

Factors affecting the clinical picture & prognosis of puffer fish poisoning in Suez city (Egypt) during year of 2008

Said S. Elshama*, Mohamed A. Zaki**, Metwally E. Metwally*

Department of Forensic Medicine and Clinical Toxicology, Faculty of Medicine, Suez Canal University.*

Marine Toxin Lab., National Institute of Oceanography and Fishery, Suez. **

Corresponding author: Said S. Elshama: saidelshama@yahoo.com

Abstract

Introduction: Puffer fish is a common form of poisoning throughout Egyptian coastal cities such as Suez city. Puffer fish contains one of the most powerful marine toxins which is called tetrodotoxin. **Aim of the work:** We attract attention of health professional to toxicity of puffer fish and factors affecting the clinical picture and outcome of poisoning which will help for early diagnosis and proper management. **Patient and Methods:** The study was carried out nine patients with history of puffer fish ingestion transferred to General Suez Hospital. Diagnosis was made on the basis of recent dietary history and clinical presentation. All cases were clinically examined, investigated and observed from admission to discharge. All patients were treated with gastric lavage, activated charcoal and symptomatic. **Results:** According to clinical grading system for tetrodotoxin toxicity, three patients had grade 1 and another three had grade 2 but, three fatal cases had grade 3 and their condition worsened and became grade 4. The onset of appearance of toxic symptoms of puffer fish poisoning was rapid. All investigations for all patients were within normal limits. Clinical manifestations of poisoning were mainly neurological, but the cardiovascular effects were not common in the majority of patients. Toxic manifestations were wide range from mild to severe according to state of preparation and clean of puffer fish. Fatal cases ate gonads and head of fish and the cause of death was respiratory failure. **Conclusion:** The factors affecting the severity and the prognosis of puffer fish toxicity are the mode of preparation, the clean and the eaten part of fish.

Keywords: Puffer fish, poisoning, tetrodotoxin, Suez city.

Introduction

Marine toxins is a vague area for physicians and clinical toxicologist in Egypt, despite it is a coastal country. Puffer fish contains one of the most powerful marine toxins which is called tetrodotoxin (Meier and White, 1995). This toxin can produce a prolonged state of suspended animation resembling death (Haddad and Lee, 2007). It was first isolated and named in 1909 by Japanese scientist Dr Yoshizumi Tahara (Tanu et al., 2002). The first recorded cases of tetrodotoxin poisoning were from the logs of Captain James Cook. He recorded his crew eating some local tropic fish (puffer fish), then feeding the remains to the pigs kept on board. The crew experienced numbness and shortness of breath, while the pigs were all found dead the next morning (Tsunenari et al., 1980). Its name derives from tetraodontiformes, the name of the order that includes the puffer fish. Fish poisoning by consumption of members of the order tetraodontiformes is one of the most potent toxins found in marine species. Tetrodotoxin has also been isolated from widely differing animal species. It is actually the product of certain bacteria such as pseudoalteromonas tetraodonis, some species of pseudomonas and vibrio (Yu and Yu, 2002).

In Japan, puffer fish poisoning remains the most common cause of fatal food poisoning because tetrodotoxin is neurotoxin and potential for severe and life-threatening effects. It is lethal more 10 times than cyanide (Noguchi and Ebeu, 2001).

Puffer fish poisoning is common in some parts of the world, it occurs only sporadically in Australia, Mexico and USA, but the majority of reported cases have occurred in southeastern Asia (Nunez et al., 2000). In Egypt, Ali et al., (1995) recorded some cases

of puffer fish poisoning in Giemsha city, Suez Gulf, and in Sharm El-Sheik. Zaki (2004) described other cases in Suez city.

In Egypt, many physicians observed sporadic cases of food poisoning after eating this specific type of fish. In the last ten years, the rate of these cases was progressive increased and made many troubles for physicians and people because of wide extreme of different clinical pictures and prognosis that ranges from complete recovery to respiratory failure and death. In Suez city, the majority of people eat puffer fish without developing any toxic manifestations, but some of them complain of different toxic signs and symptoms without any residual affection and the others die.

In this paper, we attract attention of health professional to toxicity of puffer fish which is now a common form of poisoning throughout Egyptian coastal cities such as Suez city. Therefore, this article attempts to show sufficient knowledge about factors affecting the clinical picture and outcome of puffer fish poisoning for early and clear diagnosis.

Ethical Considerations

The study was carried according to ethical principles of research. Objectives and steps of our study were explained to all patients. Written consent was obtained from patients or their legal guardians as some were critically ill.

Patients and Methods

The study was carried out in General Suez Hospital, Egypt. Nine patients from different families with different ages and sex were admitted with history of

puffer fish ingestion. Source of contamination is puffer fish which is caught from the red sea, especially the Suez Gulf which is free from any contamination (microbial contaminant and water pollutants). It was proved by researchers of National Institute of Oceanography and Fishery (Suez branch) who took multiple and frequent samples of water and fish of Suez Gulf to ensure that it was free from any pollution from industrial remnants during the same period of the research.

A presumptive diagnosis of puffer fish poisoning was made on the basis of recent dietary history and clinical presentation (Claudia et al., 2010). Complete history was taken from all patients and their relatives. All patients ate one fish and average amount of boiled rice. They did not take any medication before admission. All cases were clinically examined, investigated and observed from admission to discharge for the following parameters: onset of symptoms, clinical manifestations, blood samples for complete blood picture, renal functions (urea, creatinine), serum glutamic pyruvic transaminase (SGPT), serum glutamic oxalacetic transaminase (SGOT), blood glucose, electrolytes (sodium, potassium, calcium and phosphorous). Clinical picture was divided into grading according to clinical grading system (Wan et al., 2007). Grade 1 is characterized by perioral numbness and paraesthesia while grade 11 shows numbness of tongue, face and other areas, incoordination and slurred speech. Grade 111 is manifested by flaccid paralysis, dyspnoea and aphonia. Grade 1V is respiratory failure and coma. All patients treated with gastric lavage for one time in emergency

room, multiple doses of activated charcoal for the first two days of admission and symptomatic.

Results

Table (1) shows that total number of the patients was nine, three patients had grade 1 and another three had grade 11, but, three fatal cases had grade 111, later on, their condition worsened and had grade 1V.

Table (2) shows that values of vital signs of all puffer fish intoxicated patients were within normal limits. Clinical manifestations of puffer fish poisoning were mainly neurological. The cardiovascular effects were not common in the majority of patients.

Table (3) shows that the onset of appearance of toxic symptoms of puffer fish poisoning was early for all patients, it was developed within one hour (30 – 60 m). Three fatal cases ate gonads and head of fish. They had a grade 4 and their onset of appearance poisoning was within 30 m. The cause of death of the previous reported cases was respiratory failure. Our results showed that patient who drank a fish soup, had a grade 2 and then complete recovery.

Table (4) shows that out of six patients who ate fried fish only two patients died, while out of three patients who ate the boiled fish only one died.

Tables (5) and (6) show that renal functions and liver functions of all intoxicated patients was within normal limits.

Tables (7) shows that complete blood pictures of all intoxicated patients were within normal limits.

Tables (8) shows that serum electrolytes (Na, K, Ca and P) and random blood glucose levels of all intoxicated patients was within normal limits.

Table (1): The relationship between the grade of severity of puffer fish poisoning and number of intoxicated patients.

Grade	1	11	111	1V
Number of patients	3	3	-	3

Table (2): Values of vital signs and system affection of all puffer fish intoxicated patients during admission in the hospital.

C \ V	Blood pressure mmHg	Pulse/minute	Respiratory rate Breath/minute	Temperature C°	System affection
1	120/70	85	25	37.8	CNS Paraesthesia
2	130/90	90	24	37.5	CNS Numbness of tongue
3	100/60	85	19	36.8	CNS Incoordination
4	110/75	75	20	37.2	CNS Slurred speech
5	150/95	90	21	37.4	CNS Paralysis + CVS Hypertension
6	120/85	70	22	37.2	CNS Perioral numbness
7	140/90	90	22	37.5	CNS Paraesthesia + CVS Dyspnoea
8	110/60	80	18	37.3	CNS Coma
9	110/70	90	20	36.3	CNS Coma

C: case

CNS: central nervous system

V: vital signs

CVS: cardiovascular system

Table (3): Relationship between clinical grading system of puffer fish poisoning, onset of symptoms, eaten part of fish and outcome of all intoxicated patients.

Patient	Onset of symptoms (Minutes)	Grade of poisoning	Eaten part of fish	Outcome	Cause of death
1	>30	4	Gonads+ Flesh	Death	R.F
2	>30	1	Flesh	Recovery	-
3	>30	2	Flesh	Recovery	-
4	<30	1	Flesh	Recovery	-
5	30-60	4	Head + Flesh	Death	R.F
6	30-60	2	Soup + Flesh	Recovery	-
7	30-60	2	Flesh	Recovery	-
8	<30	4	Head + Flesh	Death	RF
9	<30	1	Flesh	Recovery	-

R.F: Respiratory failure

Table (4): The relationship between number of fatal cases and method of cooking of puffer fish.

Total number of patients	Method of cooking	Number of fatal cases
6	Frying	2
3	Boiling	1

Table (5): Renal functions of all puffer fish intoxicated patients.

R.F \ C	Reference range	1	2	3	4	5	6	7	8	9
S.Creatinine	0.6 - 1.4	0.6	0.7	0.8	0.9	0.9	0.9	1.1	1.2	1
S.Urea	45- 15	25	33	29	32	38	27	39	35	30

R.F: renal functions C: case

Reference range according to Louise (2007)

Table (6): Liver functions of all puffer fish intoxicated patients.

L.F \ C	Reference range	1	2	3	4	5	6	7	8	9
S.G.P.T	Up to 49	12	18	17	15	17	13	40	42	20
S.G.O.T	Up to 49	14	30	20	17	22	20	35	38	13

L.F: liver functions C: case S.G.P.T: serum glutamic pyruvic transaminase

S.G.O.T: serum glutamic oxalacetic transaminase Reference range according to Louise (2007)

Table (7): Parameters of complete blood pictures of all puffer fish intoxicated patients.

P \ C	1	2	3	4	5	6	7	8	9	Reference range
WBCs (10/mm)	8	9.4	9.7	5.5	5.3	10	8.1	6	8	(4-11)
Hb (g/dl)	11	13.2	13.5	12.5	12.6	11.5	14.1	13	14	M (14-18) F (12-16)
RBCs (10/mm)	4.1	4.5	4.4	4.6	4.2	4.2	4.9	4.8	4.9)F (4.5-5.5) M (4.5- 6)
HCT %	33	38.6	38.8	36	37	34	44.6	43	45	46 -33
MCV(fl)	81.3	84.9	85.2	83.9	86.2	82	91.2	90	92	96-80
MCH (pg)	28	29.9	31.7	31.2	31.4	30	32.2	30	31	34-27
MCHC (g/dl)	30	33	33.3	33.8	33.2	31	35.4	34	35	36-30
PLT (10/mm)	220	294	259	240	286	260	185	190	249	400-150

P: parameter of complete blood picture C: case

Reference range according to McKenzie (2010)

Table (8): Serum electrolytes (sodium, potassium, calcium and phosphorous) and blood glucose levels of all puffer fish intoxicated patients.

C	Reference range	1	2	3	4	5	6	7	8	9
R. glucose (mg/dl)	200<	100	110	102	96	84	156	110	100	116
Ca (mg/dl)	10.5-8.5	9.2	9.4	8.7	8.8	9.2	9.1	9	9.2	8.8
P	2.5-5	5.6	4.3	3.4	3.3	2.8	3.7	4	3.5	3.2
Na (mEq/L)	155-135	150	160	140	164	139	140	145	150	142
K (mEq/L)	5.3-3.4	3.4	3.6	3.5	3.9	3.3	4.5	4.6	4.2	3.8

C: case R: random Reference range according to **Anderson (2007)**

Discussion

In Suez city, some physicians observed cases of puffer fish poisoning, but according to the epidemiological view, pattern of distribution of cases were sporadic and random. Puffer fish poisoning is considered as an endemic because the reported cases are not increased in the number (constant rate) during one year (2008). The mortality rate of the reported cases were 33.3% during this year (number of fatal cases were shown in tables 3, 4).

Diagnosis of puffer fish poisoning is based on clinical manifestations and recent dietary history. So, a complete dietary history must be taken. The most possible source of contamination is the puffer fish (tetrodotoxin) because the boiled rice and (boiled and fried fish) exclude any microbial food poisoning. **Geo et al., (2007)** confirmed that the high degree of temperature (100 °c or more) kills the most possible of microorganisms of the food. Source of contamination is puffer fish which was caught from the red sea, especially the Suez Gulf which is free from any contamination (microbial contaminant and water pollutants).

Our cases showed that the onset of appearance of toxic symptoms of puffer fish poisoning was early, it developed within one hour because the toxin acts quickly and binds with an affinity that is not easily overcome (**Anderson, 1988**). This is consistent with **Isbister et al., (2005)**. But, it is not dependent on the severity of poisoning because symptoms of moderate and severe cases appeared within the same limits of the time, this is contrast with **Chowdhury et al., (2007)** who confirmed that onset of appearance of toxic symptoms of puffer fish poisoning depends on severity of poisoning.

Analysis of the reported cases showed that duration, severity of poisoning and outcome depends on specific eaten part of fish but not on the amount of ingested fish because the distribution of tetrodotoxin (TTX) in puffer body was not in uniformity (**Gong et al., 2003**).

Fatal cases ate gonads and head of fish. The skin and organs of the puffer fish (gonads, head, liver and intestine) contains high levels of tetrodotoxin sufficient to produce paralysis of the diaphragm and respiratory failure (**Ellis and Jelinek, 1997**). The cause of death in the present reported cases was respiratory failure and this result is consistent with **Kanchanapongkul (2001)**.

Field (1998) reported that the flesh of puffer fish may not usually be dangerous toxic and this is

consistent with condition of some patients which became completely free after ingestion of the flesh alone. **Yang et al., (1996)** indicated that the removal of the viscera and skin reduce the danger of poisoning. Therefore, toxic manifestations of reported cases were of wide range from mild to severe according to state of preparation and clean of puffer fish. **Ahasan et al., (2004)** referred that the method of cooking of puffer fish plays important role for severity of intoxication. This explains that patient drank a fish soup, had a mild degree of toxicity and a good prognosis because skin and viscera of puffer fish were removed before cooking the fish soup and the amount of tetrodotoxin was diluted by adding fresh water to form the soup.

According to the reported cases, the method of cooking has no effect on the prognosis because the two patients died from the six patients who ate fried fish, while one patient died from the three patients who ate the boiled fish. This is consistent with **Tibballs (1988)** who confirmed that the method of the cooking which depends on the high degree of temperature such as the boiled and fried fish, have not any effect on efficacy of tetrodotoxin because it is heat stable.

Clinical picture of puffer fish poisoning based mainly on neurological signs and symptoms because tetrodotoxin blocks Na channel at very low conduction (**Yamazaki and Shibuya, 1995**). There are two types of voltage-gated Na channels present in humans, the tetrodotoxin-sensitive voltage-gated Na channel ((TTX-sNa channel)) and the tetrodotoxin-resistant voltage-gated Na channel ((TTX-rNa channel). Tetrodotoxin binds to TTX-sNa channels with a binding affinity of 5-15 nanomolar, while the TTX-rNa channels bind TTX with low micromolar affinity. Nerve cells containing TTX-rNa channels are located primarily in cardiac tissue, while nerve cells containing TTX-sNa channels dominate the rest of the body. The prevalence of TTX-sNa channels in the central nervous system makes tetrodotoxin a valuable agent for the silencing of neural activity (**Kiernan and Bostock, 2000**). Results of **Kan et al., (1987)** correlate with toxic manifestations of our cases which indicated greater prominence of sensory symptoms relative to motor symptoms. The fatal cases were conscious for short time before death because of disability of tetrodotoxin to cross the blood brain barrier.

There is clinical grading system for puffer fish poisoning dependent on severity of neurological and cardiovascular involvement (**Kiernan et al., 2001**) Clinical pictures of the previous cases showed that

cardiovascular effects were not common in the majority of patients because nerve cells containing TTX-rNa channels are located primarily in cardiac tissue and this is consistent with **Isbister et al., (2005)**. Gastrointestinal manifestations were not also presented except in one patient who had nausea. This is contrast with **Ellenhorn and Barceloux (1997)**, but **Fukuda and Tani (1996)** confirmed that gastrointestinal presentation is not essential feature of puffer fish poisoning since 1941.

Conclusion

Diagnosis of puffer fish poisoning depends on signs, symptoms and history of ingestion. Clinical picture of intoxication is mainly neurological, especially sensory. Gastrointestinal and cardiovascular manifestations are not common in the majority of patients. The factors affecting the severity and the prognosis of puffer fish toxicity are the mode of preparation, the clean and the eaten part of fish. The best method of preparation of puffer fish meal which depends on the removal of viscera and skin.

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الملخص العربي

العوامل المؤثرة على الصورة الإكلينيكية وتطور حالات التسمم بأسمك القراض بمدينة السويس (مصر) خلال عام 2008

سعيد سعيد الشماع*، محمد احمد زكي**، متولي السيد متولي*
قسم الطب الشرعي والسموم الإكلينيكية – كلية الطب- جامعة قناة السويس.*
معمل السموم البحرية- معهد علوم البحار والمصايد- السويس.**

المقدمة: اسماك القراض تعتبر شكل شائع للتسمم في المدن الساحلية المصرية مثل مدينة السويس. فاسماك القراض تحتوي على واحد من أقوى السموم البحرية والتي يعرف بالتetrodotoxins. **الهدف من العمل:** لفت أنظار العاملين بالصحة للتسمم بأسمك القراض والعوامل التي تؤثر على الصورة الإكلينيكية وعلى محصلة التسمم مما يساعد على التشخيص المبكر و العلاج المناسب. **المرضى والوسائل:** تمت الدراسة على تسع من المرضى الذين تناولوا اسماك القراض ونقلوا إلى مستشفى السويس العام. ولقد تم التشخيص استنادا على التاريخ الغذائي الحديث و على الصورة الإكلينيكية. ولقد تم الفحص الإكلينيكي والفحوصات وملاحظة جميع الحالات منذ دخولها حتى خروجها من المستشفى. وتم علاج جميع المرضى بالغسيل المعوي والفحم النشط وكذلك الأعراض المصاحبة. **النتائج:** وفقا لنظام المراحل الإكلينيكية للتسمم بالتetrodotoxins، ثلاث حالات كانت تمثل المرحلة الأولى وثلاث أخرى تمثل المرحلة الثانية والثلاث حالات التي توفيت بدأت بالمرحلة الثالثة ثم تدهورت وأصبحت بالمرحلة الرابعة. بداية ظهور أعراض التسمم بأسمك القراض كانت سريعة وجميع الفحوصات التي أجريت لكل المرضى كانت طبيعية. الأعراض الإكلينيكية للتسمم كانت أساسا بالجهاز العصبي، أما التأثيرات على الجهاز الدوري كانت غير شائعة في معظم المرضى. كانت الأعراض السمية تتراوح في الشدة وفقا لطريقة تجهيز و تنظيف اسماك القراض. الحالات التي توفيت أكلت رأس السمك و البطاريخ وكان سبب الوفاة هو فشل في التنفس. **الخلاصة:** العوامل المؤثرة على شدة وتطور التسمم بأسمك القراض هي طريقة الإعداد والتنظيف والأجزاء التي تم تناولها من السمك.