

Grayanotoxin poisoning from *Rhododendron simsii* in an infant

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We report a case of severe poisoning in a 57-day-old infant who presented with vomiting, convulsions, and shock after ingesting a bottle of milk containing a decoction of *Rhododendron simsii* (紅杜鵑). The grandmother collected this toxic plant from a cultivated area, believing it was good for the airways. Grayanotoxin was detected in both the urine and plant specimens. The infant made a good recovery after requiring ventilatory support for 2 days. *Rhododendron* is a common gardening shrub in Hong Kong. Some *Rhododendron* species are poisonous and contain grayanotoxin. Intentional or accidental ingestion of toxic plants can be severe or even life-threatening. It is therefore essential that clinicians be familiar with local toxic plant species.

Introduction

Ingestion of toxic plants is a leading cause of poisoning in young children.¹ Poisoning may not be serious if the amount consumed is small or vomiting occurs early enough to prevent significant absorption. Nevertheless, plant poisoning can be a life-threatening medical emergency. The more serious poisonings usually result from mistakenly eating a toxic plant or deliberately ingesting a toxic plant for its therapeutic or toxic effects. The poisonous substances many plants contain are unknown. Close monitoring and supportive therapy are the principal management strategies. Morphological identification of the poisonous plant is helpful. Laboratory studies can sometimes determine the toxins and exclude other causes of poisoning. We report a case of grayanotoxin poisoning after the ingestion of formula milk prepared with a decoction of *Rhododendron simsii*. The diagnosis was established by the typical clinical features, identification of the plant using morphological and biochemical analysis, and detection of the target toxins in biological specimens.

Case report

A 57-day-old infant was brought to the emergency room by his grandmother because of a sudden convulsion at home. He had been coughing intermittently for a few weeks prior to admission and had been treated for acute bronchiolitis by a family physician. The grandparents were told by their friends that a plant, known as "red flower" (紅花), was good for the airways. They found the plant growing in a nearby cultivated area and took some to prepare a decoction which they then mixed with milk powder. Twenty minutes after taking this mixture the baby vomited once, then developed twitching in all four limbs and became cyanotic and unresponsive. He was brought to the emergency department immediately.

On arrival, he was unresponsive, in respiratory distress, and had poor peripheral circulation. His pulse rate was slow for his age, at around 90 to 100 beats per minute. An electrocardiogram showed sinus bradycardia and his blood pressure was 62/33 mm Hg. Both pupils were pinpoint and non-reactive to light. His lips were smacking and limbs twitching intermittently, compatible with a clinical seizure. Excessive salivation was also noted. Because of his depressed level of consciousness, he was intubated and put on mechanical ventilation. An intravenous benzodiazepam infusion was commenced and the intermittent seizure activity ceased completely 2 hours after admission.

The acute neurological presentation and its association with the recent intake of a plant decoction suggested acute poisoning. The clinical signs of a muscarinic effect and the possibility that the plant may have been sprayed with pesticides led his management team to consider a diagnosis of organophosphate or carbamate poisoning initially. A dose of atropine 0.1 mg was given intravenously. His pupils became less constricted and his perfusion improved but his serum cholinesterase level was later reported as 6662 U/L (range for children, 5320-12 900 U/L). The normal cholinesterase level made organophosphate or carbamate poisoning unlikely. The atropine injection was not repeated as his heart

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紅杜鵑木藜蘆毒素引致的一宗嬰兒中毒個案

一名57天大的嬰兒，在進食一瓶以紅杜鵑湯液沖調的牛奶後，出現嚴重中毒的徵狀，包括了嘔吐、抽搐和休克。他的祖母採摘了這有毒植物回家，誤以為它是對氣管有療效的品種。在嬰兒的尿液及植物樣本中，均找到木藜蘆毒素。他需要兩天的呼吸機器輔助，及後逐漸康復。杜鵑是香港常見的園藝灌木，某些是有毒品種，含有木藜蘆毒素。無論是刻意或意外，有毒植物所導致的中毒可以相當嚴重，甚或致命。故此，臨床醫生必須熟悉本地的有毒植物。



FIG. Picture of the *Rhododendron simsii* plant

rate had returned to normal (around 140 beats/min). Ventilatory care was continued. His heart rate normalised about 3 hours after admission but it took a day for the pupil constriction to resolve. He became more alert and was extubated 48 hours after admission. His general condition gradually improved and he recovered to normal activity levels. He was discharged from hospital on day 8. At a follow-up visit 4 months after the incident, there had been no further similar episodes and his development was normal for his age.

The patient's urine and blood were sent for toxicology studies. The plant residue and the decoction were also sent for toxicology studies. The plant was identified as *Rhododendron* species, most likely *Rhododendron simsii* (Fig). Grayanotoxin I was identified as the principal rhododendron toxin in the plant by gas chromatography mass spectrometry.^{2,3} Grayanotoxin I was also detected in the child's urine specimen. The diagnosis of grayanotoxin poisoning was therefore established.

Discussion

This is the first local report of grayanotoxin poisoning. Grayanotoxin is found in rhododendrons and other plants of the family Ericaceae. The toxin is also known as andromedotoxin, acetylandromedol, or rhodotoxin. There are various forms of grayanotoxin. The specific grayanotoxin varies with the plant species. Grayanotoxin I is the principal toxic isomer.⁴ It binds to sodium channels in cell membranes

and prevents their inactivation. Excitable tissues, including nerve and muscle cells, are maintained in a state of depolarisation, during which entry of calcium into the cells may be facilitated. This action is similar to that of another group of plant toxins: the aconitum alkaloids.⁵ Grayanotoxin has adverse effects on the cardiovascular system, including systemic hypotension, bradycardia, and atrioventricular block. In one series of cases of grayanotoxin poisoning, 15 out of 19 patients had bradycardia and hypotension. In two patients, bradycardia was severe and four patients had complete atrioventricular block.⁶ Other symptoms include nausea, vomiting, sweating, salivation, dizziness, weakness, blurred vision, convulsions, and loss of consciousness. Our patient presented with a sudden onset of seizures, bradycardia, hypotension, and excessive salivation which were all consistent with grayanotoxin poisoning. The respiratory distress may have been secondary to muscle weakness.

Grayanotoxin poisoning is mostly reported in the Black Sea region of Turkey. This involves the consumption of 'mad honey', which is honey containing rhododendron nectar. The symptoms of 'mad honey' intoxication are dose-related and occur after a latent period of a few minutes to 2 hours or more. Severe intoxication may lead to asystole although fatal poisoning has never been reported.⁷ Besides nectar, other parts of the rhododendron are also toxic. There have been reports of poisoning associated with the intake of rhododendron flowers.⁸ There was a recent outbreak of wild honey poisoning in China resulting in three deaths⁹ but the toxin was not identified so it cannot be proven that it was related to grayanotoxin.

Supportive treatment is the mainstay of therapy for grayanotoxin poisoning. Hypotension and bradycardia usually respond to the administration of fluids and atropine. The prognosis is good and the signs of intoxication generally last no longer than 24 hours.¹⁰ In our case, the patient required intubation for 48 hours and made a good recovery afterwards.

Rhododendron simsii is an evergreen shrub flowering in spring (March to April). It is the most common wild species of *Rhododendron* growing locally.¹¹ Branches and leaves of *R. simsii* are covered with stiff rusty hairs. Leaves are usually lanceolate with an entire margin. The flowers are funnel-shaped, coloured bright to deep red, and the upper petal is spotted with reddish-purple flecks. The fruit is an egg-shaped capsule, with thick hairs. This plant, interestingly, also has antitussive effects and has been used in herbal remedies to treat bronchitis.¹² Nonetheless the plant contains grayanotoxin I; the lay public should be discouraged from using it without supervision. Another *Rhododendron* species, *Rhododendron molle*, is used in traditional Chinese medicine for its insecticidal and other

TABLE. Some common toxic plants found in Hong Kong

Plant species	Toxin	Clinical toxicity
<i>Datura metel</i> (洋金花)	Anticholinergics	Confusion, tachycardia, dilated pupils, dry skin, urinary retention
<i>Strophanthus divaricatus</i> (羊角拗)	Cardiac glycoside	Gastro-intestinal upset, weakness, arrhythmias
<i>Gelsemium elegans</i> (斷腸草)	Gelsemium alkaloids	Abdominal pain, weakness, cranial nerve palsy, respiratory failure
<i>Strychnos angustiflora</i> (馬錢子)	Strychnine, brucine	Muscle rigidity, rhabdomyolysis, renal failure
<i>Abrus precatorius</i> (相思子)	Abrin (toalbumin)	Gastro-intestinal upset, bloody diarrhoea, renal failure

medicinal purposes. It is highly toxic and belongs to one of the 31 schedule 1 toxic Chinese herbs restricted for use in Hong Kong under the Chinese Medicine Ordinance. Prescription and dispensing of this herb are under strict control. Poisoning occurs readily when the herb is used in excessive doses or substituted erroneously.¹³

Besides *Rhododendron*, more than 100 toxic plants have been identified in Hong Kong and some are extremely poisonous. Among them, *Datura metel* (洋金花), *Strophanthus divaricatus* (羊角拗), *Gelsemium elegans* (斷腸草) and *Strychnos angustiflora* (馬錢子) are collectively known as the 'Top Four Toxic Plants' (四大毒草) in Hong Kong. Life-threatening plant poisonings, though less common in highly urbanised Hong Kong, have been reported. For instance, two clusters of gelsemium poisoning affecting six people were reported in 2007. One patient required mechanical ventilation for respiratory failure.¹⁴ In 2004, in another widely reported plant poisoning case, a 51-year-old woman developed acute renal failure requiring haemodialysis after taking *Abrus precatorius* (相思子), which was misidentified as *Mimosa pudica* (含羞草). The former contains a toxalbumin and inhibits protein synthesis

by inactivating the ribosome.¹⁵ Some locally available toxic plants and their associated toxicity are shown in the Table.

Confirmation of plant poisoning is difficult. Morphological identification by a botanist is helpful if the plant is available. As not all *Rhododendron* species are toxic, a specific chemical analysis to identify the toxin is important for confirming human poisonings. Laboratory studies may be the only means of confirming the presence of some plant toxins and excluding other causes of poisoning. In general, identification of the plant toxins in fresh or boiled plant samples is much easier than in biological specimens.

Conclusion

Plant poisoning can be life threatening, particularly in young children. The public should be strongly discouraged from using unfamiliar botanical products unsupervised as this is a very high-risk practice. Prompt identification and supportive therapy are the cornerstones of successful treatment. Clinicians should be familiar with locally available poisonous plants and their related toxicity patterns.

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