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Original Article

Neurological Manifestations of Puffer Fish Poisoning and It's Outcome: Study of 83 Cases

M Azizul Haque[1], Q Tarikul Islam[2], M A Razzak[3], M A Faiz[4], M Iqbal Bari[5]

Abstract

The study was carried out in Medicine and Pediatrics Department of Rajshahi Medical College Hospital, and Natore Sadar Hospital, both are located in the northern territory of Bangladesh. Period of study ranged from admission of patients till discharge. On 8th June 2008, 83 patients of Singra Upazilla Natore were admitted in Rajshahi Medical College Hospital and Natore Sadar Hospital with the history of consumption of Puffer fish. A presumptive diagnosis of Puffer fish poisoning was made on the basis of classical clinical presentations followed by Puffer fish ingestion. Blood and urine samples from 38 patients were sent to Frankfurt, Germany for toxicological analysis. The cases were clinically reviewed periodically and routine investigations were done. Report of the toxicological study confirmed the diagnosis of tetrodotoxin poisoning. Important neurological symptoms observed were peri-oral paresthesia (71), tingling over entire body (50), dizziness (35), headache (20). Muscular paralysis of the limbs was noted in 13 patients, of which 7 patients developed respiratory involvement. All the patients who developed respiratory involvement died. Early diagnosis and supportive management could ensure a safe and favorable outcome. Management of respiratory failure by ventilator support can be life saving.

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Introduction

Regarded by many as a delicacy, puffer fish is a lethal source of food poisoning with a high mortality[1].In Bangladesh puffer fish ingestion is not because of gustatory delight, rather it is a marker of poverty and ignorance. Puffer fish is also known as Fugu (in Japan), toadfish, globefish, blowfish and baloonfish.[2] It is also widely known as the blowfish or the puffer fish, because it can swell up their bellies until they resemble a ball. Puffer fish can be found in the Indian Ocean and in the South Pacific. Some can also be found in North American waters. There are nearly 100 different species of puffer fish worldwide, 38 of them found in Japan. Tetrodotoxin (TTX) is also found in the venom on the blue ringed octopus found around Australia and involved in human fatalities through bites.[3]The toxin is variously used as a defensive biotoxin to ward off predation, or as both defensive and predatory venom. The first recorded cases of tetrodotoxin poisoning were from the logs of Captain James Cook.

[1] Assistant Professor, Department of Medicine, Rajshahi Medical College, Rajshahi.
[2] Professor, Department of Medicine, Rajshahi Medical College, Rajshahi.
[3] Indoor Medical Officer, Medicine, Rajshahi Medical College Hospital, Rajshahi.
[4] Professor, Department of Medicine, Sir Salimullah Medical College, Dhaka and ex-Director General, Directorate of Health Services, Bangladesh.
[5] Professor, Department of Pediatrics, Rajshahi Medical College, Rajshahi.

Puffer fish poisoning is sporadic in Bangladesh, mostly observed in coastal areas. This outbreak is unique because of two reasons. It occurred in northern territory of Bangladesh, an area far away from the coastal areas and it is the largest outbreak of puffer fish poisoning noted in literature.

Material and Methods

On 8th June 2008, 83 patients of Singra Upazilla were admitted in Rajshahi Medical College Hospital and Natore Sadar hospital with history of consumption of puffer fish. The fishes were bought from local village market at a very cheap price and none of the affected people had any past experience of preparing, cooking and eating puffer fish. None of them was aware of the fact that the fish might be toxic. As no laboratory service for toxin bioassay was available in Rajshahi Medical College Hospital, a presumptive diagnosis of puffer fish poisoning was made on the basis of classical clinical presentations followed by puffer fish ingestion. Family members who did not consume the fish were not affected, which further strengthens our clinical diagnosis. Blood and urine samples from 38 patients were sent to Frankfurt, Germany for toxicological analysis. Report of the toxicological study confirmed the diagnosis of tetrodotoxin poisoning. All patients were treated with symptomatic treatment, maintenance of fluid and electrolyte balance and eight patients who had features of muscle paralysis were treated with neostigmine. Gastric lavage was not attempted in any patients because of late presentation. Routine investigations were done in all cases and patients were under strict clinical supervision. Some of the patients died within a few hours. In rest of the cases, symptoms gradually improved. They recovered without any residual effects and were discharged.

Results

A total of 83 patients (male 50, female 33) with history of ingestion and clinical manifestations of puffer fish poisoning were admitted in Rajshahi Medical College Hospital and Natore Sadar hospital. Such huge outbreak was partly because of sudden availability of Puffer fish (locally known as Potka fish) in local market at a very cheap rate, which prompted the local people of Singra, Natore to buy and consume it. None of the affected patients were aware of the fact that the fish might be toxic. Highest number of affected patients was in the 0-9 year age group and the lowest number was in above 60 age group. The amount of ingested Pufferfish ranged between <50 gram to 200 grams. 39 patients (46.08%) developed symptoms after consuming less than 50 grams. The interval between ingestion and onset of toxic manifestations varied between less than 30 minutes to more than 2 hours. Majority of patients (66.26%) developed symptoms within 30 minutes of ingesting Puferfish. Only 2 patients had symptom onset after 90 minutes. Most common symptom developed was peri-oral paresthesia, which was seen in 71 patients (85.54%).Other common symptoms were tingling over entire body 50 patients (60.24%), dizziness in 35 patients (42.16%).Muscular paralysis of the limbs were noted in 13 patients, of which 7 patients developed respiratory involvement. All the patients who developed respiratory involvement died. Neostigmine was given in all patients with muscular paralysis. Effect of neostigmine on patients with ascending paralysis is shown in table 5.

Table 1: Age and sex distribution of the patients (N= 83)

Age (years0	No. of patients (%)	Male (%)	Female (%)
0-9	21 (25.3)	13 (15.66)	8 (9.63)
10-19	17 (20.48)	10 (12.04)	7 (8.93)
20-29	20 (24.09)	8 (9.63)	12 (14.45)
30-39	10(12.04)	7 (8.43)	3 (3.61)
40-49	9(10.48)	8 (9.63)	1 (1.20)
50-59	5(6.02)	3 (3.61)	2 (2.40)
60 and above	1(1.20)	1 (1.20)	0 (0)
	Total=83	50 (59.8)	33 (40.2)

Table 2: Relation of clinical outcome with amount of fish ingested (N=83)

Amount of fish ingested (gm)	No. of patients affected (%)	No. of patients who improved (%)	No. of patients who died (%)
<50	39 (46.08)	39 (46.08)	0 (0)
50-100	28 (33.73)	28 (33.73)	0 (0)
101-150	10 (12.04)	4 (4.81)	6 (7.22)
151-200	6 (7.22)	4 (4.81)	2 (2.40)
>200	0 (0)	0 (0)	0 (0)

Table 3: Onset of symptoms in patients with Puffer fish poisoning (N=83)

Time (minutes)	No. of patients (%)
<30	55 (66.24)
31-60	20 (24.09)
61-90	6(7.22)
91-120	1(1.2)
>120	1(1.2)

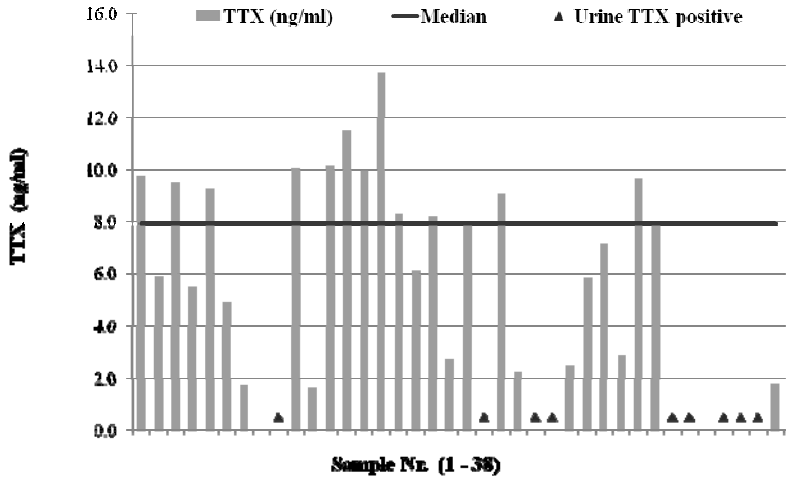
Table 4: Neurological manifestations in patients with Puffer fish poisoning (N=83)

Neurological manifestations	No. of patients (%)
Peri-oral paresthesia	71 (85.54)
tingling sensation over entire body	50(60.4)
Dizziness	35 (42.16)
Headache	20 (24.09)
Vertigo	11 (13.25)
Weakness of both upper and lower limbs	13 (15.66)
Cramps in lower limbs	8 (9.63)
Difficulty in respiration	8 (9.63)
Difficulty in speech	7 (8.43)
Blurring of vision	7 (8.43)
Weakness of jaw muscles	2 (2.4)

Table 5: Comparative outcome of treatment with neostigmine in patients of puffer fish poisoning with ascending paralysis.

Treatment	Total patients	Patients with ascending paralysis		Outcome	
		With respiratory involvement	Without respiratory involvement	improved	died
With neostigmine	8	1	7	6	2
Without neostigmine	5	5	0	0	5
Total	13	6	7	6	7

Figure 1: showing tetrodotoxin level in blood and urine samples (n=38)



Discussion

Tetrodotoxin poisoning is probably the most common poisoning along the coasts of Asia.[4] Puffer fish poisoning has been reported in many Asian countries including Thailand, Malaysia, Bangladesh, Taiwan and particularly Japan.[5,6] Tetrodotoxin (TTX) is present in high concentrations in the liver, ovaries, intestines and skin of puffer fish.[7] The amount of TTX varies widely in different species and the concentrations seasonal.[8] Tetrodotoxin blocks voltage sensitive sodium channels in nerve tissue leading to failure of depolarization and propagation of action potential in nerve tissue. TTX can act on both the central and peripheral nervous systems. This means that the motor, sensory and autonomic systems can be affected. Sensory neurons are affected first and then motor neurons at a higher dose of TTX. Furthermore, TTX can stimulate the chemoreceptor trigger zone in the medulla oblongata and depress the respiratory and vasomotor centers in that area. Paralysis and respiratory failure account for the main cause of death.[9] Sensory neurons are affected first and then motor neurons at a higher dose of TTX. It has a direct central effect on the chemoreceptor trigger zone causing nausea and vomiting, on the respiratory centre depressing respiration[10] and may cause a drop in blood pressure by relaxing vascular smooth muscle and blocking peripheral autonomic nerves.[11] Response to cholinesterase inhibitors also suggests a reversible competitive blockade at the motor endplate.[12] Tetrodotoxin is one of the most toxic substances known; it is 275 times more lethal than cyanide and 50 times more potent than strychnine or curare.[13] Tetrodotoxin is heat-stable and water-soluble, so boiling of puffer fish in water cannot destroy the toxin. The toxic dose of TTX has not been established but one dose of 1 to 2 mg of purified TTX can be lethal.[14] Reported cases from the Centers for Disease Control and Prevention (CDC) have documented toxicity with ingestion of as little as 1.4 ounces of puffer fish. Yang et al reported that the mortality rate of tetrodotoxin (TTX) poisoning in Taiwan was 13.5%[15]. In Japan, where puffer fish is considered a delicacy, there were 912 people poisoned by puffer fish from 1980 to 1999. Among the 912 people, 106 died (mortality rate 11.62%) [16]. In our study 7 patients died out of 83 patients, giving a death rate of 8.43%. Patients who lived through the acute intoxication (i.e. first 24 h) recovered without residual deficits. In our study patients who developed respiratory failure all died.

Respiratory muscle paralysis is the predominant method of death in puffer fish poisoning, so proper respiratory support may reduce the mortality. As there is no specific antidote, prevention by increased population awareness should be the first priority.

Conclusion

Early diagnosis and supportive management, especially ventilator support, could ensure a safe and favorable outcome. To improve overall management of poisoning cases, strong consideration should be given to establish a national toxicological reference laboratory.

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All correspondence to:
M Azizul Haque
Assistant Professor
Department of Medicine
Rajshahi Medical College
Rajshahi.