Case Report: Paralytic Shellfish Poisoning in Sabah, Malaysia

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Abstract. During the months of January–February and May–June 2013 coinciding with the red tide occurrence in Kota Kinabalu, Sabah, Malaysia, six episodes involving 58 cases of paralytic shellfish poisoning (PSP) or saxitoxin (STX) poisoning and resulting in four deaths were reported. Many of them were intoxicated from consuming shellfish purchased from the markets, whereas others were intoxicated from eating shellfish collected from the beach. Levels of STX in shellfish collected from the affected areas were high (mean $2,920 \pm 780$ and 360 ± 140 μg STX equivalents/100 g shellfish meat respectively for the two periods). The count of toxic dinoflagellates (*Pyrodinium bahamense* var *compressum*) of the sea water sampled around the coast was also high (mean $34,200 \pm 10,300$ cells/L). Species of shellfish containing high levels of STX were *Atrina fragilis*, *Perna viridis*, and *Crassostrea belcheri*. The age of victims varied from 9 to 67 years. Symptoms presented were typical of PSP, such as dizziness, numbness, vomiting, and difficulty in breathing. Recommended steps to prevent or reduce PSP in future red tide season include better monitoring of red tide occurrence, regular sampling of shellfish for determination of STX level, wider dissemination of information on the danger of eating contaminated shellfish among the communities, fishermen, and fishmongers.

INTRODUCTION

Paralytic shellfish poisoning (PSP) resulting from consumption of contaminated molluscan bivalves and other shellfish is a worldwide seafood toxicity problem. The neurotoxins which cause these seafood-borne illnesses are known as saxitoxins (STXs), or simply PSP toxins (or PSTs). These extremely potent and pervasive toxins are a serious toxicological health risk that affects both humans and animals. They act by blocking voltage-gated sodium and calcium channels, prolonging the gating of potassium channels,^{1,2} and preventing transduction of neuronal signals. Globally, every year more than 2,000 human cases of PSP are being reported with a fatality rate of 15%.³

STXs have at least 24 congeners, with a range of hydroxyl, carbamyl, and sulfate moieties at four sites on the back bone structure.⁴ The carbamate toxins include STX, neosaxitoxin (NEO), and gonyautoxins (GTX1–4). These are the most potent, and are most commonly found in toxic dinoflagellates. These toxins are water soluble and heat stable, but the stability varies greatly depending on the pH and the structures of toxins.⁵ Generally, however, the toxins are stable under acidic conditions.

Marine dinoflagellates of the genera *Alexandrium*, *Gymnodinium*, and *Pyrodinium* are the major sources of these toxins. In fact, most PSP are caused by *Alexandrium tamarense*, *Alexandrium fundyense*, *Alexandrium catenella*, *Gymnodinium catenatum*, and *P. bahamense*.^{6,7} Each species contains a particular suite of the toxin congeners, with a different composition and concentration which determine its overall toxicity. Interestingly, the geographic region and environmental factors also affect the toxin composition and concentration for a given species.^{8–11} These toxic dinoflagellates are ingested by filter-feeding molluscs, in particular, the bivalves in which the PSTs are accumulated.⁶

PSTs are fast-acting, and PSP symptoms generally occur within 30 minutes of consuming contaminated seafood, whereas death due to asphyxiation has been reported as soon as 3–4 hours after consumption.¹² Symptoms include tingling sensation of the lips, mouth, and tongue; numbness of extremities; paresthesias; weakness; ataxia; floating/dissociative feeling; nausea; shortness of breath; dizziness; vomiting; headache; dysphagia; and dysarthria.^{13–15} Diastolic and systolic hypertension also occurs in almost all patients.¹³ Medical treatment consists of providing respiratory support, whereas fluid therapy can be used to facilitate toxin excretion. Prognosis is good if patients survived for 24 hours, whether with or without respiratory support.^{16,17}

In Sabah, red tides or harmful algal blooms are a regular phenomenon and have been recorded as early as 1976.¹⁸ They will occur during eutrophication making the environmental conditions suitable for the dinoflagellates to grow and reproduce. When the density of the algae is high, the water appears to be discolored or murky, varying in color from purple to almost pink, normally being red or green. The main dinoflagellates affecting human health that bloom in the Sabah seas are *P. bahamense* var *compressum* (Böhm). Bivalves that feed on *P. bahamense* accumulate PSTs transferred from the dinoflagellates. These biotoxins do not harm shellfish, but they can be deadly if consumed by humans, resulting in PSP. It may take days, months, or years for shellfish to be safe to eat after a toxic bloom. PSP in Sabah has been reported yearly caused by toxin from *P. bahamense* var *compressum*. Some filter feeding fishes such as “*ikan tamban*” (slender rainbow sardine, *Dussumiera elopsoides* Bleeker), “*ikan basung*” (round scad, *Decapterus punctatus* Cuvier), and “*ikan rumahan*” (short mackerel, *Rastrelliger brackysoma* Bleeker) take in the dinoflagellates as well when they feed on the zooplankton.

Five toxins have been reported to be produced by the Malaysian *P. bahamense* var *compressum*, viz NEO, gonyautoxin V (GTX5), STX, GTX6, and decarbamoylsaxitoxin, with the first two toxins constituting about 80%.¹⁹ The cellular toxin content was also reported to be affected by temperature, salinity, and light intensity.

Other vectors have also been reported in Malaysia, for example, *Alexandrium tamiyavanichii* from Kuching, *Alexandrium*

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minutum east coast of west Malaysia, as well as *Alexandrium taylori* and *Alexandrium peruvianum*.^{20,21} Nevertheless, PSP from eating shellfish containing toxins from *Alexandrium* spp has not been reported in Malaysia yet, although both these two species produce paralytic shellfish toxins, predominantly GTX4 and GTX6.²¹ In other parts of the world, PSP outbreaks related to *Alexandrium* had been documented. For example, in Chile, intoxication of 527 people with 32 fatalities from consuming shellfish containing toxins from *Alexandrium* harvested in the Chilean Patagonia has been reported since 1972.¹² In 2002, there were two human casualties resulted from consuming ribbed mussel (*Aulacomya ater*) which contained a toxicity level of 8,575 mg of STX equivalents by 100 g of shellfish meat.

We report here PSP cases in Sabah that occurred during the months of January–June 2013. Samples of shellfish and sea water were also taken for analysis to understand better the outbreak of cases, and for making future informed decision to prevent PSP cases.

MATERIALS AND METHODS

PSP cases. Between January and June 2013, there were a total of four episodes of PSP in four localities involving 58 cases who had consumed various species of bivalves collected from Sepangar Bay or Kuala Penyu Bay (Figure 1), or purchased from the markets. All the cases were from coastal areas: squatter area in Taman Jaya Diri, Sepangar (January 1, 2013), Kota Kinabalu and Tuaran (February 12, 2013) Numbak village, Sepangar (May 24, 2013), and Rancangan Mawao village, Membakut (June 6, 2013).

Clinical investigations. All the 58 cases were brought to the nearest public hospitals, namely Queen Elizabeth Hospital in Kota Kinabalu, Hospital Tuaran, and Hospital Beaufort (for Membakut cases) for medical examination and treatment. Information on their ethnicity, age, gender, occupation, residence, shellfish consumed, symptoms, and onset of the symptoms were recorded.

Laboratory and environmental investigations. Green mussels (*P. viridis* Linn.), fan shells (*A. fragilis* [Pennant]), osyters (*C. belcheri* Sowerby), “*Dalus*” (*Meretrix meretrix* [Linn.]), “*Tuntul*” (*Turritella duplicat* [Linn.]), and “*Lokan*” (*Geloina coaxans* [Gmelin]) were collected from markets at Inanam (Kota Kinabalu) and Tuaran by the health department staff, as well as from the localities in the Sepangar Bay and Kuala Penyu Bay (with the help from the patients’ relatives) where the cases had collected the shellfish consumed. In the PSP outbreak in May–June, pelagic fish samples (round scad and short mackerel) were also collected at Sipitang, near Kuala Penyu. The STX level of these samples were analyzed by the Sabah Fishery Department Laboratory using mouse bioassay (MBA) according to the 959.08 method of the Association of Official Analytical Chemists.²² The mouse units (MU) obtained in the MBA were then converted into μg STX equivalents using the conversion factor of 0.178 $\mu\text{g}/\text{MU}$.²³

Sea water samples were also collected from various places in the Sepangar Bay, Likas Bay, and coast of Kota Kinabalu for checking the density of *P. bahamense* var *compressum*.

RESULTS

PSP cases. Details of the four episodes of STX poisoning occurring between January 1 and June 6, 2013, in Kota Kinabalu and nearby localities are given in Table 1. The number of

FIGURE 1. Map of Kota Kinabalu and surrounding areas where PSP occurred. Black dots with numbers indicate the case outbreak areas: 1. Squatter area in Taman Jaya Diri, Sepangar; 2. Kota Kinabalu and Tuaran; 3. Numbak village, Sepangar; 4. Rancangan Mawao village, Membakut. Map adapted from Google maps (www.google.com.my/maps/@5.9356184,115.9072224,11z). This figure appears in color at www.ajtmh.org.

TABLE 1
Paralytic shellfish poisoning cases recorded in Sabah from January 1 to June 6, 2013

Episode	Date (2013)	Number of cases/number exposed	Age	Case locality	Species shellfish consumed	Source of shellfish	Symptoms and clinical outcome	Attack rate
1	January 1	6/6	14.6 ± 2.9 (9–17)	Squatter area in Taman Jaya Diri, Sepangar	Fan shell (<i>Atrina fragilis</i>), “beliung”	Collected from Sepangar Bay during picnic activity	Two died (age 9, 14)	100%
2	February 12	46/91	31.3 ± 16.7 (8–67)	Kota Kinabalu and Tuaran	Green mussels (<i>Perna viridis</i>), “Kupang”	Bought from the market in Kota Kinabalu or Tuaran	Dizziness, numbness two died (age 40, 43)	50.5%
3	May 24	4/4	45.5 ± 12.0 (30–56)	Numbak village, Sepangar	Green mussels	Collected from Sepangar Bay	Dizziness, numbness and vomiting; all recovered	100%
4	June 6	2/5	18, 40	Rancangan Mawao village, Membakut	Flat oyster (<i>Crassostrea belcheri</i>), “Tiram”	Collected from Kuala Penyu Bay	Dizziness, numbness, all recovered	40%
–	–	Overall mean	30.7 ± 2.2 (8–67)	–	–	–	–	55% (58/106)

cases in each episode varied depending on the number of people who had consumed the contaminated shellfish. Three species of bivalves (*A. fragilis*, *P. viridis*, and *C. belcheri*) were found to have caused the PSP, and these were either bought from the markets or collected from the Sepangar Bay or Kuala Penyu bay (Figure 1). There were more people ($N = 46$) affected from consuming bivalves purchased from the markets, although the attack rate was 50.5%. In the case of shellfish collected from the bay for their own consumption, only the family members ($N = 12$) were affected. Forty-four cases were admitted to hospitals (four of them died; ages 9, 14, 40, and 43; 6.9% case fatality), whereas the other 14 cases were given outpatient treatment of dizziness and vomiting (medication: Prochlorperazin (stemetil) 5 mg tds for adults, and 2.5 mg bd, or tds for children). The overall mean age of all cases was 30.7 ± 2.2 and the attack rate 55% (40–100% for each episode).

Of the 58 cases (24 males and 34 females), only 24 were Malaysians. The others were from neighboring countries. Among the victims, five were below age of 10 (youngest was 8 years old), while six above 50 (oldest was 67 years old). The highest percentage was recorded for age group 11–20 (Table 2).

The most common symptoms shown by the patients were circumoral, lingual, neck numbness (83%), whereas breathing difficulty and faintness were presented by few patients (Table 3). About 35% also experienced nausea and 9% fainted.

Symptoms were presented as early as less than an hour after the consumption of the contaminated bivalves. However, most of the patients showed symptoms after 3–4 hours, whereas nine had symptoms only after more than 5 hours (Table 4).

Laboratory analysis of contaminated shellfish and sea water. Contaminated shellfish sampled in January–February had high levels of STX ranging from 590 to 3,660 (mean $2,920 \pm 780$) μg STX equivalents/100 g meat (Table 5) which is much higher than the accepted level of 80 μg /100 g meat. For the May–June samples, only the contaminated oysters *Crassostrea* from Kuala Penyu and Tuaran market had high levels (360 ± 140 μg STX equivalents/100 g meat). The other bivalve species had only 40–100 μg . Both the round scad and short mackerel were found to be free of STX.

Examination of the sea water samples collected from the area around Kota Kinabalu, Sepangar, and Likas Bay or off-shore islands showed high density of *P. bahamense* during the case outbreak period or red tide period (Table 6). The levels were particularly high in January–February 2013, with mean of $34,200 \pm 10,300$ (260–52,800) cells/L, especially in Likas Bay (52,800), Kota Kinabalu coast (KN) (68,900), and Pulau Gaya (93,900). However in May–June, the red tide appeared to be over, and no dinoflagellates were detected.

DISCUSSION

Red tides are a regular, almost yearly phenomenon in Sabah waters especially in the west coast, and the presence of

TABLE 2
Distribution of saxitoxin cases by age groups

Age group (years)	<i>n</i>	%
0–10	5	8.6
11–20	16	27.6
21–30	9	15.5
31–40	12	20.7
41–50	10	17.2
51–60	2	3.4
≥ 61	4	6.9
Total	58	

TABLE 3
Frequency of symptoms and signs among 58 patients who consumed shellfish contaminated with saxitoxin, bought from the markets or collected from the beach

Symptoms and signs	<i>n</i>	%
Circumoral, lingual, neck numbness	48	82.8
Dizziness, vertigo, headache	24	41.4
Hand and feet numbness	29	50.0
Nausea, vomiting	20	34.5
Breathing difficulty	7	12.1
Fainted	5	8.7

TABLE 4

Onset of symptoms after consuming contaminated shellfish

Time onset of symptoms	Number	%
< 1 hr	3	5
1–< 2 hr	9	16
2–< 3 hr	9	16
3–< 4 hr	18	31
4–< 5 hr	10	17
> 5 hr	9	16
Total	58	

P. bahamense can easily be detected by sampling sea water. Similarly, PSP is not new in Sabah, as it has been recorded several times previously. The earliest report of 201 cases was in 1976,¹⁸ seven of whom died. In 2009, five outbreaks occurred in Kuala Penyu, Kota Kinabalu (twice), Kota Marudu, and Penampang district with a total of 43 cases (CDC Sabah State Health Department, unpublished data). Two years later, an outbreak was recorded in Kota Kinabalu in 2011 with total of 15 cases.

This recent PSP outbreak involved 58 cases, four of whom unfortunately died, likely because of the high level of STX contained in the shellfish they consumed. The mean STX level of bivalve meat in January–February was 2,920 µg STX equivalents per 100 g meat. The oral LD₅₀ for humans is only 5.7 µg/kg, equivalent to lethal dose of 0.57 mg of STX if ingested.²⁴ In North America, the safe consumption level is set at 80 µg STX equivalents per 100 g shellfish and if this level exceeded, the shellfish growing areas for harvesting are closed.²⁵ During May–June, no mortality was reported as the contaminated oysters had comparatively less STX (360 µg STX equivalents per 100 g meat).

About the same time in coastal Tarangnan, Philippines, a similar PSP outbreak occurred in June 29–July 1, 2013, involving 31 cases, of whom two died.²⁶ All the cases had consumed green mussels, either raw, boiled, or steamed. The green mussel and oyster specimens tested had PSTs at levels

higher than the international regulatory limit. One of the fatal cases had consumed 50 green mussels. Furthermore, *P. bahamense* var *compressum* was detected in the sea water samples.

The two major toxins, NEO and GTX5 produced by *P. bahamense* var *compressum* are very toxic. The oral LD₅₀ of NEO and GTX5 have recently been reported to be respectively 2.5 and 15.9 times as toxic as STX;^{23,27} thus, the call for revision of toxicity equivalence factors of these toxins should be heeded. Similarly, the European Food Safety Authority (EFSA) basing on the established acute reference doses, consider the current EU regulatory limit for STX-group toxins was not sufficiently protective.²⁸ They suggested a level of 75 µg STX equivalents/100 g shellfish meat as opposed to the current 80 µg. However, as NEO and GTX5 found in *P. bahamense* var *compressum* are extremely potent, a level of 60 µg STX equivalents/100 g shellfish may be more appropriate.

There was much variation in the time lapsed (< 1 to > 5 hour) before symptoms appeared which is likely due to different concentration of toxin present in the bivalves consumed or the differential amount of shellfish consumed. This can be seen from the differential STX levels in the bivalves tested. Similar observation has been made previously.²⁹

It appears that the 46 cases on February 12 who were intoxicated from consuming shellfish purchased from the markets could have been prevented. This is especially so because the laboratory analysis of shellfish done on January 4 already indicated high levels of STX (590 µg STX equivalents/100 g meat, Table 5), and counts of *P. bahamense* in the sea water samples collected on January 11–February 6 showed high mean density (34,200 cells/L, Table 5). Perhaps this indicates the dissemination of information on PSP from consuming the contaminated shellfish from the authorities to the public was slow, or not reaching the important target groups such as the fishermen, the fishmongers, and the buyers of shellfish during the red tide season.

Given the fact that red tides occur regularly and that mortality has been reported regularly in the local media, why then

TABLE 5

Level of saxitoxin in bivalve and pelagic fish samples collected from the markets in Kota Kinabalu, Tuaran, Putatan, and seacoast villages in Sepangar and Kuala Penyu

Date sample collected (2013)	Source of sample	Bivalve species	Saxitoxin level (µg STX equivalents/100 g bivalve meat)
January 4	Taman Jaya Diri, Sepangar,	Fan shell	590
February 13	Inanam market, Kota Kinabalu	Green mussel	3,940
	Tuaran market, Tuaran	Green mussel	3,490
	Inanam market, Kota Kinabalu	Green mussel	3,660
Mean			2,920 ± 780
May 24	Numbak village, Sepangar	Green mussel	70
June 7	Pulau Sepangar	<i>Crassostrea belcheri</i>	70
June 10	Membakut market (Beaufort)	"Dalus" (<i>Meretrix meretrix</i>)	40–50
		"Lokan" (<i>Geloina coxan</i>)	Nil
		"Tuntul" (<i>Turritella duplicata</i>)	40
June 10	Kuala Penyu	"Dalus" (<i>Meretrix meretrix</i>)	100
		"Tuntul" (<i>Turritella duplicata</i>)	50
		<i>Crassostrea belcheri</i>	490
June 12	Sipitang	"Ikan rumahan" (short mackerel, <i>Rastrelliger brackysoma</i>)	Nil
June 17	Putatan market	"Lokan" (<i>Geloina coxan</i>)	Nil
		<i>Crassostrea belcheri</i>	Nil
June 19	Sipitang	"Ikan basung" (round scad, <i>Decapterus punctatus</i>)	Nil
June 21	Kg Penimbawan market (Tuaran)	<i>Crassostrea belcheri</i>	220
Mean for contaminated <i>Crassostrea</i>			360 ± 140

The current safe level for saxitoxin is 80 µg of STX equivalents per 100 grams of meat.

TABLE 6

Level of *Pyrodinium bahamense* var *compressum* in sea water samples taken from the sea and islands around Kota Kinabalu, at a depth of 1 and 3 meters during the outbreak of PSP

Date (2013)	Sampling site	Number of samples	<i>Pyrodinium bahamense</i> cells/L
January 11	Likas Bay	4	52,800 ± 340
January 18	Serusup (Sg Tuaran)	2	770 ± 250
January 23	Likas Bay	2	260 ± 140
January 23	Pulau Sepangar	2	960 ± 560
January 23	Pulau Gaya	4	810 ± 270
January 23	Sepangar Bay (TLDM)	2	5,320 ± 2,960
January 23	Kuala Menggatal	2	1,540 ± 1,500
February 6	Likas Bay	2	1,640 ± 40
February 6	Kota Kinabalu coast (KN)	2	68,900 ± 2,100
February 6	Pulau Gaya	2	93,900 ± 2,300
Mean			34,200 ± 10,300
May 9	Kota Kinabalu coast (six samples), Pulau Gaya (2), P. Sepangar (1), Likas Bay (2), Tanjung Aru (2), Petagas (2)		Nil
June 7	Kota Kinabalu coast (6), Pulau Gaya (1)		Nil
June 11	Kota Kinabalu coast (1), Pulau Sepangar (1)		Nil

The safe level for *P. bahamense* < 7,000 cells/L.

do PSP still occur in Sabah? The lack of communication to the community at large on the danger of consuming contaminated shellfish during red tide season could be a major reason. The following actions can be taken by the government to ensure that such PSP outbreak does not occur again or at least being minimized.

Firstly, an efficient sentinel monitoring system for harmful algal bloom and contaminated shellfish is urgently needed. This would provide an early-warning system for PSP toxin levels. Such system would require extensive and close coordination among Sabah Department of Health, Fishery department, local health office, industry, fishermen, and volunteers, which is not something unachievable. Sea water and shellfish and filter-feeding fish should be sampled weekly or biweekly when the harmful algal bloom is expected or detected. Presently, the Fisheries Department carries out monthly sampling of sea water from designated sampling points and analyzed for dinoflagellate density. The results are conveyed to Sabah State Health Department. If the level is above the normal level, Sabah State Health Department will issue out alert letter or press statement if multiple localities are involved. Extensive health promotion should then commence immediately.

Secondly, when red tides are imminent or present, the health promotion activities and awareness promotion of the hazards of eating contaminated shellfish should be conducted on a wide scale. Posters of warning of contaminated shellfish should be posted in markets where these are sold. Similarly, warning posters should be displayed along the beaches and bay of Sabah where shellfish are collected for consumption. At the same time, samples of shellfish sold in the markets should be sampled and the presence of STX determined. Lowest doses causing mild symptoms of PSP in humans vary between 120 and 304 µg/person, and lowest doses associated with severe intoxications/fatalities vary between 456 and 576 µg STX/person.³⁰ When shellfish toxicity exceeds the safety consumption level (≥ 80 µg/100 g tissue³¹), the shellfish market should be closed to avoid food poisoning from consuming the toxic shellfish. Furthermore, contaminated shellfish in the market should be confiscated and destroyed.

Lastly, it is important to note that there is a lag of about a week between the peak of causative dinoflagellate density and the peak level of shellfish toxicity. The latter usually reaches a maximum after most of the dinoflagellates have

disappeared from the environment. This would imply that although the red tide may be over, the shellfish may not be safe to be consumed still. This explains PSP cases in Membakut who had consumed the oysters. Although the sea water samples in May–June did not show any dinoflagellates (Table 6), the oysters sampled in Kuala Penyu locality still had high STX level (490 µg STX equivalents/100 g meat). Thus, sampling of shellfish and determination of the STX level should continue until it is deemed safe for consumption.

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