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Neurological Considerations of Envenomation by Flower Sea Urchin (*Toxopneustes pileolus*): A Review

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Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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Review Article

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ABSTRACT

The flower sea urchin (*Toxopneustes pileolus*) sting is characterised by severe pain, followed by a brief paralysis of facial muscles that may create confusion with the diagnosis of similar clinical conditions like facial palsy and an episode of myasthenia gravis (MG), at the first glance. The epidemiological history, paralysis of face muscles occurring in scuba divers, following a sting, by the sea urchin, distinguishes the venomation by the flower sea urchin, from the other conditions. Its awareness to the medical professionals, assumes paramount importance in avoiding misdiagnosis. Another distinguishing feature of the envenomation, is its self limiting nature and the sting's effect wears of within a few minutes to hours besides being nonreccurent. Though two toxins, contractin and Pedixin are identified, the possible mechanisms involved in the sting paralysis are not clearly elucidated. The similarity of symptomatology with MG suggests a possible mechanism of action of the sea urchin toxin, similar to that of MG involving the myonueral junction. The various mechanisms disrupting the signal transmission at the myoneural junction are explored. The article is aimed at creating awareness among the medical profession about the sting paralysis, its transient and reversible nature and also suggest possible mechanisms that may be involved in the sting paralysis,to give impetus to future research, in this direction.

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1. INTRODUCTION

The flower sea urchin is described as the most poisonous sea urchin in 2014 Guinness book of world records. Medically significant envenomation is reported with flower urchin sting. The actual incidence of flower sea urchin envenomation is not exactly known. But the toxin's effect is well documented. The occurence of few cases of anaphylaxis are also reported.

There is a void in this interdisciplinary matter, between the clinicians under whose observation envenomation cases may come, and biologists who are experts in matters of biology of the urchin. Hence this article attempts to bridge this gap between the both, for a concerted effort for better understanding of the sting paralysis. The biology information may be repugnant to a clinician and the medical details may be disgusting to a biologist, as in any other interdisciplinary matters, calling for a balanced approach to the details broached.

2. BIOLOGY OF THE FLOWER URCHIN

Toxopneustes pileolus, the commonly known as flower urchin, derives its name from its flower-like pedicellariae. It is considered highly dangerous of all sea urchins species. Toxopneustes means “toxic foot”. Pedicellariae are the toxic appendages of the flower urchin.

2.1 Taxonomy

2.1.1 Habitat

They are found among coral reefs, coral rubble, rocks, sand, and seagrass beds .They are found at depth upto 90 meters from these surface [1]. They may exhibit “covering phenomena “partially burying themselves on the substrate [2].

2.1.2 Distribution

Flower sea are widespread in distribution and are commonly seen in the tropical Indo-West Pacific sea [3]. They can be found north from Okinawa, Japan, to Tasmania, Australia etc. [4].

Table 1. Taxonomy of *Toxopneustes pileolus*

Phylum: Echinodermata
Class: Echinoidea
Order:Camarodonta
Family: Toxopneustidae
Genus: Toxopneustes
Species: *Toxopneustes pileolus*

2.1.3 Identification

The flower sea urchin has the general morphology like any other sea urchin except for the coloured pedicellariae, which assume circular shape when open and triangular shape when closed or closing. The spines are tiny and found beneath the pedicellariae, acting as clause by which the urchin hooks to the prey.

2.1.4 Toxin storage and injection into the prey

The toxin of flower sea urchin is stored in the pedicilleriae. Unlike other sea Urchins, which use spines to inject the venom, flower sea urchin uses pedicellariae to store and inject its toxin into its prey. [5] The pedicellariae attach by means of its claus to the prey, and in which process they may be torn from the stalk. The detached pedicellariae, can remain stuck to the victims skin and can inject toxin repeatedly for few hours [6,7]. So it is very important to dislodge the pedicellariae if they are stuck on the human skin to reduce the effect of the envenomation. The amount of the toxin injected depends on the size of the pedicellariae.

2.1.5 The toxins

Two toxins from the pedicellariae venom of flower urchins iare broached n two studies [8] and a third toxin whose status is uncertain and some bioactive lectins are reported in the literature.

The salient points of the toxins are summarized in the Table 2.

Table 2. Toxins of flower sea urchin

1. Contractin A:
Discovered in 1991.
It Interferes with the transmission of signals at nerve endings caused hemagglutination [9,10].
It caused contractions in the smooth muscles, in guinea pig [11].

2. Peditoxin:
Discovered in 1994. It is a a protein toxin It is composed of the protein pedin and the active prosthetic group pedoxin. Pedin itself is non-toxic, but it magnifies the effects of pedoxin. When combined together into the holoprotein peditoxin, even low doses resulted in anaphylaxis-like shock and death. [12]In low doses in mice, pedoxin caused Lowering of the body temperature muscle relaxation sedation and anesthetic coma. At higher doses - convulsions and death.
3. UT841
It is the third toxin isolated in 2001.it is not settled whether it is distinct or identical to contractinI [13]. In addition to these toxins, the following lectins are also isolated as components of the toxin, whose role is not clear.
4. The lectins:
lectins; SUL-I, SUL-II, SUL-IA, and SUL-III (SUL stands for "sea urchin lectin") have also been isolated from flower urchin venom [14]

3. DISCUSSION

The first hand information of the flower sea urchin sting, resulting in paralysis of the facial muscles, is provided in 1930, by Tsutomu Fujiwara the Japanese marine biologist who suffered an accidental sting on his hand. He described his experience in a paper published in 1935: [15,16]. The same in his own words is reproduced verbatim below.

“After a while, I experienced a faint giddiness, difficulty of respiration, paralysis of the lips, tongue and eyelids, relaxation of muscles in the limbs, was hardly able to speak or control my facial expression, and felt almost as if I were going to die. About 15 minutes afterwards, I felt that pains gradually diminish and after about an hour they disappeared completely. But the facial paralysis like that caused by cocainization continued for about six hours”.

3.1 Limitations of Symptomatology

Due to sudden and unexpected accident, the additional/accurate description of symptoms might not have been possible for the narrator-biologist. Not much improvement to the original discreption of the symptomatology is made afterwards. No case seems to have come under the observation of the discerning eye of a physician, who could have added some signs or could have observed still subtler manifestations, as is well said by the great pathologist, Boyd ie ‘what the mind doesn’t know,the eye doesn’t see'. Hence is the stressed importance of involvement of both the biologist and a clinician in the future research.

The mechanism of the envenomation is not fully understood. The biologist who originally ascribed that the symptom complex looked like cocainization. How and why he felt so is known only to him. None of the symptoms, he described match with known features of acute cocaine intoxication.The symptomatology matches with two clinical entities. –The facial palsy and Myasthenia gravis ((MG) episode, at least superficially. Hence the two diseases are briefed to find whose mechanism of action, the toxin might resumble.

3.2 The Facial Palsy (Paralysis)

It is of two types the UMN (upper motor neuron) and LMN (lower motor neuron) type. The symptoms described show involvement of both lower and upper part of the face paralysis which is inconsistent with the diagnosis of UMN type, because of the bilateral upper motor neurone innervation spares the upper half of the face involvement in the UMN, type of the facial palsy.

The presence of weakness of limb in addition, eliminates LMN type (Bells Palsy) as it shows no such limb involvement, the paralysis being limited to both of the upper and lower half of face muscles. So, the mechanism of facial palsy cannot be the same as that of the paralytic symptoms described under the flower sea urchin sting.

The other disease, myasthenia gravis, which is due to loss of nerve transmission at the myoneural junction, involving the nuerotransmitter, acetylcholine. The anology is limited to the myoneural junction involvement in both and otherwise have no parallel in aetiology or clinical course. The name myasthenia gravis, means “grave, or serious, muscle weakness.” in Latin. The muscle is fatigued on prolonged usage and the disease runs a prolonged course with exacerbations from time to time. The

neuromuscular dysfunction has an autoimmune basis in MG unlike the sting paralysis which is sought to be explained by other than autoimmune mechanisms.

3.3 Myoneural Junction Involvement

The symptomatic resemblance to Myasthenia gravis (MG) suggests a possibility that the flower sea urchin toxin might be working at the myoneural junction. The axon of the post synaptic nerve fiber ends in the nicotinic type of acetylcholine receptor on the sarcollemal membrane of the skeletal muscle. The space in between is called synaptic cleft. The electrical action potential received at the axon fiber releases the synaptic vesicles, from the presynapticnerve ending. The packets containing acetylcholine which is the chemical neurotransmitter that makes the muscle contract. In the absence of acetylcholine, the muscle gets fatigued or paralysed.. In myasthenia gravis the acetyl choline is either destroyed by the over active enzyme, the cholinesterase. Or the post synaptic nicotinic acetylcholine receptors are blocked by the auto-antibodies produced by the body (hence MG is considered as an autoimmune disease). The blockade is reversible as production of acetylcholine by inhibiting the cholinesterase by drugs like neostigmine, results in once again restoration of chemical neurotransmission causing the muscle to contract. The role of cholinesterase-like activity could be possible mode of action of the flower sea urchin toxin as the symptoms match with those of MG as shown in Table 1. The transient nature of the facial muscle paralysis by the toxin is perhaps due to its quick bio-degradation, when normal acetylcholine transmission is restored. The question of the role of the auto-antibodies does not arise as the toxin is foreign and the exposure is limited to single episode.

Table 3. Showing the resemblance in symptomatology of MG and sting paralysis

Symptom –	MG. -	Toxin
1.Weakness of the eye. muscles.	+	+
2.Drooping of eyelids.	+	+
3.Change in facial expression.	+	+
4.Blurred vision.	+	+
5.Impaired speech	+	+
6.Difficulty in breathing.	+	+
7.Weakness of limbs.	+	+

3.4 Possible Role of PGE 2M

PGE2 negatively regulates the release of acetylcholine and also cause smooth muscle contraction and modulates the cholinesterase output [17]. This could cause a brief disturbance in the synaptic transmission, resulting in reversible paralysis of facial muscles as seen in the case of the flower sea urchin. The PGE2 is an eicosanoid, which could be of the sea urchin origin as its involvement in hyperspermia is well documented [18] or could be induced by inflammatory response of the body against the toxin, injected. The role if any of PGE2 needs to be studied in future research as it could explain both the nictinic receptor blockade and muscarinic acetylcholine receptor stimulation.

3.5 Role of Muscurinic Acetylcholine Receptors

[19,20] muscarinic receptor mediated stimulation of the acetylcholine may result in smooth muscle contraction as is seen with the envenomation by the toxin. The muscarinic receptors of acetylcholine (situated at the parasympathetic nerve endings) have many types like M1 to M5. [14] Stimulation of particular type elicits particular response. The Type 3 mediates the gastrointestinal intestinal secretions, and sweat secretions. in abscence of which in the toxicity can be explained by the fact that M3 receptors may not be stimulated by the toxin, yet can cause smooth muscle contraction. Stimulation of M2 is shown to inhibit or reduces the heart rate. M4 is responsible for bronchospasm. Thus stimulation and inhibition of muscurinic cell effects can be modulated by different types of M (muscarinic) receptors.

3.6 Possible Role of Calcium Ions in Mechanism of Sting Paralysis

Transient neuromuscular junction disturbances are noted in case of use of the drug Verapamil and aminogycoside group of antibiotics. So, they represent a different mechanism of neuromuscular blockade which is transient and inconsequential. Sharing such features being Transient and reversible nature, it is possible that the flower urchin toxin might work this way also. This suggestion is for the future research in this direction. The action potential arrived at the axon of the pre synaptic nerve fibre causes ca++ion channels to open with release of ca++ which causes the release of synaptic vesicles

containing the acetylcholine. These acting on the sarcollemal membrane of the muscle and opens up sodium ion channels. This causes Na ions to enter into the muscle cells and potassium ions coming outside which cause depolarization of the membrane resulting in setting up of action potential that causes muscle contraction. If the calcium reflux is blocked at the presynaptic nerve terminal, the acetylcholine release can be stopped and the muscle looses its tone and is relaxed or paralyzed .Aminoglycosides antibiotics and the drug Verapamil cause calcium ion depletion and hence exhibit neuromuscular junction disturbance. So if the toxin has the potentiality of inhibiting the calcium ion release at the pre synaptic nerve terminal that also can explain its observed effect on the mayo-neural junction. This possibility need to be investigated by the future research.

Other mechanisms of the toxin exerting its effect on the myoneural junction:

- Depolarisation of the muscle membrane: like the drug succinylcholine
- Competitive blockade: like the drug – pancurium.

3.7 Management

The management is symptomatic, necessitating the prophylactic use of antibiotics (to prevent secondary infection of the site of bite), liberal use of analgesics (pain management), supportive therapy like I.v fluids (in case of shock), steroids (at the discretion of the treating physian) for any allergic manifestations, surgical toilet of the bite wound and active immunization against tetanus. If the patient develops anaphylaxis, the usual protocols for treating the same is necessary. Since most of the patients make spontaneous recovery, allaying the apprehension of the patient, his relatives and the treating doctor (!), is all that might be required additionally.

4. CONCLUSION

The article is aimed at suggesting a clinician-biologist symbiosis for future research on the flower sea urchin envenomation. It is also intended to create awareness of the existence to the physicians working in emergency departments. Areas of potential future research are suggested. The possible mechanisms of envenomation of the flower sea urchin are discussed.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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