A Young Girl Presenting with Acute Respiratory Failure and Paralysis Due to a Suspected Taiwan Banded Krait Bite

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Abstract
We describe the clinical course of a 13-year-old Taiwanese girl presented with a change in consciousness (GCS: E1VeM1), generalized paralysis, and respiratory failure accompanied with transient hypertension. She required ventilator support for six days and all the neurologic deficits gradually recovered. We considered all the differential diagnoses of acute paralysis and respiratory failure. Neurotoxic snake bite was highly suspected. Her serial neurologic examinations were recorded in detail. If one has a clear understanding of the evolution of characteristic features, a specific diagnosis and treatment are possible. (J Pediatr Resp Dis 2013;9:69-73)

Key words: Acute respiratory failure, Mechanical ventilation, Envenomation, Taiwan banded Krait, Neurotoxic snake, Bungarotoxin.

INTRODUCTION
Envenomation by one of the six common species of venomous land snakes in Taiwan mountain areas is common. It is often impossible to identify the offending snake after envenomation. Clinical manifestation after snake bite often falls into either the neurotoxic or the hemotoxic group.1-3 In Taiwan, three venomous snakes, the sharp-nosed pit viper, the Taiwan Habu and the bamboo viper, produce hemotoxins. However, the Taiwan cobra and the Taiwan banded krait produce neurotoxins. Mixed toxins, combining hemotoxins and neurotoxins, are secreted by Russell’s pit viper.1 In the past, patients often received both the anti-hemorrhagic and anti-neurotoxic polyvalent anti-venom for treatment.

We report the clinical course that a girl presented with acute respiratory failure, brainstem dysfunction and appeared to be in a coma status.

CASE REPORT
A 13-year-old previously healthy girl lived on a mountain located in the middle of Taiwan. In autumn of 2009, she was bitten by an unknown animal at midnight while she had been sleeping home. The wound was small and bled. At that time, there was one lizard found on her bed. One hour later, she presented to the emergency department (ED) of a regional hospital with epigastric pain, dizziness, and mild numbness of her mouth and hands. Acute gastritis was impressed. After symptomatic treatment, discharge was arranged. The numbness progressed and tremor of her four extremities was noted about 5 hours after the bite. She could not swallow any oral medication in pill form. On her way back to the ED, consciousness change, extremities paralysis, and cyanosis were noted. Blood pressure was 158/97 mmHg, pulse rate was 147 beats/min and body temperature was 36.5°C. There was no spontaneous
breathing and pupils were dilated. Endotracheal tube was inserted with mechanical ventilation. Emergent brain computed tomography showed no evidence of hemorrhage or mass lesion. After initial stabilization, Glasgow coma scale (GCS) was scored as E1VeM1, the patient was transferred to a tertiary medical center. Because of hypertension and two small bite marks on her left fifth finger, two vials of neurotoxic snake anti-

venom were given on the way to the center about 9 hours after the bite.

On arrival at the ED of the tertiary medical center, 10 hour after the bite, the patient’s pupils were dilated without light reflex. (Figure 1) She presented with no spontaneous breathing and her four extremities were cold and wet. Her vital signs were blood pressure: 172/106 mmHg, pulse rate: 131 beats/min and body

| Table 1. All the neurology examinations during the first 7 days hospitalization. |
|---------------------------------|------|------|------|------|------|------|------|
| Highest BP (mmHg)               | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 |
| GCS                             | E3M6Ve| E3M6Ve| E3M6Ve| E4M6Ve| E4M6Ve| E4M6Ve| E4M6Ve|
| Highest BT(°C)                  | 36.9  | 37    | 37.4  | 37.7  | 37.4  | 37.3  | 37.2  |
| Highest HR                      | 131   | 126   | 114   | 123   | 128   | 114   | 121   |
| Spontaneous breathing           | (-)   | (+)   | (+)   | (+)   | (+)   | (+)   | (+)   |
| Ptosis*                         | Eye closed | +++ | +++ | ++ | ++ | + | normal |
| Pupils size (OU)/ light reflex  | 7mm/(-)| 6mm/(-)| 5mm/(-)| 4mm/(+) | 3mm/(+) | 3mm/(+) | 3mm/(+) |
| Extra ocular motion             | fixed | fixed | fixed | Upward and downward limited | normal | normal | normal |
| Corneal reflex                  | absent | (+) | (+) | (+) | (+) | (+) | (+) | (+) |
| Gag reflex                      | (-) | decreased | decreased | decreased | decreased | decreased | decreased | (+) |
| 11th CN function†               | Drowsy | Cannot evaluate | (+) | (+) | (+) | (+) | (+) | (+) |
| 12th CN function ‡              | Drowsy | Cannot evaluate | (+) | (+) | (+) | (+) | (+) | (+) |
| Deep tendon reflex              | absent | 3+ | 3+ | 2+ | 2+ | 2+ | 2+ |
| Babinski sign                   | (-) | (-) | (-) | (-) | (-) | (-) | (-) |
| Muscle power (Upper / Lower extremities) | 0 / 0 § | 2 / 3 | 4 / 4 | 5 / 5 | 5 / 5 | 5 / 5 | 5 / 5 |

BP: blood pressure. GCS: Glasgow Coma Scale. BT: body temperature. HR: heart rate. OU, both eyes. CN: cranial nerve.

* +++ severe ptosis, ++ moderate ptosis, + mild ptosis.
† 11th CN function: (+) Shoulder elevation.
‡ 12th CN function: (+) Tongue protruding.
§ Muscle power: all toes were scaled as 2.
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Figure 1. Negative pupillary light reflex: pupils dilatation, 12 hours after the bite.

Figure 2. The wound of envenoming (left small finger): minimal swelling and little hemorrhage, 12 hours after the bite.

temperature: 36.9 °C. In addition, a doctor found that the patient was able to move her toes on command. After being transferred to the pediatric intensive care unit, GCS was corrected to E1VeM6. Physical examination revealed that the wound at her left small finger was small with minimal local erythematous change and swelling. (Figure 2) The patient was drowsy and ventilator-dependent totally dependent on the ventilator. Oculocephalic reflex and deep tendon reflexes for the four extremities were all absent. Muscle power of the four extremities was absent except that her toes were scaled as two. Gag reflex could be observed during oral suction, but the reflex was weak. All the neurologic examinations are listed in Table 1.

During the hospitalization, as it was highly suspected that the patient had a neurotoxic snake bite, another six vials of neurotoxic snake anti-venom were administered about eleven to sixteen hours after the bite (a total of eight vials include two vials on the ambulance). Tetanus toxoid was also prescribed after admission to prevent tetanus infection. Hypertension and tachycardia were controlled by propranolol and doxazocin mesylate. We sent stool, gastric juice, and blood samples to the centers for disease control (CDC) to make a differential diagnosis between botulism and other neurotoxic causes of paralysis, and the results were all negative. On the second day in hospital, the patient could open her eyes spontaneously with obvious ptosis. Because of her drowsy consciousness and increased deep tendon reflex, we arranged an electroencephalography (EEG) and brain magnetic resonance imaging (MRI). The EEG showed no epileptiform discharge and slow activities diffusely with a rhythm ranging from 6 to 7 Hz, which means mild and diffuse cortical dysfunction. Brain MRI showed negative findings.

The ventilator mode was set to an assist control mode on the first day due to the patient being totally ventilator dependent. The ventilator rate setting was 18 breaths/min. There was normal breathing sound. Her saturation was 100% under room air supplement. Chest X ray showed negative finding. On the second day in hospital, some spontaneous breathing effort was observed. The ventilator setting was shifted to synchronized intermittent mandatory ventilation (SIMV) mode. However, there were still episodes of apnea. On the 7th day in hospital, the last neurologic deficits of ptosis and extraocular muscle paralysis subsided and extubation was performed. Afterwards, a Taiwan banded krait was found in the patient’s house. The patient felt mild but persistent muscle weakness for 2 months after discharge.

DISCUSSION

We assumed that this girl presented acute paralysis and respiratory failure after dysphagia due to a neurotoxic snake bite, although the serology commercial kit to detect the Taiwan spectacle cobra bite was not done in this patient. The respiratory failure was not the result of bronchospasm or alveolar lung disease. It was caused by peripheral muscle paralysis. In addition, her wound was small and little hemorrhagic. Thus, the clinical doctor easily ignored the possibility of envenomation. According to the presentation of the wound, we could
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not differentiate a snake bite from a lizard bite. It was reasonable to suspect a snake bite because there is no toxic lizard in Taiwan. We believe that the Taiwan banded-krait found at the patient’s home was perhaps pursuing its food, the lizard. Then the krait accidentally bit the patient’s left fifth finger while she was sleeping.

There have been several reports about krait bites occurring at night while people were sleeping in the fields or on the floors of huts in India. It is important for clinical doctors to identify krait bite by detailed history taking. We should keep in mind that patients perhaps go to the hospital before neurotoxic symptoms onset, and most of the onset symptoms are nonspecific. Besides, late onset of respiratory failure will occur after a Taiwan banded krait bite. Anyone who is suspected as being bitten by an unknown snake should be placed under observation for eight hours or more. Cranial nerve dysfunction, such as ptosis, pupils dilatation, limited extra-ocular mobement (EOM) and diminished gag reflex, even no spontaneous breathing could be related to the toxin blocking the receptor at the neuromuscular junction.

There are two types of neurotoxic snakes in Taiwan, the Taiwan banded krait and the Chinese cobra. Neurotoxic snake bite in Taiwan is not an unusual issue, and the diagnosis depends on history and clinical symptoms. The Taiwan banded krait has strong venom, and the toxic symptom include numbness, abdomen pain, ptosis, diplopia, inarticulate, drooling, and pupil dilation at the early stages. Then, the numbness will progress in the direction to the heart and fatal respiratory muscle paralysis will occur several hours later. The standard treatment is anti-venom injection within a reasonable period of time as the administration of anti-venom eight hours after the bite will not help the patient to recover from respiratory failure because the neuromuscular junction will have been damaged. If the patient cannot receive the anti-venom in time they require ventilator support to stabilize the patient and wait for recovery. The local symptoms of Taiwan banded krait bite are generally mild painful, with little hemorrhage and swelling. Our patient had a typical wound presentation, which was difficult to detect needle-like tooth marks. (Figure 2)

Bungarotoxin from the Taiwan banded krait has been found since 1944, and its curare-like properties and site of action have been well-studied since the 1960s. The site of action was primarily peripheral in origin and blocking takes place at the neuromuscular junction. Three types of bungarotoxin have been isolated: alpha-, beta-, and gamma-bungarotoxin. Alpha-bungarotoxin blocks neuromuscular transmission by an irreversible combination with the motor end-plate acetylcholine receptor, leading to failure of muscle contraction. Thus, it resulted in not only skeletal muscle but also fetal respiratory muscle paralysis. Whereas beta- and gamma-bungarotoxin exhibit neuromuscular function at presynaptic sites by causing acetylcholine release and depletion. In addition, the entire parasympathetic nervous system and preganglionic neurons of the sympathetic nervous system are cholinergic, which means related to the neurotransmitter acetylcholine. As we know, acetylcholine is a neurotransmitter, which acts on two types of receptors, the nicotinic and muscarinic receptors. In parasympathetic nerve transmission, acetylcholine acts in two stages: When stimulated, the preganglionic parasympathetic nerve releases acetylcholine and acts on nicotinic receptors at the effector organs. Because parasympathetic nerve is more acetylcholine dependent than sympathetic nerve, we can postulate that when the acetylcholine receptors are blocked, the sympathetic activity will surpass parasympathetic activity and cause the hypertension. Our patient had tachycardia with hypertension. The symptoms are characteristic sign of increased sympathetic tone and matched bungarotoxin effect on automonic nerve system. Snake anti-venom use promptly is crucial for patients bitten by the Taiwan banded krait; because the irreversible blocking of alpha-bungarotoxin will limit the anti-venom function after eight hours after envenomation. This patient received a total of 8 vials of anti-venom about nine hours after envenomation. There was persistent respiratory failure after the antivenom use.

According to the reports in the literature, Bungarotoxin is a big molecular which is theoretically hard to cross the blood-brain-barrier. However, the
basal forebrain, and brainstem complexes are also cholinergic. There were still reports which demonstrate that alpha-bungarotoxin is also a selective antagonist of the α7 nicotinic acetylcholine receptor in the brain. In our patient, dizziness was also the initial complaint. Conscious change without response presented at the first ED. Although she could sometimes follow the instructions of the doctor to move her toes, she was sleepy and could not remember how she was transferred and treated in the first two days in hospital. In addition, increased deep tendon reflex, which was noted on the second day in hospital, suggested upper motor neuron signs. Thus, we conclude that Bungarotoxin perhaps cross the blood-brain-barrier at low dosages. Further research in this field is warranted.

We also considered other differential diagnoses with regards to acute paralysis, including autoimmune disorder such as Guillain-Barre syndrome, transverse myelitis; food borne illness such as botulism or swellfish poisoning; electrolytes imbalance such as hypokalemia, hypomagnesemia hypophosphatemia or hypocalcemia; and rare infectious disease such as poliomyelitis. We had excluded above possibilities by laboratory tests and brain MRI. Regarding the possibility of botulism, we traced the food intake history of the patient to rule this out. Her family denied the patient had ingested honey, marinated meat, swellfish, or dried bean curd recently. Furthermore, she did not have any other dirty wounds. A blood sample to CDC also did not find evidence of botulism intoxication.

CONCLUSION

According to the patient’s presentation, we should keep in mind that cranial dysfunction symptoms, such as pupils dilatation, negative oculocephalic reflex and no spontaneous breathing, are not equal to brainstem death. Reviewing the patient’s serial symptoms, if anyone has gastrointestinal symptoms and rapidly progressing paralysis and respiratory failure. Toxin, especial neurotoxic snake bite should be one of the differential diagnoses.

REFERENCES