CASE REPORT

Acute respiratory failure due to Nicotiana glauca ingestion

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Abstract

Background: A variety of organisms produce potent toxins that impact human health through compromising respiratory function.

Case report: We describe a rare case of abrupt respiratory failure after *Nicotiana glauca* ingestion in a previously healthy sixty years old female patient. She presented complaining for gait instability and malaise after ingestion of cooked leaves of the wild plant and two hours after the onset she developed respiratory failure for which she was intubated and mechanically ventilated for two days. The patient fully recovered and was discharged from the hospital.

Conclusion: Anabasine, the plant's main active ingredient, can cause severe systemic intoxication due to its nicotinic receptor agonist action with respiratory muscle paralysis being the main effect. Hippokratia 2013, 17, 2: 183-184

Keywords: *Nicotiana glauca,* anabasine, respiratory failure

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Introduction

Nicotiana glauca Graham (Solanaceae) or tree tobacco is an evergreen perennial plant, belonging to the same genus with cultivated tobacco *(N. tabacum L.)*. Morphologically, it may be distinguished from tobacco due to the non-pubescent (glabrous) leaves and the yellow flowers[1] (Figure 1). It is a treelike shrub that may reach a height of 6 m, which usually grows in open and disturbed areas, in well-drained deep soils. Even though *N. glauca* is native to south America, it has been introduced to other continents and currently it is wide-spread and naturalized also in the Mediterranean countries, both in the mainland but also in the islands[1]. Many medicinal uses have been described by ethnobotanists[2], even though all parts of this plant contain harmful substances. In particular, among those, *N. glauca* contains substantial quantities of a toxic pyridine alkaloid chemically related to nicotine, named anabasine. Anabasine has been shown to cause severe and often fatal intoxication in humans. According to the literature, *N. glauca* produces a nicotinic-cholinergic syndrome with muscle weakness and autonomic instability as the main manifestations[3]. This case report involves a patient with acute respiratory failure after consuming *N. glauca* boiled leaves. Additionally, we discuss the associated molecular mechanisms.

Case report

A previously healthy sixty years old woman presented to the emergency department complaining for gait instability and malaise, shortly after ingesting the cooked leaves of a wild plant. Two hours after onset, she developed respiratory difficulty with an oxygen saturation of 80% on room air (pO_2: 49mmHg, pCO_2: 52mmHg). Evaluation showed a slightly tachypneic patient with diminished breath sounds bilaterally. Furthermore, with supplemented oxygen of 35%, the oxygen saturation was raised to 94%. She kept complaining of blurred vision and feeling unwell. Computed tomography of the chest revealed basilar atelectasis and no evidence of pulmonary embolism, pneumothorax, or new infiltrates. On the way back to the ward, respiratory movements become very shallow and the oxygen saturation dropped again. The systolic blood-pressure was 150 mmHg and the heart rate 94 bpm. Due to the already failing respiratory system, a decision to intubate the patient was made. Echocardiographic evaluation of the patient was unremarkable. After two days in the intensive care unit, she was transferred to the medical ward and finally, five days later, she was discharged from our hospital, free of symptoms. On her follow up, one month after her discharge, she remains well, without any symptoms. A specimen of the plant species was sent to a specialized center (Laboratory of Systematic Botany and Phytogeography, School of Biology, Aristotle University of Thessaloniki) where it was identified and deposited in the Herbarium of Aristotle University of Thessaloniki. The identification was made by using the keys of Flora Europaea[1], while the nomenclature follows the International Plant Names Index (IPNI)[4]. Unfortunately, there is no available antidote for nicotinic agonists. Management includes mechanical ventilation until the effect has worn off.

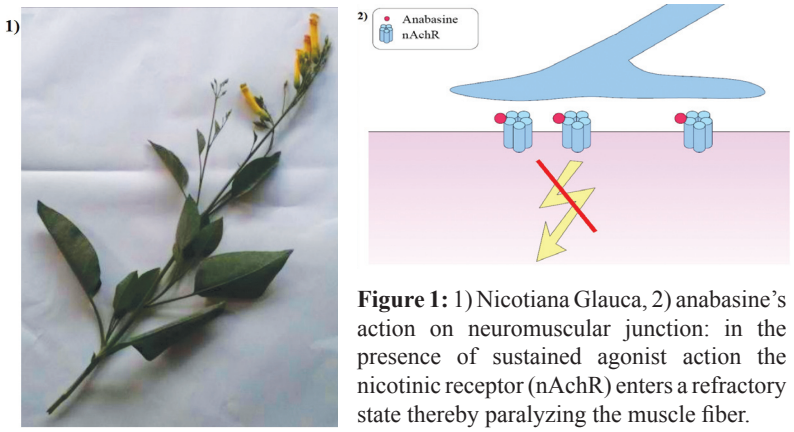

Figure 1: 1) Nicotiana Glauca, 2) anabasine's action on neuromuscular junction: in the presence of sustained agonist action the nicotinic receptor (nAchR) enters a refractory state thereby paralyzing the muscle fiber.

Discussion

Anabasine, also known as neonicotine, is the predominant alkaloid isolated from the tree tobacco plant *(Nicotiana glauca)* where it exists as a rakemic mixture of two enantiomers. Anabasine has also been isolated from the toxic plant Anabasis aphylla and the poison gland of several *Messor* (ants) species. It is a highly toxic basic compound (pKa=11) and has been used as a botanical insecticide in the past[5]. So far, there are sixteen cases reported in the literature[3]. The median lethal dose (LD50) for rats is 16 ± 1 mg/kg and 11 ± 1 mg/kg for S and L enantiomers accordingly[6]. Pharmacokinetic studies performed in humans showed an elimination half-life of 15.9 hours (SD: 5.3, range: 10.1-26.8), on the basis of urine excretion rates[7]. To better understand the clinical aspects of anabasine toxicity, the current understanding of anabasine molecular targets will be presented.

Similarly to nicotine, anabasine is a nicotinic receptor (nAchR) agonist with an additional weak acetylcholinesterase inhibitor activity[6,8,9]. nAchRs belong to a group of pentameric ligand-gated cation channels first isolated from Torpedo, characterized by the pharmacological activity of nicotine. Together, with muscarinic receptors, it comprises the two classes of receptors mediating achetylocholine signaling. They are found in the central nervous system, neuromuscular junction, autonomic nervous system ganglia and adrenal glands. The human genome encodes 16 different nicotinic receptor subunits. This enables functional nicotinic receptors to have a potentially diverse range of sensitivity towards agonists and differ in their physiological properties[10]. In comparison to nicotine, anabasine shows increased potency and efficacy to neural α7 and fetal muscle nAchR. Clinical observations and experimental data published so far generally agree with the notion that anabasine acts as a neuromuscular blocking drug. On the contrary, action on neural α4β2 nAchR is minimal[6]. Additionally, the pre-Botzinger complex, a rhythm generating network located within the ventrolateral medulla which is essential to the generation of respiratory rhythm in mammal, express α4β2 nAchR[11]. Thus, the possibility that anabasine can compromise respiratory control centrally as nicotine is limited. Furthermore, despite the reported dysautonomia[6], nicotine is fifteen times more potent at the gaglion type α3β4 nicotinic reseptor[8]. An important consideration relevant to the above mentioned data is that the functional potencies of anabasine and nicotine have been assayed in models systems that are not always easily comparable to humans. Secondly, in addition to anabasine there are smaller quantities of nicotine that may contribute to the clinical picture[12]. Additionally, the percentage of the primary active ingredients may vary widely depending on the plant's growing conditions and the type of preparation ingested.

In conclusion, *Nicotiana glauca* intoxication should be considered in patients with acute respiratory failure after a wild plant meal. Special attention should be made in differentiating respiratory failure from the most known plant *Datura stramonium* in which anticholinergic syndrome is produced and physostigmine administration is indicated.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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