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Review Article

Puffer Fish Poisoning

M Azizul Haque[1], Q Tarikul Islam[2], A R M Saifuddin Ekram[3]

Abstract

Puffer fish poisoning occurs sporadically throughout the world, especially in the coastal areas. It contains tetrodotoxin which can cause death by muscular paralysis, respiratory depression, and circulatory failure. Early diagnosis and supportive management could ensure a safe and favorable outcome. In this review article, we have tried to explore the pathophysiology, clinical features, and treatment of puffer fish poisoning.

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Introduction

Though many people consider it a delicacy, puffer fish (Lagocephalus scleratus) is a lethal source of food poisoning with a high mortality[1]. Puffer fish is also known as Fugu (in Japan), toadfish, globefish, blowfish and baloonfish[2]. It is 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. Their lifespan depends on the different species. However, there are well-established methods of extinction for puffer fish as a whole in Japan as Japanese consumes about 20,000 tons of blowfish per year, 6,800 tons in imports. In Japan, 100 annual human fatalities due to ingestion of toxic puffer have been reported until 1960 [3]. The rate of deaths in recent years has decreased substantially with improved legislation of Fugu preparation and marketing.

The highly toxic Red Sea porcupine fish may have prompted the biblical injunction: ".... and whatsoever hath no fins and scales ye may not eat; it is unclean unto you" (Deuteronomy 14:9-10). The puffer fish is illustrated on an Egyptian tomb of the fifth dynasty dated 2500 BC[4]. Captain Cook was poisoned by it in 1774[5] and the voodoo poisons of Haitian folklore responsible for "zombification" reportedly contains tetrodotoxin[6]. Puffer fish, or Fugu, is a delicacy in Japan where specially trained chefs prepare it. The small amount of toxin present in correctly prepared fish produces a mild tingling around the mouth, which, together with the thought of sharing a potentially fatal dish with friends, supposedly adds to the gastronomic experience[7]. Pufferfish belongs to the order Tetraodontoidea which also includes ocean sun fish and porcupine fish[8]. Tetrodotoxin (TTX), is also found in the venom on the blue ringed octopus found around Australia and involved in human fatalities through bites[9]. 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. He recorded his crew eating some local

[1] Assistant Professor, Department of Medicine, Rajshahi Medical College, Rajshahi.
[2] Professor , Department of Medicine, Dhaka Medical College, Dhaka.
[3] Professor, Department of Medicine, Rajshahi Medical College, Rajshahi.

tropic fish (Pufferfish), and 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. In hindsight, it is clear that the crew received a mild dose of tetrodotoxin, while the pigs ate the Pufferfish body parts that contain most of the toxin, thus killing them. The toxin was first isolated and named in 1909 by Japanese scientist Dr. Yoshizumi Tahara.

Toxicity of Tetrodotoxin

Tetrodotoxin poisoning is probably the most common poisoning along the coasts of Asia[10]. Puffer fish poisoning has been reported in many Asian countries including Thailand, Malaysia, Bangladesh, Taiwan and particularly Japan[21,22]. Tetrodotoxin (TTX) is present in high concentrations in the liver, ovaries, intestines and skin of puffer fish[11]. The amount of TTX varies widely in different species[12]. 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. Paralysis and respiratory failure account for the main cause of death[13]. 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[14] and may cause a drop in blood pressure by relaxing vascular smooth muscle and blocking peripheral autonomic nerves[15]. Response to cholinesterase inhibitors also suggests a reversible competitive blockade at the motor endplate[16]. 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[17]. 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[18]. 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. Tetrodotoxin also is found in the gastropod mollusc; in the eggs of horseshoe crabs; in newts of the genus Taricha; in the skin of Atelopid frogs; and in the skin and viscera of porcupine fish, globefish, balloon fish, blowfish, sunfish, toadfish, blue-ringed octopus, and some species of salamanders.

Clinical Features

Initial symptoms include lip and tongue paresthesia, followed by facial and extremity paresthesia and numbness. Salivation, nausea, vomiting, and diarrhea with abdominal pain develop early. Motor dysfunction with weakness, hypoventilation (may be from dysfunction of central and peripheral nervous systems), and speech difficulties then develop. A rapid ascending paralysis occurs over 4-24 hours. Extremity paralysis precedes bulbar paralysis, which is followed by respiratory muscle paralysis. Deep tendon reflexes are preserved early in the course of paralysis. Finally, cardiac dysfunction with hypotension and arrhythmias (bradycardia), central nervous system (CNS) dysfunction (e.g., coma), and seizures develop. Patients with severe toxicity may have deep coma, fixed non-reactive pupils, apnea, and loss of all brain stem reflexes. Death can occur within 4-6 hours. Typically, death occurs from respiratory muscle paralysis and respiratory failure. Yang et al reported that the mortality rate of tetrodotoxin (TTX) poisoning in Taiwan was 13.5%[19]. 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 rate11.62%)[20]. Patients who live through the acute intoxication (i.e. first 24 h) usually recover without residual deficits. Recovery takes days to occur.

Clinical grading system for tetrodotoxin poisoning based on signs and symptoms

Grade 1: Perioral numbness with or without gastrointestinal symptoms.

Grade 2: Numbness involving tongue, face and distal areas; early motor paralysis and incoordination; slurring of speech; normal reflexes.

Grade 3: Generalized flaccid paralysis; dyspnoea or respiratory failure; aphonia.

Grade 4: Hypoxia and severe respiratory failure; cardiovascular effects including hypotension, bradycardia and arrhythmia[23].

Diagnosis of Tetrodotoxin poisoning

No specific laboratory test that confirms tetrodotoxin ingestion exists; thus, dietary history is the key for diagnosis. Mouse bioassays for paralytic shellfish toxin (i.e., saxitoxin) exist that are positive with tetrodotoxin and research chromatography techniques, but neither is available in the acute clinical situation. Tetrodotoxin also may be detected by fluorescent spectrometry.[17]

Treatment

There is currently no effective antidote to tetrodotoxin poisoning. Treatment is entirely supportive and may involve mechanical ventilation or inotropic support[24]. Activated charcoal is said to effectively bind the toxin[25]. As tetrodotoxin is less stable in an alkaline environment, gastric lavage with 2% sodium bicarbonate solution may help removing the unabsorbed toxin[26]. Gastric lavage and activated charcoal is said to have role if instituted early. Advocated treatments yet to be of proved benefit include cholinesterase inhibitors (neostigmine), naloxone, cysteine, gastric lavage with sodium bicarbonate,[25] antihistamines, and steroids[23] Future effective treatment is a possibility. When monoclonal neutralizing antibody was injected into mice poisoned with oral tetrodotoxin it resulted in 100% survival compared with 0% survival in the control group[27]. No reports have yet appeared of its use in man. Nothing equivalent to anti-venom has been developed--presumably because the toxin acts quickly and binds with an affinity that is not easily overcome.

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 could ensure a safe and favorable outcome. Although puffer fish poisoning is uncommonly encountered in our daily practice, physicians should be familiar with the clinical presentations and management and get prepared to handle such potentially life-threatening intoxication.

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