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Case Report

Extraocular Muscle Paresis Caused by Snakebite

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A 51-year-old man presented with binocular diplopia on the three days after the snakebite in the fifth finger of the right hand by an *Agkistrodon blomhoffi* (mamushi). In the primary position he had an exotropia and right hypertropia, which became apparent when his head was tilted to the right. From ocular angle of deviation measured by synoptophore and Hess chart test, he was diagnosed as having medial rectus muscle paresis as well as inferior oblique muscle paresis of the left eye. Elevation deficit on right gaze in the left eye had remained during three days. Our case suggested that the occurrence of subjective binocular diplopia is an important clinical sign for the onset of general abnormalities caused by snakebite.

There are only 2 types of venomous snake, *Agkistrodon blomhoffi* (Japanese pit viper, “mamushi” in Japanese) and *Rhabdophis tigrinus* (“yamakagashi” in Japanese), in the Japanese Temperate Zone.

Although the venom of *A. blomhoffi* mainly consists of hemolytic toxins, it has thin neurotoxin which sometimes leads to myasthenia gravis⁽¹³⁾⁽²⁾. Some report that the patient bitten by *A. blomhoffi* has extraocular muscle palsy caused by neurotoxin. However, the majority of bitten patients have solely medial rectus muscle palsy⁽⁵⁾⁽¹²⁾, and cases accompanied by inferior oblique muscle are very rare.

CLINICAL CASE

A 51-year-old man, who had been treated with antivenom for snakebite of *Agkistrodon blomhoffi* (mamushi) two years before, was admitted to an emergency room because he was again bitten by a snake in the fifth finger of the right hand. He recognized the snake as *A. blomhoffi* by its appearance, and tied up his upper arm with a vinyl cloth and brought himself to our hospital on foot.

His injured finger was markedly edematous, and the wound was incised and disinfected. He was given with 6000 units of equine freeze-dried antivenom after the desensitization. On the following day, creatin kinase (CK) value and C reactive protein (CRP) value rose up to 895IU/l and 0.44mg/dl, respectively. The edema, pain and hemorrhage in the right arm persisted for three days, but no necrotic changes were seen around the injury. He did not have eye symptom at the first time of snake bite two years ago. But now he felt diplopia on the third post-injury day. Corrected visual acuity was more than 20/20 in both eyes and no abnormal changes in refraction and pupil reactions were observed. In the primary position he



FIGURE 1. Diagnostic position of photograph on the 4th day after the snakebite. Exodeviation and hypertropia with left eye fixating is seen at the primary position. Ocular motility does not show obvious limitation.



FIGURE 2. Head tilt tests showed abnormalities in extraocular muscle reactions.

FOS			UP10°	FOD			
RIGHT 10°	-2° R/L9° IN 8°	-1° R/L3° IN 6°	-1° R/L3° IN 6°	-1° R/L6° IN 5°	±0° R/L4° IN 2°	+1° R/L2° IN 2°	LEFT 10°
	-2° R/L9° IN 8°	-1° R/L3° IN 6°	-1° R/L2° IN 6°	-2° R/L7° IN 5°	-1° R/L5° IN 2°	±0° R/L3° IN 2°	
	-2° R/L7° IN 7°	-1° R/L3° IN 6°	-1° R/L2° IN 6°	-1° R/L5° IN 5°	±0° R/L3° IN 5°	+1° R/L2° IN 2°	
DOWN 0°							

FIGURE 3. Ocular deviation in diagnostic position of gaze measured by using synoptophore.

had an exotropia of 4 prism diopters (PD) and right hypertropia of 4PD at distance and an exotropia of 10PD and right hypertropia of 5PD at near measured by prism and alternate cover test, respectively. Obvious limitation of the eye movement was not seen (Figure 1). Left hypertropia became apparent when his head was tilted to the right (Figure 2). Right eye hypertropia measured by using synoptophore was greatest on attempts to look right upgaze with fixation on the left eye; i.e., -2° horizontal, 9° vertical and 8° intorsion (Figure 3). Hess chart also showed insufficient motility of the left eye at right upper gaze with the fixation on the left eye (Figure 4). The patient was diagnosed as having paresis of the medial rectus muscle and inferior oblique muscle of the left eye based on these results. On the sixth post-injury days, the patient felt regression of diplopia, and CK and CRP values returned to normal levels. After the recovery, his eye position showed neither exotropia nor hypertropia.

SNAKE BITE AND OCULAR MUSCLE PARESIS

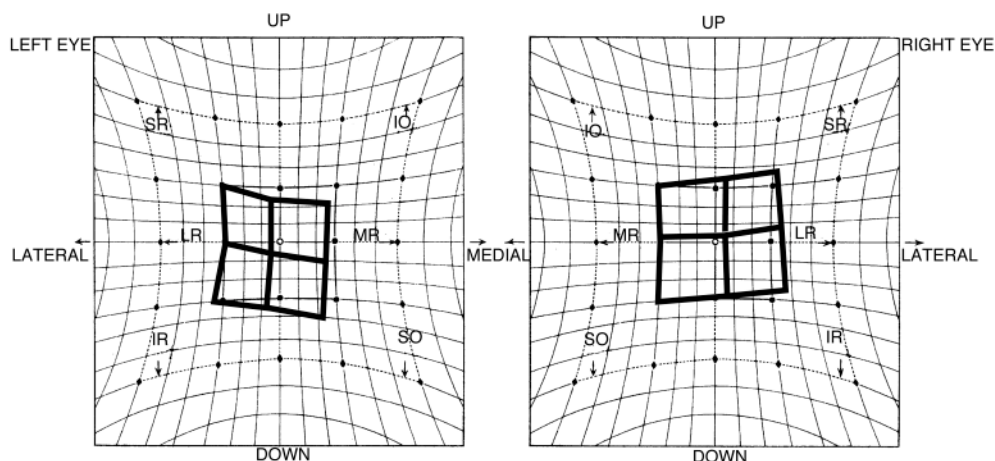


FIGURE 4. Hess chart showed a greatest right eye hypertropia on right up gaze.

No angle of deviation was seen in the head tilt position. Defective movements in right up direction were not observed by using synoptophore or Hess chart test.

DISCUSSION

After snakebites by *A. blomhoffi*, focal edema, ache, focal necrosis, muscle degeneration⁽¹⁰⁾, disseminated intravascular coagulation or hemolysis and acute renal failure⁽⁹⁾ have been reported. Extraocular muscle palsy is not a rare symptom in the patients with snakebites by cobra whose venoms are mainly neurotoxin⁽⁷⁾. Venoms of *A. blomhoffi* mainly consist of hemorrhagic or thrombotic toxin⁽⁶⁾⁽¹⁴⁾, but they also have faint neurotoxic effects that lead to ptosis and/or diplopia in mild cases and myasthenia gravis in severe cases. In Japanese literature, although some cases of extraocular muscle paresis have been reported, this is the first report that presents a case being diagnosed as having inferior oblique muscle paresis. Many investigators have pointed out that neurotoxin acts not on central but on peripheral nervous systems⁽¹³⁾⁽⁸⁾. The reason why extraocular muscle, especially medial rectus muscle, tends to be affected is unknown. Neurotoxins of snake venom are thought to be some kinds of phospholipase A2 enzymes. They are postsynaptic (alpha type) in death adder⁽¹⁶⁾, whereas presynaptic (beta type)⁽¹⁵⁾ and postsynaptic⁽³⁾ in *Agkistrodon halys pallas*. Neurotoxin of *A. blomhoffi* is presynaptic type called beta-agkistrodotoxin. It interferes neurotransmitter release by blocking Ca^{2+} dependent K^+ current and fast K^+ current⁽¹⁷⁾. Hence the further basic investigations on the property of the receptor or the structural difference between skeletal muscles and extraocular muscles are expected.

The majority of reports describe that the occurrence of extraocular muscle palsy is observed within 24 hours from the injury due to snake-bite. There exists no case report in which the extraocular muscle paresis occurs more than 48 hours after the injury. The reason why the occurrence of muscle paresis was delayed in our case was thought that the amount of venom injected was not considerable and the patient had been sensitized when he was previously bitten by a snake. Many reports indicate that the symptom exists for 7 to 14 days. In our case, the symptom remitted 3 days after the occurrence of the extraocular muscle paresis. The reason for this was thought to be same as above.

The availability of antivenom is controversial. Kimoto et al.⁽⁴⁾ point out antivenom is effective against the venom of *A. blomhoffi*. However, Seneviratne et al.⁽¹¹⁾ assert that

antivenom is ineffective against the venom of other snakes. There are some case reports⁽⁸⁾⁽¹³⁾ in which spontaneous remission of extraocular muscle palsy due to *A. blomhoffi* bite is obtained without using antivenom. Recently, some investigators⁽¹⁾ indicate that monospecific ovine Fab fragment antivenom is useful to reduce side effects such as anaphylactic shock. However, such kind of antivenom effective against the venom of *A. blomhoffi* has not been developed yet.

In a previous report, patients who express systemic symptom wholly have extraocular muscle paresis⁽¹³⁾. Our experience of this patient suggested that the occurrence of subjective binocular diplopia is an important, sensitive and specific clinical sign for the onset of general abnormalities caused by snakebites.

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