

Tetrodotoxin-Mediated Delay in Aconitine Toxicity: A Murder in Okinawa

Y. Ohno

Department of Legal Medicine
Nippon Medical School
Bunkyo-ku, Tokyo
Japan

TABLE OF CONTENTS

INTRODUCTION	140
I. CASE HISTORY	141
II. MEDICOLEGAL INVESTIGATION	141
A. Aconitine	142
B. Tetrodotoxin	143
III. EPILOGUE	143
ACKNOWLEDGMENT	143
REFERENCES	144
ABOUT THE AUTHOR	144



* Corresponding author: Dr. Youkichi Ohno, Department of Legal Medicine, Nippon Medical School, 1-1-5 Sendagi, Bunkyo-ku, Tokyo 113-8602, Japan; +81 3 3822 2131 (voice); ohno@nms.ac.jp.

Tetrodotoxin-Mediated Delay in Aconitine Toxicity: A Murder in Okinawa

REFERENCE: Ohno Y: Tetrodotoxin-mediated delay in aconitine toxicity: A murder in Okinawa; *Forensic Sci Rev* 26:139; 2014.

ABSTRACT: Aconite (wolfsbane) plants, which belong to the genus *Aconitum* (Ranunculaceae family), contain highly toxic alkaloids, including aconitine, mesaconitine, hyaconitine, and jesaconitine, in all of their parts. The relevance of this plant material is illustrated by the case of a Japanese female who died suddenly in 1986 and was autopsied in Okinawa by the author. The detection in 1987 of *Aconitum* alkaloids in her blood using gas chromatography/selected ion monitoring (GC/SIM), which was newly developed for this case, demonstrated that she had died from aconite poisoning.

KEY WORDS: Aconite, aconitine, hyaconitine, jesaconitine, life insurance, mesaconitine, murder, pufferfish, sodium channel, tetrodotoxin.

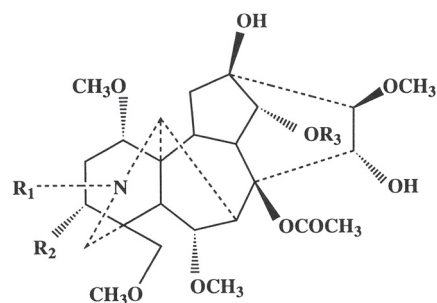
INTRODUCTION

Aconite plants, which belong to the genus *Aconitum* in the plant family Ranunculaceae, contain extremely toxic alkaloids, such as aconitine, mesaconitine, hyaconitine, and jesaconitine, mainly in their roots, leaves, and stems (**Figure 1; Structure 1**). The fatal dosage by oral administration (per os) for humans is in the range of 2–4 mg of pure aconitine, or 1 g of the raw root.



Figure 1. Aconite plant (photograph taken in spring).

The genus *Aconitum* contains about 300 species of herbaceous flowering perennials (often used decoratively), which grow in alpine climates or cooler regions of the northern temperate zones. Their flowers, which mainly grow in spike-like clusters, are usually purple or blue (**Figure 2**) and are often used for flower arrangements (Ikebana) in Japan. Additionally, the roots of aconite plants (known as Bushi or Uzu in Japan) are considered indispensable for Sino-Japanese traditional herbal medicine (Kampo medicine). Since the raw roots of aconite plants are highly toxic, they are usually processed in ways that hydrolyze their highly poisonous constituents to their



Aconitine	R ₁ = C ₂ H ₅	R ₂ =OH	R ₃ = -OC-C ₆ H ₅
Mesaconitine	R ₁ = CH ₃	R ₂ =OH	R ₃ = -OC-C ₆ H ₅
Hyaconitine	R ₁ = CH ₃	R ₂ =H	R ₃ = -OC-C ₆ H ₅
Jesaconitine	R ₁ = C ₂ H ₅	R ₂ =OH	R ₃ = -OC-C ₆ H ₄ -OCH ₃

Structure 1. Chemical structures of *Aconitum* alkaloids.



Figure 2. Aconite flowers (photograph taken in autumn).

deacetyl and debenzoyl derivatives before medical use. In Europe and India, *Aconitum* alkaloids have also been used in homeopathic medicine.

Aconitum alkaloids such as aconitine, mesaconitine, hyaconitine, and jesaconitine induce both atrial and ventricular arrhythmia when administered systemically, and death can result from the ventricular fibrillation caused

REFERENCES

1. Catterall WA: Neurotoxins that act on voltage-sensitive sodium channels in excitable membranes; *Ann Rev Pharmacol Toxicol* 20:15; 1980.
2. Isono H, Uda H, Sawamura R, Suzuki T, Suzuki Y, Hasegawa A: *Forensic Chemistry* (Japanese); Hirokawa Publishing: Tokyo, Japan; p 161; 1984.
3. Mizugaki M, Ohyama Y, Kimura K, Ishibashi M, Ohno Y, Uchima E, Nagamori H, Suzuki Y: Analysis of *Aconitum* alkaloids by means of gas chromatography/selected ion monitoring (Japanese); *Eisei Kagaku* 34:359; 1988.
4. Ohno Y, Chiba S, Uchigasaki S, Uchima E, Nagamori H, Mizugaki M, Ohyama Y, Kimura K, Suzuki Y: The influence of tetrodotoxin on the toxic effects of aconitine in vivo; *Tohoku J Exp Med* 167:155; 1992.
5. Ono T, Hayashida M, Tezuka A, Hayakawa H, Ohno Y: Antagonistic effects of tetrodotoxin on aconitine-induced cardiac toxicity; *J Nippon Med Sch* 80:350; 2013.



ABOUT THE AUTHOR

Y. Ohno

Youkichi Ohno graduated from the School of Medicine, Tohoku University, Japan, in 1978, and from the forensic medicine course at the Graduate School of Medicine, Tohoku University, in 1982. He was an associate professor at the University of the Ryukyus, Okinawa, from 1985 to 1990, when he transferred to Nihon University, and has been a professor at the Department of Legal Medicine, Nippon Medical School, since 1992. He is one of the most famous forensic pathologists in Japan, partially due to the role he played in solving this complicated murder case.