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Aconite poisoning in camouflage

隱藏的烏頭中毒病例

The Toxicology Reference Laboratory has confirmed 10 cases of aconite poisoning from March 2004 to May 2006. In four of these 10 cases, the aconite herb was not listed in the written prescription. We report these four cases to highlight the problem of 'hidden' aconite poisoning.

在2004年3月至2006年5月期間，醫院管理局毒理學實驗室確認了10宗烏頭中毒的個案。其中四宗，藥單上均沒有列明烏頭這草本植物。本文報告這四宗病例以帶出烏頭中毒的潛在問題。

Introduction

In Hong Kong, Chinese medicine coexists with orthodox western medicine. Eighteen percent of the population consults herbalists first for treatment of an illness.¹ As is the case with western pharmaceuticals, some herbs are toxic and must be used with caution. Generally, herbal poisoning is more difficult to manage. This is in part due to inadequate knowledge about the safety and efficacy of Chinese medicine. In Taiwan it was reported that 47% of the potentially toxic effects of Chinese traditional medicines were either unknown or could not be found in the literature.² Hence, toxicological problems associated with the use of herbal medicines may not be readily recognised. A multidisciplinary approach is advocated, but not every hospital has a full team able to handle the problem.³

In Hong Kong aconite herbs are the most common cause of severe herbal poisoning.^{4,5} Aconite herb poisoning has been known since ancient times. In western countries, aconite poisoning usually occurs after ingesting the wild aconitum plant.⁶ In Asia most aconite poisoning cases are related to the use of aconitum rootstocks in traditional medicines.⁷⁻¹⁰ Both *Radix Aconiti* (川烏) and *Radix Aconiti Kusnezoffii* (草烏) have been used in Oriental *materia medica* for the treatment of various musculoskeletal disorders. Aconitum alkaloids are the active ingredients and the source of toxicity. The amount and type of aconitum alkaloids are the main factors determining the severity of intoxication. For the same plant, the level of active ingredient is affected by the time of harvest and method of processing.¹¹ Additionally, prolonged decoction is essential to reduce the toxicity of these herbs before consumption.

It is imperative that all medical staff managing these patients be able to recognise the clinical features of aconite poisoning. These patients usually present with paraesthesia, numbness in the mouth and limbs, weakness, and bradycardia. Ventricular dysrhythmias and refractory cardiovascular collapse occur in severe poisoning.¹²⁻¹⁴ Diagnosis should not be difficult in typical cases. If a herbal prescription is available, recognising the potentially toxic herbs among the non-toxic ones provides a big clue. However, interpretation of herbal formulae is a skill that needs to be sharpened. Moreover, inadvertent contamination occurs. The Toxicology Reference Laboratory confirmed 10 cases of aconite poisoning from March 2004 to May 2006 but in four of these 10 cases, no aconite herb was listed in the written prescription. We report these four cases to highlight the problem of 'hidden' aconite poisoning.

Case series

Case 1

After taking a decoction of Chinese herbal medicine for treatment of low back

Key words:

Aconitum;
 Drugs, Chinese herbal;
 Poisoning

關鍵詞：

歐烏頭；
 藥物，草本；
 中毒

Hong Kong Med J 2006;12:456-9

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pain, a 20-year-old man presented to an emergency department with sudden onset of weakness, sweating, vomiting, and shortness of breath. On admission, his consciousness was impaired and circulatory failure was evident. His systolic blood pressure was 70 mm Hg. Electrocardiography revealed ventricular tachycardia. Cardioversion was attempted unsuccessfully. Amiodarone was given immediately and the patient was intubated and managed in the intensive care unit. The cardiac arrhythmia was refractory to standard therapy. During bouts of ventricular tachycardia his pulse became imperceptible on occasion. Following prolonged cardiopulmonary resuscitation, aggressive supportive management and temporary pacing, the patient was stabilised. Subsequent electrocardiography and electrophysiological studies were normal. The patient fully recovered and was discharged after 3 weeks of hospitalisation.

This patient had taken a similar decoction 2 months before the event without problem. A Chinese medicine pharmacist studied the prescription and found that it did not include any cardio-toxic herb. These 17 components had been prescribed: Radix Cyathulae (川牛膝), Cortex Eucommiae (杜仲), Fructus Lycii (杞子), Rhizoma Anemarrhenae (知母), Radix Dipsaci (川斷), Semen Sinapis (白芥子), Rhizoma Atractylodis (蒼術), Rhizoma Atractylodis Macrocephalae (白朮), Radix Saposhnikoviae (防風), Herba Epimedii (淫羊藿), Herba Hedyotidis Diffusae (百花蛇), Fructus Aurantii (枳殼), Radix Paeoniae Alba (白芍), Radix Clematidis (威靈仙), Rhizoma Smilacis Glabrae (茯苓), Rhizoma Cibotii (狗脊), and Fructus Amomi (春砂仁). Leftover herbal broth and a urine sample collected on the day of admission were screened for common toxins. Surprisingly, yunaconitine was found in both samples. Yunaconitine, an aconitum alkaloid found in Radix Aconiti from Yunnan, is as highly toxic as aconitine.¹⁵ Its presence confirmed aconite poisoning.

To identify the source of the aconite contamination, another pack of unused herbs kept by the patient was examined. The herbs matched those prescribed. The unused herbs were decocted for analysis. No aconitum alkaloid was detected. Hence, it is logical to conclude that the herbs taken by the patient on the day of admission contained Radix Aconiti. The source of the herbs, however, remains a mystery.

Case 2

A 27-year-old woman developed chest discomfort, dizziness, numbness, and weakness 1 hour after ingesting a decoction of Chinese herbal medicine. She arrived at an emergency department 30 minutes after the onset of symptoms. Upon presentation, she appeared unwell. Her blood pressure was 95/73 mm Hg and the pulse rate was 55 beats per minute. Electrocardiography showed a sinus bradycardia with first-degree heart block. She was hospitalised and the symptoms resolved completely in 24 hours with supportive therapy alone. This patient had enjoyed good past health

and gave no history of cardiac disease. Shortly before the episode, she had a cough and consulted a herbalist. She was prescribed a formula containing 19 herbs. A review of the prescription showed Rhizoma Anemarrhenae (知母), Rhizoma Polygonati (黃精), Cortex Moutan (牡丹皮), Rhizoma Dioscorea Batatis (山藥), Radix Rehmanniae Preparata (熟地), Radix Rehmanniae (生地), Rhizoma Smilacis Glabrae (茯苓), Rhizoma Alismatis (澤瀉), Periostracum Cicadae (蟬蛻), Radix Isatidis (板藍根), Rhizoma Paridis (支花根), Rhizoma Belamcandae (射干), Radix Panscis Quinquefolii (花旗參), Radix Glycyrrhizae (甘草), Radix Platycodi (桔梗), Radix Saposhnikoviae (防風), Rhizoma Atractylodis Macrocephalae (白朮), Fructus Corni (山萸肉), and Semen Oroxyli (千層紙). Herbal poisoning was suspected but none of the herbs was known to give rise to such a clinical picture. The herbal remnants were dried for examination. Among the remnants, one item did not match any of the prescribed herbs but appeared to be a piece of aconitum rootstock. In addition, yunaconitine was detected in both the leftover herbal broth and the patient's urine. The findings confirmed that this was another case of 'hidden' aconite poisoning with atypical clinical features.

Case 3

A 51-year-old woman, with a history of optic neuritis, was admitted with sudden onset of neck rigidity, dizziness, numbness of the extremities, and weakness. Two hours before presentation, she had ingested a bowl of herbal decoction with the following herbs: Radix Saposhnikoviae (防風), Radix Rehmanniae (生地), Herba Schizonepetae (荊芥), Rhizoma Pinelliae (法夏), Periostracum Cicadae (蟬蛻), Rhizoma Smilacis Glabrae (茯苓), Radix Scutellariae (黃芩), Radix Gentianae Macrophyllae (秦艽), Radix Bupleuri (柴胡), Radix Dipsaci (川斷), Radix Angelicae Pubescentis (獨活), Citrus Reticulatae Pericarpium (陳皮), Ramulus Uncariae cum Uncis (鉤藤), Herba Taraxaci (蒲公英), and Flos Lonicerae (忍冬). The patient had taken the same herbs, which were prescribed for treatment of influenza, without problem earlier. On examination the patient had a blood pressure of 105/63 mm Hg and a pulse rate of 63 beats per minute. Electrocardiography showed sinus rhythm. The hypotension responded to fluid therapy. Routine laboratory investigations were unremarkable. Her symptoms subsided spontaneously the next day, but remained unexplained. Leftover herbal decoction and a urine specimen were analysed and yunaconitine was found in both specimens. This confirmed another case of 'hidden' aconite poisoning.

Case 4

A 45-year-old woman became ill 1 hour after taking herbal broth prescribed for a menstrual problem. She presented to an accident and emergency department with tongue numbness, nausea, dizziness, and generalised weakness. Her blood pressure was 91/44 mm Hg and pulse rate was 58 beats per min. Electrocardiography showed a junctional bradycardia. She was hospitalised and her symptoms

improved after supportive treatment. The herbal formula taken contained the following herbs: Radix Codonopsis (黨參), Radix Astragali (黃芪), Radix Paeoniae Alba (白芍), Rhizoma Smilacis Glabrae (茯苓), Radix Angelicae Sinensis (當歸尾), Radix Dipsaci (川斷), Rhizoma Chuanxiong (川芎), Radix Rehmanniae Preparata (熟地), Talcum (滑石), Semen Cuscutae (菟絲子), and Radix Angelicae Dahuricae (白芷).

'Hidden' aconite poisoning was suspected. Leftover herbal broth and a urine sample collected on the day of admission were analysed. Yunaconitine was found in both samples, confirming the diagnosis.

Discussions

Aconite poisoning can be life-threatening.¹⁶ We have confirmed 10 cases of aconite poisoning in 2 years. In four of them, an aconite herb was not prescribed. 'Hidden' aconite poisoning, hence, is not uncommon. Moreover, this may be just the tip of an iceberg with some cases going unrecognised.

Diagnosing 'hidden' aconite poisoning is a clinical challenge. The presentation can be non-specific. Although aconite poisoning has been repeatedly reported in the Chinese medical literature, it is still a condition with which orthodox medical practitioners are unacquainted.¹⁷ Furthermore, many toxins have a similar presentation.¹⁸⁻²⁰ A high index of suspicion is essential. These four cases also underscore the importance of timely and appropriate collection of samples for laboratory confirmation.

When a patient presents with unexplained numbness, weakness, and cardiovascular symptoms, the possibility of aconite intoxication should be considered. The differential diagnoses include plant and animal toxins such as digoxin-like cardiac glycosides, andromedotoxin, tetrahydropalmatine compounds such as Jin bu huan (金不換), veratrine, ciguateric toxins, and shellfish poisoning.²¹ All four cases presented with numbness and weakness shortly after taking a herbal decoction. The temporal relationship strongly suggested herb-related toxicity. However, none of their prescriptions contained aconite herbs. Yet aconitum alkaloids were detected in the urine specimens and leftover herbal broth. In one case, a piece of aconitum rootstock was also identified. Aconite was thus considered the 'hidden' cause of their acute poisoning.

In these four cases of 'hidden' aconite poisoning, there was no common herbal item listed in all the herbal prescriptions. Systematic erroneous substitution of other herbs by an aconite herb was thus unlikely. In our opinion, inadvertent contamination with an aconite herb is a possible explanation. Intuitively, a mix-up between aconite herbs and other herbs can occur at a number of stages, including harvesting, during processing, transportation, storage, and dispensing. The fresh aconitum rootstocks are

extremely toxic and must be processed before use. The level of toxicity decreases after prolonged boiling, which is a standard decoction requirement for these herbs. Naturally this particular procedure will not be carried out if the presence of an aconite herb is not intended. 'Hidden' aconite poisoning, hence, is far more dangerous than intentional use of aconite.

Yunaconitine was the aconitum alkaloid detected in all four cases. It is not one of the common toxins (aconitine, hypaconitine, and mesaconitine) seen in aconite poisoning.²² The diagnosis would have been missed in these four cases if laboratory screening for yunaconitine was not included. The presence of yunaconitine suggests that the mix-up occurred in aconitum species of Yunnan origin.

The frequent occurrence of 'hidden' aconite poisoning has a public health significance for our community. This mistaken substitution with aconite herbs can occur randomly and result in severe poisonings. Our report only represents the tip of the iceberg, as the contamination source is often not detectable. It also highlights the importance of quality assurance in herbs with low margins of safety. Efforts should be made to enhance the safety of herbs through the promotion of Good Agricultural Practice and Good Manufacturing Practice. It is hoped that reporting of these cases can increase awareness of this problem among health care professionals and lead to improvement of control measures.²³

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