A case series of puffer fish poisoning
河豚中毒個案系列

CK Wan 尹志強, SH Tsui 徐錫漢, HK Tong 唐漢軍

Puffer fish poisoning caused by tetrodotoxin, a potent neurotoxin, is uncommon in Hong Kong. We report a total of seven cases of puffer fish poisoning with different levels of severity. Two of them developed respiratory distress and subsequently required endotracheal intubation and respiratory support while the others presented with numbness and mild weakness. Most of them experienced perioral numbness as the first symptom. The mean time of symptoms onset was approximately 94 minutes. All of our patients survived the intoxication. (Hong Kong J Emerg Med. 2007;14:215-220)

河豚毒素為強烈的神經毒素，其引致的河豚中毒在香港並不常見。本章報告7個不同嚴重程度的河豚中毒個案。其中2人出現呼吸困難及其後需要氣管內插管及呼吸器支持，而其他人則呈現麻木及輕度無力。他們大多數最初的病徵為感覺口周麻木。病徵開始的平均時間大約為94分鐘。所有中毒病者均生存。

Keywords: Fishes, food poisoning, tetrodotoxin

關鍵詞：魚、食物中毒、河豚毒素

Introduction

The mortality rates of puffer fish poisoning (PFP) vary among different series and countries. Some articles quoted it to be as high as 50%. However, it is believed that the mortality rate is much lower in areas with modern medical facilities and care. 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%). Most of these cases were due to preparation of puffer fish by untrained people. Notably, puffer fish poisoning occurs sporadically but only one fatality has also been reported in Hong Kong.

Case presentation

From November 2005 to November 2006, there were 2 incidents of puffer fish poisoning involving a total of 7 patients presenting to our department. The first incident involving 3 patients occurred in November 2005. Three Chinese sailors caught a puffer fish weighted 250 grams in Hong Kong waters. The skin, head and viscera were cut. The flesh and bone were boiled with cabbage and rice noodles for 15 minutes. They had eaten the flesh, cabbage, rice noodle and soup about 6.5 hours before attending our department.

The second incident occurred in November 2006. We received a cluster of 4 cases of PFP. Four sailors from Mainland China caught a puffer fish weighted about
400 grams in Hong Kong waters. The viscera were removed. The head, skin, flesh and bone were cooked with cabbage and ginger in boiling water for 10 minutes. They had drunk the self-prepared puffer fish soup and eaten the flesh six hours before attending our department.

Their clinical profiles and outcomes are summarised in Table 1. The diagnosis of puffer fish poisoning was made basing on their typical clinical presentation and the history of puffer fish ingestion. The differential diagnoses included paralytic shellfish poisoning, ciguatera fish poisoning, organophosphate poisoning and rarely botulism.\(^1\)

Patient 1 to 4 belonged to the 2006 incident (bigger fish) while Patient 5 to 7 belonged to the 2005 incident.

Patient 1 was a 40-year-old man who developed generalised weakness and numbness 60 minutes after eating the puffer fish and soup, followed by throat congestion, difficulty in swallowing and drooling of saliva. On examination, he was fully conscious and

**Table 1. Summary of the clinical profile and outcome of the 7 cases of puffer fish poisoning**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex / Age (year)</th>
<th>Onset (minutes)</th>
<th>Symptoms</th>
<th>Severity grade*</th>
<th>Duration of mechanical ventilation (hours)</th>
<th>Duration of ICU admission / total hospital stay (days)</th>
<th>Residual symptoms on discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M 40</td>
<td>60</td>
<td>Generalised weakness and numbness; throat congestion; drooling of saliva</td>
<td>3</td>
<td>21</td>
<td>1 / 5</td>
<td>Mild residual lower limb weakness</td>
</tr>
<tr>
<td>2</td>
<td>M 39</td>
<td>Immediate</td>
<td>Vomiting; perioral, finger and toe numbness; drooling of saliva; difficulty in breathing; generalised weakness; dysarthria</td>
<td>3</td>
<td>18</td>
<td>1 / 4</td>
<td>Nil</td>
</tr>
<tr>
<td>3</td>
<td>M 34</td>
<td>15</td>
<td>Numbness over fingertips, tongue and perioral area; dry mouth; dizziness; mild limb weakness; abdominal discomfort</td>
<td>2</td>
<td>NA</td>
<td>0 / 1</td>
<td>Nil</td>
</tr>
<tr>
<td>4</td>
<td>M 34</td>
<td>15</td>
<td>Numbness over perioral area, fingers and toes; very mild weakness</td>
<td>2</td>
<td>NA</td>
<td>0 / 1</td>
<td>Nil</td>
</tr>
<tr>
<td>5</td>
<td>M 54</td>
<td>210</td>
<td>Numbness over fingers, nausea, dizziness; mild limb weakness</td>
<td>2</td>
<td>NA</td>
<td>0 / 0</td>
<td>Nil</td>
</tr>
<tr>
<td>6</td>
<td>M 55</td>
<td>150</td>
<td>Numbness over perioral area, fingers and toes; vomiting; dizziness; generalised weakness</td>
<td>2</td>
<td>NA</td>
<td>0 / 1</td>
<td>Mild truncal ataxia</td>
</tr>
<tr>
<td>7</td>
<td>M 37</td>
<td>210</td>
<td>Finger numbness; mild weakness</td>
<td>2</td>
<td>NA</td>
<td>0 / 0</td>
<td>Nil</td>
</tr>
</tbody>
</table>

*Refer to Table 3; NA=not applicable; ICU=intensive care unit
afebrile. The blood pressure was 161/101 mmHg and the pulse rate was 111 beats per minute. The oxygen saturation was 100% on 2 litres of oxygen per minute. He had generalised hypotonia with power grade 3 over 5. In view of rapid ascending paralysis and subjective respiratory distress, he was intubated and mechanically ventilated and transferred to the intensive care unit (ICU). He was mechanically ventilated for 21 hours and then extubated uneventfully. The total hospital stay was five days. Upon discharge, he only had slight weakness of the lower limbs.

Patient 2 was a 39-year-old man who presented with vomiting and numbness over the perioral area, toes and fingers immediately after the ingestion of puffer fish and soup. He then complained of difficulty in breathing. On presentation, he was conscious and afebrile. The blood pressure was 133/84 mmHg and the pulse rate was 73 beats per minute. The respiratory rate was 24 per minute. The oxygen saturation was 98% on 2 litres of oxygen per minute. The power of limbs was grade 5. He was not intubated initially in our department but was closely monitored in the ICU. Approximately one hour after admission, he was intubated because of progressive dyspnoea and the development of dysarthria. The duration of mechanical ventilation was 18 hours. He stayed in hospital for four days and was discharged uneventfully.

Patient 3 and 4 stayed in the general medical ward for one day. Their symptoms lasted about 24 hours.

Patient 5 and 7 presented with numbness and mild limb weakness about 210 minutes after the ingestion of puffer fish. When they attended our department, their symptoms were subsiding. Their vital signs were stable and they were discharged directly from our department after observation for about three hours. Follow up was not arranged because they went back to China by ship soon after discharge.

Patient 6 presented with numbness over the perioral area, fingers and toes, then followed by repeated vomiting, dizziness and generalised weakness. The power of the limbs was full. He was closely monitored and managed in our observation ward. The numbness lasted about seven hours. He developed no respiratory distress. He discharged himself against medical advice after approximately 20 hours of stay. Upon discharge, truncal ataxia persisted but he could walk with a wide-based gait.

### Discussion

Puffer fish poisoning has been reported in many Asian countries including Thailand, Malaysia, Bangladesh, Taiwan and particularly Japan.\(^4\)\(^7\) Mortality and relatively large scaled incidents have been reported. How et al reported that 6 sailors were intoxicated in one incident in which 1 patient died.\(^7\) Ahasan et al reported an incident of puffer fish poisoning involving 37 patients with 8 of them died due to respiratory failure.\(^4\)

Between 1993 and 2006, there were 10 reported incidents of puffer fish poisoning involving 23 patients, including the data of this case series, with one death in Hong Kong (Table 2). More than 60% of them were not local residents.\(^8\) Lau et al reported 7 Vietnamese

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of incidents</th>
<th>No. of person involved</th>
<th>Fatality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>1994</td>
<td>1</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>2000</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>2001</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2005</td>
<td>3</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>2006</td>
<td>2</td>
<td>5</td>
<td>0</td>
</tr>
</tbody>
</table>
boat people in Tai A Chau Detention Centre intoxicated after eating puffer fish caught from Hong Kong waters. One of them died. The rest survived the intoxication and made an uneventful recovery. The single mortality was a 17-year-old male who developed limb numbness and dyspnoea two hours after ingestion of the abdomen of the puffer fish. A diagnosis of PFP was made in the Detention Camp Clinic. However, he developed cardiopulmonary arrest while being transferred to hospital by helicopter. On arrival at Queen Elizabeth Hospital, he was in asystole. Although circulation returned after resuscitation, he died eight hours after admission. 

It was postulated that the mortality might be avoided if active airway management and respiratory support had been initiated earlier.

The mortality rates of PFP are difficult to calculate. It was estimated to be as high as 50%. Such high rate may be over-represented by reports from developing countries and old reports. Yang et al reported that the mortality rate of tetrodotoxin (TTX) poisoning in Taiwan was 13.5%. The mortality rate of PFP in Hong Kong, including data of this series, is 4.35% (1/23). The low mortality rate of PFP in Hong Kong may be due to the different dose ingested, different species of puffer fish, high quality of acute medical service and early medical consultation.

In our case series, although Patient 1 to 4 had fast onset of symptoms, they attended our department late. They might not be aware of the early warning signs and symptoms and the seriousness of PFP. In order to avoid mortality in the future, education of the public should be reinforced. In Japan, chefs are required to be specially trained and pass the examination in handling puffer fish. People should be advised not to eat puffer fish prepared by themselves and should seek medical care immediately once they develop symptoms of PFP. However, such message may not reach the Chinese seamen from Mainland China.

The toxic dose of TTX has not been established but one dose of 1 to 2 mg of purified TTX can be lethal. The relatively mild symptoms experienced by Patient 3 to 7 may be due to the relatively low dose of TTX ingested. It will be interesting to know if there is any correlation between the blood or urine concentration of TTX and the severity of clinical symptoms.

Tetrodotoxin is heat-stable and water-soluble, so boiling of puffer fish in water cannot destroy the toxin. However, it is less stable in alkaline medium. High concentrations of TTX can be found in liver, gonads, skin and intestines of puffer fish. The amount of TTX varies widely in different species and the concentration is seasonal. It is a common belief that all puffer fish would become more toxic in their spawning seasons. The spawning periods of two locally found puffer fish, namely Takifugu niphobles (Jordan and Snyder) (Figure 1) and Takifugu alboplumbens (Richardson) are from October to February (four consecutive months) and December to February (two consecutive months) respectively. Contrary to the common belief, they were relatively less toxic during their spawning seasons. The species of puffer fish ingested by our patients, however, could not be identified because there was no remnant of the puffer fish left.

Tetrodotoxin can also be found in porcupine fish, goby, shellfish, California newt, parrotfish, blue-ringed octopus, starfish, angelfish and xanthid crabs. Food poisoning caused by goby was reported in the Guangdong province in April 2007. Yongeichthys criniger (a toxic goby) was wrongly identified as the non-toxic and edible mudskippers, resulting in one death. Besides eating puffer and goby fish, dried porcupine fish may be another source of TTX poisoning. One patient was reported to develop symptoms of TTX poisoning after drinking a soup prepared from dried porcupine fish that was bought from a local market.

![Figure 1. Takifugu niphobles (source: Dr. Shao Kwang-Tsao).](image-url)
Tetrodotoxin blocks voltage sensitive sodium channels in nerve tissue leading to failure of depolarisation 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 centres in that area. Paralysis and respiratory failure account for the main cause of death.\textsuperscript{1,14}

Patients usually experience symptoms within six hours after ingestion.\textsuperscript{1} The clinical toxicity of TTX poisoning can be graded into 4 stages according to the neurological and cardiovascular features (Table 3).\textsuperscript{15} The clinical course of Patient 2 revealed that the respiratory paralysis could occur rapidly. Thus, close monitoring and early respiratory support is of paramount importance.\textsuperscript{16} On the other hand, patients usually recover without any residual deficit if they live through the first 24 hours.

Despite the long history of puffer fish poisoning, there are no antidotes or antitoxins available. The mainstay of treatment is supportive.\textsuperscript{1,16,17} Aggressive resuscitation may revive patients from critical conditions. Loke and Tan reported a severe case of PFP. A 69-year-old lady was intoxicated after eating the roe of puffer fish. She developed cardiorespiratory arrest shortly after arriving at the accident and emergency department. She was aggressively resuscitated and mechanically ventilated. Eventually she survived the intoxication.\textsuperscript{6}

After institution of appropriate airway management and circulatory support, gastrointestinal decontamination including gastric lavage and activated charcoal may be considered if the patient presents early.\textsuperscript{1} For example, gastric lavage with 2% sodium bicarbonate solution may help removing the unabsorbed toxin.\textsuperscript{17} None of our patients in this case series had received any gastrointestinal decontamination because of late presentation to hospital.

Apart from supportive management, other agents like monoclonal antibodies and 4-aminopyridine have been shown to be beneficial in TTX poisoning in animal studies only.\textsuperscript{18,19}

### Conclusion

We reported a series of seven cases of puffer fish poisoning presenting with different levels of severity. Early diagnosis and supportive management could ensure a safe and favourable outcome. Although puffer fish poisoning is uncommonly encountered in our daily practice, emergency physicians should be familiar with the clinical presentations and management and get prepared to handle such potentially life-threatening intoxication.

### Acknowledgement

We would like to thank Dr. Shao Kwang-Tsao (Acting Director/Research Fellow, Research Center for Biodiversity, Academia Sinica, Taiwan) for his kind permission of using the photo of *Takifugu niphobes*.

### Table 3. Clinical grading system for tetrodotoxin poisoning based on signs and symptoms\textsuperscript{15}

<table>
<thead>
<tr>
<th>Grade</th>
<th>Clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Perioral numbness with or without gastrointestinal symptoms</td>
</tr>
<tr>
<td>2</td>
<td>Numbness involving tongue, face and distal areas; early motor paralysis and incoordination; slurring of speech; normal reflexes</td>
</tr>
<tr>
<td>3</td>
<td>Generalised flaccid paralysis; dyspnoea or respiratory failure; aphony</td>
</tr>
<tr>
<td>4</td>
<td>Hypoxia and severe respiratory failure; cardiovascular effects including hypotension, bradycardia and arrhythmia</td>
</tr>
</tbody>
</table>
References

12. Yu CF, Yu PH. The annual toxicological profiles of two common puffer fish, Takifugu niphobles (Jordan and Snyder) and Takifugu alboplumbeus (Richardson), collected along Hong Kong coastal waters. Toxicon 2002;40(3):313-6.