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Red Sea Puffer fish Poisoning: Emergency Diagnosis and Management of Human Intoxication

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ABSTRACT

Regarded by many as a delicacy, puffer fish (*Lagocephulus scleratus*) is a source of food poisoning with a high mortality. It contains tetrodotoxin which cause death by muscular paralysis, respiratory depression, and circulatory system failure. On December 23rd, 2004 seven patients from the same family were admitted to the general Suez Hospitals with history of consumption of puffer fish. Important manifestations were observed peri-oral tingling, weakness of both legs, floating or lightness sensations, headache and abdominal pain. All patients were treated by gastric lavage, intravenous fluid, active charcoal and injection of Neostigmine. The cases were clinically reviewed periodically and routine biochemical and hematological investigations were done. Also, toxicity studies for the patients gastric lavage was occurred. Results of toxicities test confirmed the presence of tetrodotoxin in the muscle of consumed fish. No significant changes in complete blood picture, blood glucose level, liver and renal function tests of patients were observed. While a marked disturbance was recorded in the serum levels of sodium, potassium, calcium and phosphorus of the patients throughout the medical care time. Complete recovery for all patients was reached after four days. Puffer fish has no specific treatment. Health professionals should have sufficient knowledge regarding its clinical manifestations, complications and management. People awareness should be raised towards potential risk of eating puffer fish. It may be a must to establish a public agency that deal with collection of this fish, monitoring its toxicity and dealing with its safe flesh either for local consumption or for exportation.

INTRODUCTION

Numerous deaths from eating puffer fish have been reported from all over the world. Many puffer fish species contain tetrodotoxin (TTX) which is a potent marine neurotoxin (Yang *et al.,* 1995). The concentration of TTX may vary due to season, geographic location, sex and organ tissue (Noguchi *et al*., 1997; Nunez *et al*., 2000 and Yu and Yu 2002). The liver, gonads, intestines, and skin of these fish contain TTX that can cause death in approximately 60 % of persons who ingest it (Ellenhorn and Barceloux, 1988).The majority of reported cases have occurred in southeastern Asia including Japan, Malaysia, Taiwan , Hong Kong, and Korea (Kan, 1987; Yang *et al.,* 1996; Kanchanapongkul, 2001). Ababou *et al.,* (2000) recorded that, in Marco, 3 persons were intoxicated after ingestion of puffer fish eggs and one of them died. In Pakistan, eight patients died from a total of forty-five persons developed manifestations of puffer fish poisoning (Ahasan *et al*., 2003). Although puffer fishes are rarely consumed as food in Egypt, many cases of intoxication resulted from consumption of these fishes have been occurred. Clark and Gohar (1953); Ali *et al*., (1995) and Ali (1996) recorded some cases of puffer fishes poisoning in Giemsha on the Gulf of Suez, in Hurgada and

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in Sharm El-Sheik on the Red Sea, respectively, without referring to any clinical symptoms of poisoning cases, age, and sex of patient, the first medical aid, the duration of the gastrointestinal and neurological features, the time of recovery and/or the time of death. Zaki (2004) described the clinical manifestations, age, sex and time elapsed between the ingestion and the death of eight cases from 11 cases of puffer fishes poisoning in Suez City.

Although Puffer fish is available in Egypt and Puffer fish poisoning is sporadic, ignorance regarding its proper cooking process may lead to serious clinical hazards including fatality. Since intoxication of Puffer fish is uncommon for many physicians, the increase in the rate of sporadic poisoning promoted us to report this paper. Possibly it is the first article in Egypt which deals with the clinical troubles and the management of human intoxication.

PATIENTS AND METHODS

On December 23rd, 2004 seven patients from the same family were admitted to the Suez Hospital with history of consumption of Puffer fish. Puffer fish was bought from the Attaka Port. A preliminary diagnosis of puffer fish (tetrodotoxin) poisoning was made on the basis of recent dietary history and the observed clinical symptoms of the cases. All patients were treated with gastric lavage, intravenous fluid, active charcoal and injection of Neostigmine. The cases were clinically reviewed intensively in the first 6 hours and a routine investigation was done daily. Age and sex of patients, onset of symptoms in minutes after the ingestion of the fish and the clinical features of the admitted cases were recorded. The gastric lavage and blood samples of patients were taken for further analyses.

Assay of toxicity

The gastric lavage of all intoxicated persons was subjected for assessing the toxicity of TTX according to mouse assay method (Kawabata, 1978).

Blood Collection and handling

The blood of patients was collected in heparinized and non heparinized tubes in the first and the second days on intoxication. The heparinized tubes were used for hematological parameters. Blood Samples in the non heparinezed tubes were allowed to clot at room temperature for 1h. Serum samples was obtained by centrifugation at 1000 g. for 20 min. Blood and serum samples were investigated at once.

Haematological assays

Haematological parameters including white blood cells count (WBC_S); red blood count (RBCs); haemoglobin content (Hb); hematocrit value (HCT); mean cell volume (MCV), mean cell haemoglobin (MCH); mean cell haemoglobin concentration (MCHC); and blood platelets count (PLT) were measured automatically by cell counter (ADIVA 60-ct- System is a fully automated hematology analyzer, Bayer Health Care, Germany).

Biochemical assays

All determinations were performed spectrophotometrically (Biosystems, BTS 310, Spain) using commercial available specific kits (Spain react, Spain; Human, Germany; SGM, Italy; Biocon, Germany; Bio Merieux, France and Teco Diagnostics, USA). Serum samples were subjected to determination of glucose (Trinder,1969); urea (Chaney and Marbach, 1962); Cratinine (Fabiny & Ertingshausen, 1971); ALT and AST (Gella *et al*., 1985); sodium (Maruna, 1958); potassium (Terri and Sesin, 1958); calcium (Gitelman, 1967) and phosphorus (Kesler and Morris, 1964).

RESULTS

Table (1) shows a total of 7 persons (1 male + 2 children + 4 females) ingested puffer fishes during their lunch meal and developed features of tetrodotoxin poisoning. The amount of fish taken during meal

individually varied. The intoxicated persons having significant manifestations were admitted to the hospital. Body temperature of six intoxicated persons decreased 1or 2 ^{o}C (Table 1).

Table (2) illustrates the time taken for onset of symptoms varied from 15 minutes to 120 minutes post ingestion.

Table (3) elucidates the toxicity of gastric lavage of all poisoned persons. The cases 4 and 6 who exhibited severe symptoms of toxicity had 25 and 5 MU respectively in their gastric lavage. Although, the gastric lavage of the remaining patients showed no toxicity, the mice injected with their extracts resulted in toxicity manifestations and death after 30 minutes.

Table (4) demonstrates the important symptoms observed on the first day, second day and the third day.

Tables (5 & 6) show no significant effect of TTX on complete blood picture, serum glucose, kidney and liver function tests of all patients, while serum electrolytes (Na, K, Ca and P) showed a significant disturbance in their levels through out 48 hours post ingestion of puffer fish.

DISCUSSION

Although puffer fish poisoning is very few in Egypt, our paper highlights the seriousness of TTX intoxication and its potential to be life-threatening (Zaki, 2004). In addition, such paper is to attract the attention especially physicians to the dangerous of such poisons, its symptoms and the available supportive treatment as early recognition of the condition and supportive care in a modern intensive care unit should ensure a safe outcome.

The flesh of the puffer fish is considered delicious in Suez City, Egypt as well as in other countries such as Japan, Taiwan, China, the Philippines and Mexico. In Suez City, it is prepared by removing the head, skin, gonads, intestine and liver and then is soaked in a water with acetic acid 5 %. While, in Japan, it is prepared by chefs specially trained and certified by the Government. Poisoning incidents, in Japan, decreased in the recent years by imposing quarantine rule and creating public awareness after extensive study of the toxicity and toxin properties of puffer (Noguchi and Ebesue, 2001). On the other hand, in Egypt, poisoning usually occurs after eating fish caught and prepared by unauthorized handlers (Zaki, 2004). Although, our cases bought only the flesh, they suffered the poisoning. This may be due to diffusion of TTX from skin, ovary and/ or liver during improper cleaning by handlers. In addition, the patients might not handle and cook the fish properly.

The early diagnosis of puffer fish poisoning is based on the observed clinical manifestations and recent dietary history. Clinical grading system for tetrodotoxin poisoning based on symptoms and signs present (after Fukuda and Tani 1949): Grade I: perioral numbness and paraesthesia, with or without gastrointestinal symptoms (mainly nausea).Grade II: numbess of tongue, face and other areas (distal); early motor paralysis and incoordination; slurred speech; normal reflexes. Grade III: generalized flaccid paralysis, respiratory failure (dysnoea), aphonia and fixed/dilated pupils; patient still conscious. Grade IV: severe respiratory failure and hypoxia, hypotension, bradycardia and cardiac dysrhythmias; unconsciousness may occur.

According to the above grading, patients 1, 2 and 7 belong to grade I. Patients 3 and 5 followed grade II. However, cases 4 and 6 showed all symptoms of grade II, and some manifestations of grade III. This grade variation of intoxication may depend on cooking practice, amount taken, age, vomiting after ingestion and post-ingestion management. The vomiting was the common symptom of gastrointestinal features in the survival victims. Such survival may be attributed to the rapid stomach evacuation and subsequent decrease the dose of absorbed toxin.

In spite of long history of TTX intoxication, no antidotes or antitoxins to TTX is invented so far. Treatment is supportive including gastric lavage, intravenous fluid and in some cases injection of Neostigmine (Sun, 1995).

The non significant results of complete blood pictures, blood glucose level and liver and renal function tests of patients may be ascribed to good and fast management of treatment. Consequently, the absorbed dose of toxin was less to stimulate severe bio deterioration. Such view is confirmed by the present results where 6 of patients exhibited gastric lavage of insignificant toxicity. This is in agreement with the results of Yu and Yu (2002) where they considered the non toxic dose is less than 10 MU/g.

The disturbance in the serum levels of electrolytes of the patients throughout the medical care time may be due to vomiting (Varley, 1988) and intravenous fluid.

Since, puffer fishes are relatively available in Egypt. People may like such fishes because the fish are thought to be a very delicious, beneficial in potency, analgesic for backbone pain, curiosity and/or due to its low cost. It may be a must to establish a public agency that deal with collection of these fish, monitoring its toxicity and deals with its safe flesh either for local consumption or for exportation. On the other hand, the rest of fish (especially gonads and liver) which contain higher level of TTX can be used as a source of the toxin to be used pharmaceutically.

Table (1): Age and Sex distribution of patient admitted with puffer fish poisoning

Case Number	Age (Year)	Sex	Body Temperature
1	8	Female	36
2	11	Female	35
3	17	Female	36
4	20	Female	37.5
5	24	Female	35
6	45	Female	36
7	55	Male	36

Table (2): Onset symptoms in patients with puffer fish poisoning and toxicity level of gastric lavage

Case Number	Onset of symptoms (in minutes)	Toxicity level in gastric lavage (in Mouse Unit)
1	< 30	Less than 5
2	< 30	Less than 5
3	< 30	Less than 5
4	61-90	25
5	< 30	Less than 5
6	31- 60	5
7	91-120	Less Than 5

Table (3): Clinical features in patients with puffer fish poisoning in relations to days

Clinical features	**No. of patients developing symptoms**		
Symptoms	**1 st day**	**2 nd day**	**3rd day**
A slight numbness of the lips and tongue Tingling and numbness around oral cavity	7	4	----
Tingling and numbness throughout the body	7	3	---
Sensations of lightness or floating	2	---	----
Nausea and Headache	7	5	2
Vomiting	5	3	1
Increase of temperature of face	4	-----	-----
Cooling of Terminals	4	----	----
Abdominal pain	5	4	1
Reeling or difficulty in walking	1	----	--
Weakness of both lower limbs	2		
Difficulty in respiration	2	----	
Difficulty in speech	2		
Unconsciousness	2		

Table (4): Blood WBCs, HB, RBCs, HCT, MCV, MCH, MCHC and PLT in some patients .

	Normal Control	**1**	**2**	**3**	**4**	**5**	**6**	**7**
WBCs (10^3/mm)	(4-11)	N. S	9.4	9.7	5.1	5.3	N. S	8.1
Hb (g/dl)	Ch 11-14 M: 14-18 F: 12-16	N. S	13.2	13.5	12.5	12.6	N. S	15.8
RBCs (10^6/mm)	Ch 11-14 M: 14-18 F: 12-16	N. S	4.6	4.4	4.06	4.15	N. S	4.9
HCT %	Ch 11-14 M: 14-18 F: 12-16	N. S	38.6	38.8	35.9	36.6	N. S	44.6
MCV		N. S	83.9	88.2	88.4	88.1	N. S	91.2
MCH (Pg)		N. S	28.7	30.7	30.8	30.2	N. S	32.3
MCHC (g/dL)		N. S	34.2	34.7	34.8	34.3	N. S	35.4
PLT (10^3/mm^3)	150-400	N. S	294	259	240	286	N. S	184

N.S: No sample was collected for CBC from Patients No 1 & 6

Table (5): Serum glucose, creatinin, urea, GPT, GOT, sodium, potassium, calcium and phosphorous in all patients.

	Normal Control	1	2	3	4	5	6	7
Random Blood Sugar (mg/dl)	< 200	N.D* / N.D**	110* / N.D**	102* / N.D**	96* / N.D**	84* / N.D**	156* / N.D**	176* / N.D**
S. Creatinine (mg/dl)	F: 0.6-1.2 M: 0.7-1.4	N.D / 0.6	0.6 / 0.7	0.8 / 0.9	0.9 / 0.9	0.9 / 0.9	0.7 / 0.9	1.0 / N.D
Blood Urea (mg/dl)	15-45	N.D / 25	33 / 30	29 / 28	32 / 34	38 / 36	27 / 24	30 / N.D
S. G.P.T (U/L)	Up to 49	N.D / 12	10 / 18	16 / 17	14 / 15	17 / 16	12 / 13	20 / N.D
S. G.O.T (U/L)	Up to 49	N.D / 14	24 / 30	17 / 20	15 / 17	20 / 22	17 / 20	13 / N.D
S. Na (mEq/L)	135-155	N.D / 150	146 / 160	140 / 164	144 / 164	139 / 164	118 / 144	144 / N.D
S. K (mEq/L)	3.4-5.3	N.D / 3.4	3.5 / 3.3	3.2 / 3.9	3.1 / 3.5	3.1 / 3.3	3.5 / 4.1	3.1 / N.D
S. Ca (mg/dl)	8.5-10.5	N.D / 9.2	9.3 / 9.4	8.7 / 9.5	8.8 / 9.5	8.6 / 9.2	8.4 / 9.1	8.8 / N.D
S. P (mg/dl)	A. 2.5-5 Ch. 4-7	N.D / 5.6	4.3 / 4.1	3.4 / 4.2	2.2 / 3.7	2.8 / 4.2	3.7 / 4.1	3.2 / N.D

* First day
** Second day
A = Adult
Ch = child
S.= Serum

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