ABSTRACT

Cases of snakebites especially with an elapidae are considered as a medical emergency. However, in some cases of elapidae envenomation, bite signs might be unpredictable.

**Case:** Dorsal surface of the second finger of a 39-year-old man was bitten by *N. Naja Oxiana* less than half hour before his admission. On arrival, patient had clear bilateral ptosis, mydriasis, reduced light reflex of pupils and sialorrhea. Other muscles power had no problem. The patient was agitated due to suffocation secondary to respiratory muscle paralysis, during half hours of hospitalization. He was intubated and mechanically ventilated. He was treated by antivenom, 10 vials as attack dose, 5 vials as repeated dose that was repeated three times and 2 vials every 8 hours as maintenance dose. He received antibiotic for local superinfection. Although, he did not receive any acetylcholinesterase inhibitors, he was extubated 48 hours later. The patient was discharged on the 7<sup>th</sup> day in good general condition with oral antibiotic prescription and no complication except local cellulitis. In conclusion, for efficient treatment of patients bitten with elapidae, we need to find the best course of treatment using the adequate antivenom as fast as possible.

**Keywords:** Snake Envenomation, Antivenoms, Elapid Snakes, Neurotoxin Disorders

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**\*Correspondence:** Mohammad Moshiri; Email: Moshirim@mums.ac.ir

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## Introduction

There are 3,500 species of snakes all around the world, which can be divided into three categories including toxic, semi-toxic, and none-toxic. The toxic group includes elapidae and viperidae (1).

Cases of snakebites especially with an elapidae are considered as a medical emergency. Although, the level of toxicity depends on many factors (1). Clinical signs in snake bites are mainly due to the effect of alphaneurotoxin, cardiotoxin and hematotoxin, however, in some cases of elapidae envenomation, bite signs might be unpredictable (2, 3).

A 39-year-old man was bitten by elapidea who developed respiratory arrest very soon. The rapid onset of neurological symptoms in this patient was notable, which made it a rare case that should be reported.

## Case report

On April 2, 2019, a 39-year-old male patient was admitted to Toxicology Emergency Unit of Imam Reza Hospital, Mashhad at 3:30 pm. He got bitten half an hour before admission. While he was sightseeing around the city, he sat on a rock, and suddenly, felt a burning sensation on his left hand and noticed a big, long snake beside him. He came to the emergency room immediately. He was bitten on the dorsal surface of the second finger. On arrival, patient had clear ptosis of the eyelids alongside mydriasis and pupil's response to light was slow. He also had sialorrhea. However, other muscles including the muscles of head, neck, limbs, and trunk had no problem. Patient's gag reflex was normal. His vital signs were as following: Pulse rate= 85 beats/min, Blood pressure= 130/80 mmHg, Respiratory rate = 18 cycles/min, and electrocardiogram results included Rate= 71 beats/min, Axis= 52°, QTc= 380 msec, QRS= 80 msec, without any ST and T changes.

A common sign for snake bites is the presence of two puncture wounds from the animal's fangs, which was confirmed in this

case. However, other signs such as redness, swelling, bleeding or blisters were not observed. The bitten finger was splinted and placed at the same level of the heart.

At 4 PM, the patient was agitated due to suffocation secondary to respiratory muscle paralysis, however, he was able to understand the medical team's conversations clearly and answered them with no struggle. The bag-valve-mask (BVM) ventilation was performed immediately. In order to keep him relaxed, the medical team informed him about his condition and assured him that they were totally aware of his situation and they were performing all necessary actions. Then, he was treated by lidocaine, midazolam, and fentanyl to tracheal intubation, however, initial attempts were unsuccessful due to the patient's drug addiction, past history of cervical disk surgery, neck prosthesis, and anterior position of his larynx. Therefore, the patient was intubated under GlideScope guidance using 200 mg of propofol, 400 mg of fentanyl, and 4 cc of lidocaine. He was treated by infusion of fentanyl 100 mg/h and midazolam 5 mg/h with monitoring of blood pressure, and he was ventilated mechanically.

At 4:30 pm, the antivenom (hexavalent snake antivenom immunoglobulin, 10 mml, Razi institute, Iran) infusion was started according to the protocol (1). At first, 10 vials were injected slowly over a one-hour period. Injection speed started slowly, and then, increased.

At 9 pm, the patient was transferred to intensive care unit (ICU). Within 24 hours after ICU admission, vital signs were normal, however, sinus bradycardia (42-52 beats/min) were reported but no specific treatment were taken regarding bradycardia due to the patient's normal blood pressure and stable hemodynamic. His wound was bandaged and tetanus vaccine and immunoglobulin were given. Because the coagulation tests were normal, heparin 2000 U was administered every 12 hours. The lab tests results are summarized in Table 1.

**Table 1.** A summary of laboratory results of case bitten by *Naja Naja Oxiana* treated in Imam Reza Hospital, 2019

Day	1		2		3	4	5	6
Time⇒	15:30	20:00	8:00	20:00	8:00	8:00	8:00	8:00
Lab Test (Unit)↓								
White blood cells (×1,000)	8.5	14.1	15.7	10.4	8.3		9.1	9
Hemoglobin (mg/dL)	15.1	14.7	15.6	12.1	12.7		12.8	12.8
Hematocrit (%)	42.6	41.3	42.5	33.9	34.9		34.7	35.7
Platelets (×1,000)	221	257	143	143	225		244	230
Phosphorus (mg/dL)		3.2						
Potassium (mEq/L)		3.7		3.5	3	3.4		3.4
Calcium (mg/dL)		9.3						8.7
Sodium (mEq/L)		141		135	141	138		134
Magnesium (mg/dL)		1.9						
Creatinine (mg/dl)		1.0		1.0	1.0	1.0		1.1
Urea (mg/dl)		40		23	21	16		19
Blood sugar (mg/dL)		120		93	111	121		
Alkaline phosphatase (U/L)		187						
Alanine aminotransferase (U/L)		19						
Aspartate aminotransferase (U/L)		17						
Prothrombin time (seconds)	11.5	14.6	11.7	14.5	13.2	13.6	14.8	14.9
International normalized ratio (INR)	0.93	1.14	0.93	1.13	1.06	1.05	1.09	1.19
Partial thromboplastin time (second)	21	63	23	28	30	36	24.8	30
PH		7.38		7.39				
PO <sub>2</sub> (mmHg)		58.2		58.2				
PCO <sub>2</sub> (mmHg)		41		41				
HCO <sub>3</sub> (mEq/L)		24		24				
Base excess		0.2		3.9				
O <sub>2</sub> sat (%)		86.7		44.8				
C-reactive protein (CRP)							Negative	
Erythrocyte sedimentation rate (min)							24	

According to the comments of infectious disease specialist, cefazolin was started (one gram every 6 hours). Due to the lack of improvement in patient's breathing and diaphragm paralysis, 5 vials of antivenom were injected three times every six hours, and then, 2 vials were administered every 8 hours for 24 hours. Also, according to the neurologist consult, the patient was not a candidate for Physostigmine administration. After 48 hours and discounting patient's sedative drugs, gradually, his respiratory muscles function improved and he was able to breathe spontaneously, thus, he was extubated, while he was fully conscious. Given the patient's history of addiction, he received 2.5 mg of methadone (subcutaneously) every 12 hours. Bradycardia was also eliminated at this time. In the same time period, the ptosis and sialorrhea were also eliminated and there was no need for suction.

On the third day of ICU hospitalization, the liquid oral intake was started and the patient was transferred to the poisoning ward. Also, due to local swelling of his left hand, soft tissue

sonography and Doppler sonography of the upper extremity vessels were requested. Ultrasound of the left hand revealed inflammation and edema and subcutaneous soft tissue strain with no abscess or collection, and Doppler color examination revealed increased arterial blood flow due to distal limb inflammation. The possibility of compartment syndrome was rejected by orthopedist.

On the fourth day, regular diet was started. On the fifth day, the amount of wound secretion increased but his sedimentation rate (ESR) was 24 minutes and C-reactive protein was negative. According to the infectious disease specialist comments, the antibiotics regime was changed into clindamycin 900 mg every 8 hours and ciprofloxacin 400 mg every 12 hours. The patient was discharged on the 7<sup>th</sup> day in good general condition with oral antibiotic prescription and recommendation for outpatient visit to the orthopedic clinic due to deep surface cellulitis without any abscess.

## Discussion

Cobra bites are among the most dangerous bites, which kill a large number of people in Asian countries annually. Most of these patients lose their lives due to their late arrivals in clinic centers or choosing a clinic without enough facilities (3, 4).

The venom of cobra snake is a neurotoxin that shows signs of neuromuscular paralysis and is the leading cause of death. Two types of neuromuscular toxins with pre- and post-synaptic blockings properties have been identified in venom of cobra snakes (2, 3). Presynaptic neurotoxins belong to phospholipase A2 toxins. This toxin is abundant in *Naja Naja Oxiana*, which is the native snake of the region. Therefore, it is likely that our patient had been bitten by it. This toxin targets motor nerve terminals, such as the neuromuscular junction, and enters the cell through binding to the terminal axons and endocytosis. In consequences, the number of synaptic vesicles is depleted and acetylcholine secretion is inhibited (5, 6). This process is an irreversible process, and therefore, its recovery requires nerve regeneration and time (7). This is a good interpretation for treatment with acetylcholinesterase inhibitors (AChEIs), such as physostigmine, which is not satisfying in presynaptic toxin intoxication, and synaptic remission requires a long period of time (8), therefore, in case of complete paralysis, it may require a long time to recover. Thus, well-timed actions and quick diagnosis is very important. In this patient, early diagnosis, and sufficient amount of antivenom, which neutralized the toxin in patient's circulatory system, helped reducing the patient's treatment time.

In this case, diaphragm and respiratory muscles paralysis occurred approximately one hour after the bite, which occurred much faster than expected. These symptoms usually occur within the first 3 to 24 hours after bites (3, 9). The one-hour delay is required for toxin to attach to the axon and exert its activity, therefore, there is usually a delay between the onset of symptoms and the time patient was bitten (1, 3, 9). In the current patient, the symptoms (ptosis) had developed in less than half an hour after the bite. However, given the patient's symptom on arrival, the medical team diagnosed rapidly and used antivenom as soon as possible. Even though, patient showed respiratory paralysis and

respiratory problems prior to that. Therefore, the appearance of symptoms of facial or local muscle paralysis in a patient with a cobra snake can be a sign for future respiratory paralysis, although it may be unpredictable at the time (1).

Venom of cobra snake contains post-synaptic toxins, which are also found in *Naja naja Oxiana*, the native snake of the region (10). These toxins bind to the acetylcholine receptor at the neuromuscular junction and cause paralysis. This does not damage the cell, and therefore, it is reversible with antivenom, and there is no need to prescribe acetylcholinesterase inhibitors (3), although some authors recommend treatment with these drugs for postsynaptic paralysis as adjuvant therapy (1). In the current patient, as antivenom therapy improved his symptoms and stopped the progression, while he was ventilated mechanically, no acetylcholinesterase inhibitors were administered.

In this patient, due to life-threatening symptoms, 10 vials of antivenom were initially infused as attack dose. Then, due to lack of proper response and progressive symptoms, he received another 5 vials of antivenom three times a day. Antivenom therapy had been continued until the physicians were convinced that there is no new symptom or symptom progression was stopped and the remained symptoms were related to the presynaptic blocking and the patient should be given time.

In conclusion, for efficient treatment of patients bitten with *Elapidae*, we need to find the best course of treatment using the adequate antivenom as fast as possible.

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## Authors' contributions

M.M and B.D find the case and treated him; M.R and P.R wrote the manuscript search on the literatures; P.R and M.M edited them. All authors accept final draft. M.M. is corresponding author.

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### Informed Consent

The informed consent was obtained from the patient.

### Conflicts of interests

The authors declare that there is no conflict of interests.

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