

## INTOXICATION WITH *ATROPA BELLADONNA* L. AND SEVERE ANTICHOLINERGIC SYNDROME

Chibishev Andon

University Clinic for Toxicology and Urgent Internal Medicine, Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia  
*e-mail: acibisev@gmail.com*

### Abstract

*Atropa belladonna* L., family *Solanaceae*, or also known as a deadly nightshade, is a plant which foliage and berries contain a high concentration of alkaloids and is extremely toxic. When these substances are being accidentally ingested, they tend to block the postganglionic parasympathetic fibers and muscarinic receptors in the central nervous system, thus causing an emergency clinical state known as anticholinergic toxic syndrome. In this article we present two cases of this rare clinical syndrome.

**Keywords:** *Atropa belladonna*, parasympathetic block, anticholinergic syndrome

### Case report

*Atropa belladonna* L., family *Solanaceae*, is a plant from the *Solanaceae* family, with specific greenish leaves and small, brownish berries, both extremely toxic. Foliage and berries contain a high concentration of alkaloids, such as atropine, scopolamine and hyoscyamine<sup>[1]</sup>. When these substances are accidentally ingested, they tend to block the postganglionic parasympathetic fibers and also the muscarinic receptors in the central nervous system, thus causing a specific clinical state known as anticholinergic toxic syndrome (ATC)<sup>[2-3]</sup>.

During ancient ages, herbal extracts from this plant were used as eye drops by rich women in order to cause mydriasis and to make their eye expression more attractive. Some countries still use these extracts in the pharmaceutical industry, producing drugs for bradycardia correction, analgesics or neural pain and muscle spasm reliefs.

Intoxication with *Atropa belladonna* L., family *Solanaceae*, is caused by an ingestion of the berries and these types of poisonings have been described both in children and adults<sup>[4-6]</sup>.

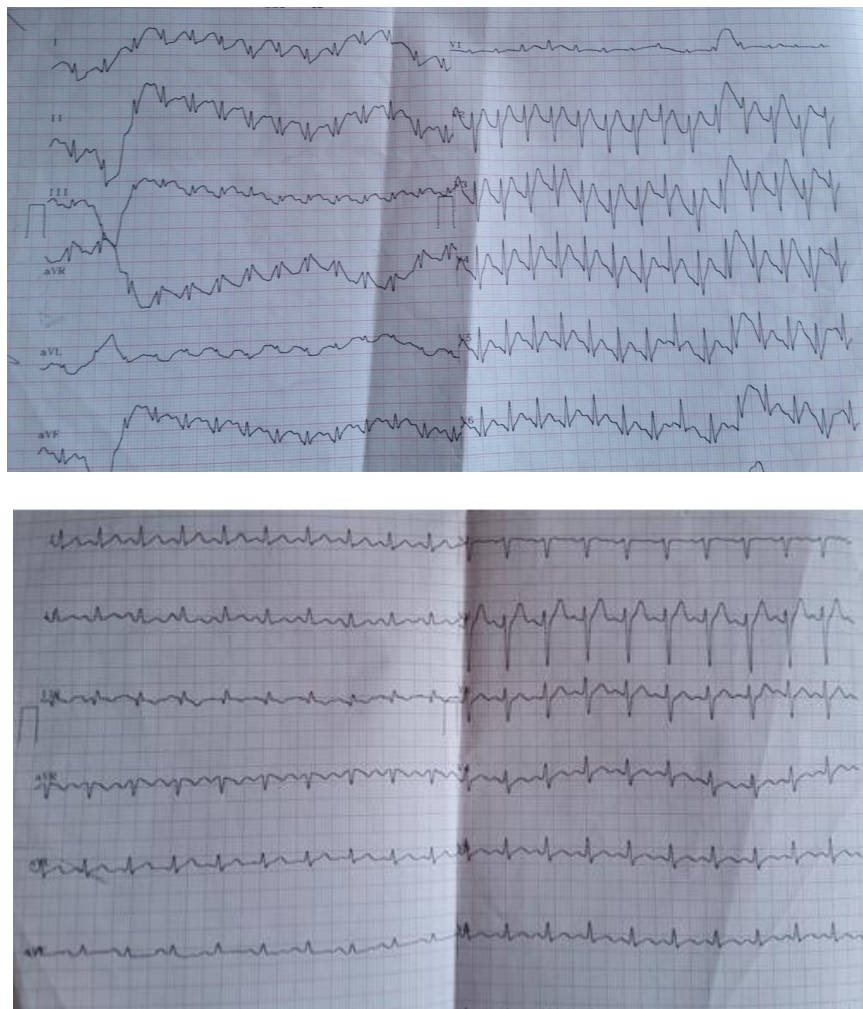
In this article we present two cases of adult males intoxicated with *Atropa belladonna* L., family *Solanaceae*, after consuming it during their mountain walk.

The first one is 37 and the second one is 36 years old; both of them consumed unknown types of berries, found along the hiking path in the local wood. They arrived at our emergency unit after being primarily evaluated and shortly treated at the local hospital. We immediately hospitalized them at the intensive care unit and both of them were conscious, but confused, agitated, aggressive and logorrhic. Their skin was extremely red and warm, especially in the face and neck area. Their mouth and mucosal membranes were quite dry, while their pupils were notable mydriatic, with slow response to light and without proper accommodation. Intensive care monitors showed tachycardia, tachypnea and hypertension in both patients, more severe in the first one, who reported that he consumed more than 10

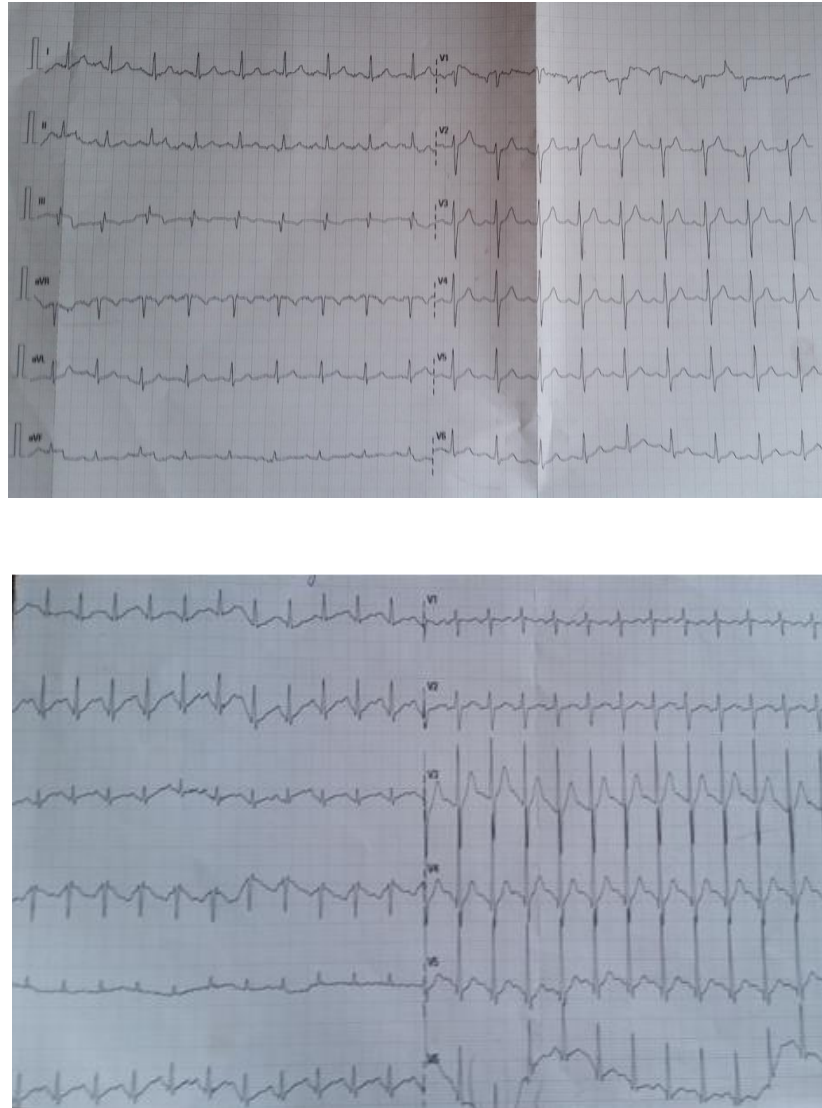
berries. Oxygen saturation was 90-92%. Laboratory analyses showed leukocytosis and elevated level of acetylcholinesterase.

A sample from the plant was brought to us by family members and relatives of the patients and we were able to start an identification process in order to provide a specialized treatment. After consulting our laboratory plant experts and albums for toxic plants, we found out that the intoxication was caused by the plant *Atropa belladonna* L.

Both patients received parenteral treatment with 5% Dextrose, Ringer lactate and Saline solutions, vitamin therapy and mild sedation. Neostigmine was given at a dose of 1.5 mg during the first hour after hospitalization and additional 1 mg during the next three hours. Clinical state of our patients was remarkably improved 12 hours after receiving the initial treatment. Both patients were hospitalized at the intensive care unit during the next 5 days, after which they were dismissed from hospital in a stable health state.



**Fig. 1.** ECG findings on admission



**Fig 2.** ECG findings in the ICU

*Atropa belladonna* L., family *Solanaceae*, is a specific kind of plant that contains certain alkaloids and esters of tropane acid. It belongs to the family of *Solanaceae* and it can reach height of a 1.5-2 m. Its berries are cherry-sized with an extremely sweet and pleasant taste. It is native to England and its distribution extends through central and southern Europe to Iran. It is typically found in woods and thickets, but is also often found in disturbed areas, waste places, and roadsides where it typically spreads rapidly in a weed-like manner. It has naturalized in certain parts of the U.S., mostly in dumps, quarries and disturbed ground in parts of New York, Michigan, California, Oregon and Washington. Herbal extracts from this plant contain racemic atropine, hyoscyamine and scopolamine in a high concentration. In its earlier stages of growth its seeds contain mainly hyoscyamine, while its mature berries contain mainly atropine<sup>[7-11]</sup>.

Our clinical cases exhibited typical *Atropa belladonna* L., family *Solanaceae* intoxication, caused by ingestion of mature berries. In both cases, we noticed a specific anticholinergic toxic syndrome, with its characteristic symptoms, such as mydriasis, tachycardia, red and warm skin.

According to literature, intoxications with *Atropa belladonna* L., family *Solanaceae*, are usually accidental, although there are few cases where these berries were consumed with suicidal intent. The majority of intoxications is accidental and can be seen among nature lovers, people who spent plenty of their free time in the woods, where they consume this plant due to curiosity<sup>[12]</sup>.

Clinical signs and symptoms develop as a result of the toxic effects of herbal alkaloids. Substances as L-atropine, hyoscyamine and hyoscine cause changes in the central and peripheral nervous system. Depending on the amount ingested, patients can develop clinical state of a short-term amnesia, hallucinations, agitation, logorrhea, mydriasis, dry skin and mucosal membranes, tachycardia, fever and urinary retention. The most severe cases can suffer from respiratory and cardio-circulatory failure. In some cases, we can only see lethargy and convulsions, which in a short time can lead to a comatose state with a poor prognosis. Patients that have ingested *Atropa belladonna* L., family *Solanaceae*, usually have leukocytosis, hyperglycemia and metabolic acidosis<sup>[13-17]</sup>.

Both of our patients suffered from accidental intoxication with *Atropa belladonna* L., family *Solanaceae*, and developed typical anticholinergic syndrome.

The severity of the intoxication depends on the quantity of ingested berries. Toxic dose for adults is approximately 10 berries, while ingestion of more than 15 berries can be fatal. In children, toxic dose is 5 berries, while 10 berries are usually fatal. Children that live in mountain villages, near the wood, can often be victims of these kinds of poisonings, mainly due to an accidental ingestion of the berries that resemble to those of blueberry and raspberry<sup>[18]</sup>. Clinical manifestations in our patients were similar to those described through literature, whereas patient number 1, who had ingested greater amount of berries, had slightly more severe clinical state.

When the reason for acute intoxications is known, these patients can be treated appropriately in a short time after hospitalization and in these circumstances the prognosis can be quite positive. On the other hand, diagnosis of these poisonings in the emergency unit can be extremely difficult because they often look like acute psychotic state or severe traumatic central nervous system damage. Some of the cases can be similar to suicidal or accidental intoxications with antihistaminic drugs, phenothiazines, neuroleptics, antipsychotics or antidepressants<sup>[19,20]</sup>. When patients arrive in the emergency unit completely conscious and contactable, they can immediately explain in details what kind of berries they ingested. In opposite, we must contact their families, closest relatives, or try to find a sample of the plant that they had ingested.

Patients with *Atropa belladonna* L., family *Solanaceae* intoxication should be immediately hospitalized in the intensive care units and closely monitored. During the first 4-6 hours, we can perform gastric lavage, with water or saline solution, and also use active medical charcoal. In severely agitated patients, we use sedatives, usually benzodiazepines. They are parenterally given vitamins in high dose. The main drug that must be used is neostigmine (Prostigmine), which is a reversible inhibitor of the cholinesterase effects<sup>[21-23]</sup>.

Our patients received contemporary therapeutic protocol and after 6 hours they had improvement in their clinical state. Their complete treatment lasted for 3 days, after which they were dismissed from hospital in a stable health condition.

*Conflict of interest statement.* None declared.

## References

1. Southgate HJ, Egerton M, Dauncey EA. Lessons to be learned: a case study approach. Unseasonal severe poisoning of two adults by deadly nightshade (*Atropa belladonna*). *J R Soc Promot Health* 2000; 120(2): 127–30. doi: 10.1177/146642400012000212.
2. Mowry JB, Spyker DA, Cantilena LR Jr, McMillan N, Ford M. 2013 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 31st Annual Report. *Clin Toxicol (Phila)* 2014; 52(10): 1032-283. doi: 10.3109/15563650.2014.987397.
3. Joshi P, Wicks AC, Munshi SK. Recurrent autumnal psychosis. *Postgrad Med J* 2003; 79: 239–40.
4. Lan X., Zeng J., Liu K., Zhang F., Bai G., Chen M., Liao Z., Huang L. Comparison of two hyoscyamine 6 $\beta$ -hydroxylases in engineering scopolamine biosynthesis in root cultures of *Scopolia lurida*. *Biochem. Biophys. Res. Commun.* 2018;497:25–31.
5. Caksen H, Odabaş D, Akbayram S, Cesur Y, Arslan S, Uner A, *et al.* Deadly nightshade (*Atropa belladonna*) intoxication: an analysis of 49 children. *Hum Exp Toxicol* 2003; 22(12): 665-8. doi: 10.1191/0960327103ht404oa.
6. Trabattoni G, Visintini D, Terzano GM, Lechi A. Accidental poisoning with deadly nightshade berries: a case report. *Hum Toxicol* 1984; 3(6): 513-6. doi: 10.1177/096032718400300607.
7. Zhao T, Li S, Wang J, Zhou Q, Yang C, Bai F, Lan X., Chen M, Liao Z. Engineering tropane alkaloid production based on metabolic characterization of ornithine decarboxylase in *atropa belladonna*. *ACS Synth. Biol.* 2020;9:437–448
8. Alizadeh A, Moshiri M, Alizadeh J, Balali-Mood M. Black henbane and its toxicity - a descriptive review. *Avicenna J Phytomed* 2014; 4(5): 297-311. PMID: 25386392; PMCID: PMC4224707.
9. Zeng L, Zhang Q, Jiang C, Zheng Y, Zuo Y, Qin J, *et al.* Development of *Atropa belladonna* L. Plants with High-Yield Hyoscyamine and without Its Derivatives Using the CRISPR/Cas9 System. *Int J Mol Sci* 2021; 22(4): 1731. doi: 10.3390/ijms22041731.
10. Cock I. The safe usage of herbal medicines: counter indications, cross-reactivity and toxicity. *PharmacognCommun* 2015; 5(1): 2-50. doi: 10.5530/pc.2015.1.2.
11. Vangoori Y, Janapati S. Evaluation of anti-inflammatory effect of Belladonna (a homeopathic drug) in experimental animals-rats. *Int J Pharma Bio Sci* 2013; 4(3): 111-115.
12. Glatstein M, Alabdulrazzaq F, Scolnik D. Belladonna Alkaloid Intoxication: The 10-Year Experience of a Large Tertiary Care Pediatric Hospital. *Am J Ther* 2016; 23(1): e74-7.
13. Lange A, Toft P. Poisoning with nightshade, *Atropa belladonna*. *UgeskrLaeger* 1990; 152:1096.
14. Karadaş S, Selvi Y, Mustafa Ş, Selvi F, Reşit Ö, Özgökçe F. *Datura Stramonium* Zehirlenmesi: Psikiyatrik Belirtilerle Başvuran Olgu. *Düşünen Adam Psikiyatri ve Nörolojik Bilimler Dergisi.* 2011;24:152–4.
15. Spina SP, Taddei A. Teenagers with Jimson weed (*Datura stramonium*) poisoning. *Cjem* 2007; 9: 467–8. doi: 10.1017/s1481803500015530.
16. Fatur K, Kreft S. Nixing the nightshades: Traditional knowledge of intoxicating members of the Solanaceae among hallucinogenic plant and mushroom users in Slovenia. *PLoS One.* 2021 Feb 22;16(2)

17. Maffè S, Paffoni P, Laura Colombo M, Davanzo F, Dellavesa P, Cucchi L, Zenone F, Paino AM, Franchetti Pardo N, Bergamasco L, Signorotti F, Parravicini U.G, Toxicology, *Ital Cardiol (Rome)*. 2013 Jun;14(6):445-55.
18. Laffargue F, Oudot C, Constanty A, Bedu A, Ketterer-Martinon S. Deadly nightshade (*Atropa belladonna*) intoxication in a 2-year-old child. *Arch Pediatr* 2011; 18(2): 186–8. doi: 10.1016/j.arcped.2010.11.006.
19. Tulin F, Kirpınar I. Psychiatric Aspects of a Case with Deadly Nightshade Intoxication. *Journal of academic emergency medicine* 2011; 10(2): 86–88. doi: 10.4170/jaem.2009.96658.
20. Lee MR. Solanaceae IV: *Atropa belladonna*, deadly nightshade. *J R Coll Physicians Edinb* 2007; 37(1): 77–84.
21. Davies F, Gupta R. Apparent life threatening events in infants presenting to an emergency department. *Emerg Med J* 2002; 19: 11–16. doi: 10.1136/emj.19.1.11.
22. Chadwick A, Ash A, Day J, Borthwick M. Accidental overdose in the deep shade of night: a warning on the assumed safety of 'natural substances'. *BMJ Case Rep* 2015; 2015: bcr2015209333. doi: 10.1136/bcr-2015-209333.
23. Cıkla U, Turkmen S, Karaca Y, Ayaz AF, Turedi S, Gunduz A. An *Atropa belladonna* L poisoning with acute subdural hematoma. *Hum Exp Toxicol* 2011; 30(12): 1998–2001. doi: 10.1177/0960327111407225.