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Anticholinergic syndrome due to 'Devil's herb': when risks come from the ancient time

G. A. PICCILLO,[1] L. MIELE,[2] E. MONDATI,[3] P. A. MORO,[4] A. MUSCO,[1] A. FORGIONE,[2] G. GASBARRINI,[2] A. GRIECO[2]

Division of Emergency Medicine,[1] Cannizzaro Hospital, Catania, Department of Internal Medicine,[2] Università Cattolica del Sacro Cuore. Policlinico A. Gemelli, Rome, Department of Internal Medicine and Systemic Pathologies,[3] University of Catania, Catania, Poison Control Centre,[4] Niguarda Cà Grande Hospital, Milan, Italy

SUMMARY

We describe a case of *Mandragora autumnalis* poisoning which occurred in a 72-year-old female patient who had eaten the venenous *M. Autumnalis*, picked near her home, mistaking it for the edible *Borago Officinalis*. *M. Autumnalis* is a solanaceous plant, common in the Sicilian countryside, which contains a variable concentration of solanum alkaloids, causing gastrointestinal irritation, and tropane alkaloids, with anticholinergic properties. Unluckily, *M. Autumnalis* is often mistaken for the edible *B. Officinalis*, likewise widespread in Sicilian countryside. The diagnosis of *Mandragora* poisoning was made on the basis of clinical symptoms and signs of anticholinergic syndrome associated with a history of vegetable meal of uncontrolled origin, moreover analysing the vegetable obtained from gastric lavage. Decontamination and symptomatic treatment were useful in our patient to control acute poisoning.

Keywords: Mandragora autumnalis; Borago officinalis; Atropa belladonna; toxic plant; poisoning; physostigmine; solanaceous alkaloids; anticholinergic syndrome; cholinergic antagonists

INTRODUCTION

Anticholinergic syndrome due to the adverse or toxic effects of several drugs is not an infrequent occurrence in the emergency department, and a differential diagnosis must be made. Causative agents such as drugs (tricyclic antidepressants, antihistamines, antiparkinsonism drug overdose), adverse effects from the ophthalmic use of atropine or scopolamine plasters and sympathomimetic syndrome due to cocaine, amphetamines or other drugs should be considered. Less frequently, agents, such as some types of vegetables, should be keep in mind to avoid medical mistakes. Only an accurate history and physical examination should lead to identification of the causal agent, allowing correct patient assessment and treatment.

Mandragora Autumnalis is a solanaceous plant that grows wild in the Sicilian countryside. It is an annual herb with oblong ovate leaves and blue violet flowers, which if eaten is to able to provoke an anticholinergic syndrome (1,2,3), and it must not be mistaken for 'mandrake' or American *Mandragora* (4).

Correspondence to:
Dr Luca Miele, MD, Department Internal Medicine, Università Cattolica del Sacro Cuore, Policlinico 'A. Gemelli', Largo Gemelli 8-0168 Roma, Italy
Tel.: + 39 630155451
Fax: + 39635502775
Email: lumie@lycos.it

Because of the 'human body' shape of its root and its narcotic and poisonous effects, from ancient times this plant, also known as 'Devil's herb', was believed to be an aphrodisiac and to have magic and medical properties. In 1518, Niccolò Machiavelli wrote the famous Italian tale 'Mandragola', underlining the 'medical' use of a *Mandragora* potion for infertility treating.

We report a case of anticholinergic syndrome due to unintentional assumption of *Mandragora* with clinical effects of its alkaloids.

CASE REPORT

A 72-year-old Sicilian woman, affected with hypertension on treatment with enalapril, was admitted to our Emergency Division hallucinated, confused and very agitated with psychomotor impairment.

For 2 h before arriving at hospital, she had been suffering from increasing abdominal pain, nausea and progressive behaviour disturbance, alarming her relatives.

At admission, she was tachypnoic (25 b/min) and tachycardic (heart rate 110 beats/min), it was present flushing and her skin was dry and hyperaemic, and symmetrical unreactive mydriasis and xerostomia were present. The body temperature was 37.3 °C. She presented rise of BP (185/98 mmHg).

On neurological evaluation was no present CNS depression and all the reflexes (palpebral, corneal, cutaneous, cough,

deglutition and osteotendineous) were accentuated. Abdominal examination indicated the presence of a large bladder due to urinary retention: 600 mL of urine was withdrawn via a catheter. All the laboratory data, evaluated as haemochrome, glycaemia, urea, creatinine, serum electrolytes, bilirubin, total proteins, transaminases, LDH, alkaline phosphatase, GGT, cholinesterase, CPK, CK-MB, amylase, lipase, APTT, AP and fibrinogen, resulted within normal range. The drug screen resulted negative.

All signs were suggestive for anticholinergic syndrome, so a detailed clinical history from relatives was taken. Because it was excluded sympathomimetic or drug responsibility, we hypothesised a possible plant containing anticholinergic alkaloids or tropane derivatives. In fact, the history, obtained with the help of a patient's relative, revealed that 4 h earlier the woman had eaten a vegetable picked up in the countryside near her home town. In addition, our toxicology unit carried the analysis of vegetable tracks, which got through gastric lavage that revealed the presence of *M. Autumnalis*, which confirmed our diagnosis.

Suspecting plant anticholinergic poisoning, we performed gastric lavage and administered activated charcoal (20 spoons in five doses orally), and cathartic-magnesium sulphate (30 g orally) to decontaminate the patient. Two doses of 10 mg diazepam (Valium^{TM}, Roche spa, Milan, Italy) intravenously were able to control the anxiety, agitation and tachycardia with complete resolution of the symptomatology. No readministration of the drug was necessary. As a matter of urgency, we called in all the members of the family to evaluate their clinical state. None of them, luckily, had eaten the poisonous plant, so they did not exhibit symptoms of anticholinergic syndrome.

After clinical observation for 72 h in our ward, the patient was asymptomatic, and she was discharged healthy.

DISCUSSION

Our patient unintentionally ate leaves of *M. Autumnalis* (Figure 1B), mistaking this plant for the edible *Borago Officinalis* (Figure 1A). Both grow in sunny Mediterranean areas, have similar leaves and small, blue violet flowers with five petals, so may be confused by an inexpert picker.

The alkaloids of the tropane group, particularly atropine, hyoscyamine and scopolamine, act on the peripheral and central nervous systems (5). Scopolamine is the principal alkaloid in the genera *Mandragora* and *Scopolia* (6). These substances have parasympatholytic properties, producing similar peripheral effects (salivary and bronchial gland activity, mucosal dryness due to inhibition of sweat, reduced gastrointestinal motility, urinary retention), while having different central actions: hyoscyamine stimulates the cerebral cortex, whereas scopolamine is depressant and produces sedative and hypnotic effects (7). Between the alkaloids of the nicotine group, the only toxicologically active one is nicotine, which is present in large quantities only in the leaves of the *Nicotiana* species.

The family Solanaceae includes plants that have been used, since ancient times, for food (tomato, potato), medicines or poisons (*Atropa belladonna*, *Mandragora officinalis*), or as enjoyment (*Nicotiana tabaccum*, *Datura stramonium*). Besides neuroactive alkaloids, Solanaceae also contain solanines, glycoalkaloids producing gastrointestinal irritation and causing nausea, vomiting and diarrhoea (8). Other Solanaceae plants with anticholinergic properties, such as *A. belladonna*, *D. stramonium* and *Hyoscyamus niger*, are easily found in Italy and not infrequently produce acute poisoning, in both adults and children (7,8). In fact, the berries of *A. belladonna*, sometimes mistaken for the edible *Vaccinium myrtillus*, can produce a classic anticholinergic syndrome. *D. stramonium*, also called 'Jimson Weed', is intentionally used by adolescents to experience hallucinations, producing sometimes fatalities (7,9).

M. Autumnalis is often mistaken for the edible *B. officinalis* by inexpert pickers or is intentionally used as a hallucinogen. The exact toxic dose of these plants is undeterminable, because the alkaloid content of vegetables is variable due to factors that affect growth (season, characteristics of soil and climate), genetic features of the particular species and individual variability. Furthermore, the alkaloid concentration differs in different parts of the same plant. The alkaloid 'mandragorin' is a mixture of hyoscyamine and hyoscine. The alkaloid content of dried *M. Autumnalis* is 0.4–0.7% in the roots and 0.3–0.4% in the leaves (3,6).

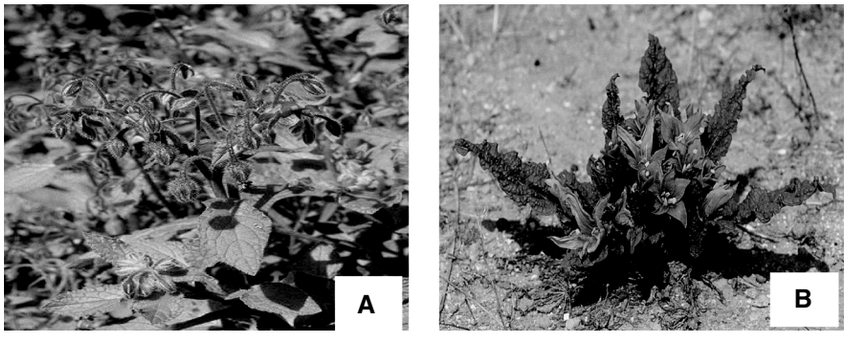

Figure 1 Appearance of *Borago officinalis* (A) and *Mandragora autumnalis* (B) in their natural environment. Note the strong similarity of the two plants, which can very easily be mistaken for one another

The maximum concentration of alkaloids is found in the *Mandragora* roots, which were not eaten by our patient. Usually, ingestion of a few leaves, seeds, berries or pieces of roots can produce poisoning, characterised by nausea and vomiting, disorientation, delirium or mental status depression, mydriasis, tachycardia, flushed and dry skin, xerostomia, decreased gastrointestinal motility and urinary retention. All the symptomatology of anticholinergic syndrome is summed up in the Anglo-Saxon refrain: 'hot as a hare, blind as a bat, dry as a bone, red as a beet, mad as a hen'. Severe poisoning may produce seizures and coma and is potentially life threatening (10).

The gastrointestinal symptoms, which were more accentuated in our patient presenting with abdominal pain, are ascribable to the solanine content, while the parasympatholytic effects are characteristic of tropane alkaloid toxicity (7).

In cases of poisoning due to oral exposure, the treatment consists of gastric decontamination, administration of activated charcoal and cathartic treatment, and supportive therapy (8,11,12). Antidote therapy with physostigmine may be required in severe poisoning (13,14). Because, in the anticholinergic syndrome, the gastrointestinal motility is reduced, gastric lavage and activated charcoal administration are useful even several hours after exposure, and a cathartic may be administered if not contraindicated.

In our case, gastric lavage was performed, and activated charcoal plus magnesium sulphate was orally administered. Diazepam, the drug of choice if seizures are present, was administered to control anxiety, delirium and hyperactivity, reducing also tachycardia and hypertension, and to achieve in our patient complete disappearance of the symptoms. The use of physostigmine in the management of acute anticholinergic toxicity is still controversial due to the adverse effects of this drug and the possibility of control with symptomatic therapy (15). Because the toxic anticholinergic effects are due to the antagonism of acetylcholine at the neuroreceptor site, the anticholinesterase action of physostigmine is effective because it specifically reverses this antagonism by increasing the acetylcholine available to the receptor site (5,7). In recent years, the role of physostigmine as an antidote for anticholinergic poisoning has been questioned (10,13,14).

It is recommended that it should not be used routinely, or just to keep a patient awake, and is absolutely contraindicated if cyclic antidepressants have been coingested as it may precipitate seizures and intractable cardiac arrest (7). Moreover, physostigmine has a short duration of action (20–60 min), which is often too short to control the longlasting anticholinergic signs and symptoms caused by these poisons (7). The use of physostigmine as an antidote should therefore only be considered in severe cases: in comatose patients with hypoventilation or for the treatment of intractable seizures, hypotension or dysrhythmias in the setting of anticholinergic poisoning. On the contrary, it has a rapid and specific action and seems more effective than benzodiazepines in treating the symptoms of anticholinergic toxicity (15).

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REFERENCES

1 Jimenez-Mejias ME, Montano-Diaz M, Lopez Pardo F et al. Atropine poisoning by Mandragora autumnalis. A report 15 cases. *Med Clin (Barc)* 1990; **95**: 689–92.
2 Frohne D, Pfander HJ. *A Colour Atlas of Poisonous Plants*. London, England: Wolfe Publishing Ltd, 1983.
3 Piccillo GA, Mondati EG, Moro PA. Six clinical cases of Mandragora autumnalis poisoning: diagnosis and treatment. *Eur J Emerg Med* 2002; **9**: 342–7.
4 Frasca T, Brett AS, Yoo SD. Mandrake toxicity. A case of mistaken identity. *Arch Intern Med* 1997; **157**: 2007–9.
5 Hardman JG, Limbird LE, Molinoff PB, Ruddon RW, Gilman AG, eds. *Goodman & Gilman's. The pharmacological basis of therapeutics*. Whitby, ONT: Mc Graw-Hill Ryerson Ltd, 1996.
6 Oshima T, Sagara K, Tong YY, Zhang G, Chen YH. Application of ion-pair high performance liquid chromatography for analysis of hyoscyamine and scopolamine in solanaceous crude drugs. *Chem Pharm Bull (Tokyo)* 1989; **37**: 2456–8.
7 Klasco RK, ed. *POISINDEX® System.* Greenwood Village, Colorado: Thomson Micromedex, 2001.
8 Chan TY. Anticholinergic poisoning due to Chinese herbal medicines. *Vet Hum Toxicol* 1995; **37**: 156–7.
9 Dyer S. Plant exposures: wilderness medicine. *Emerg Med Clin North Am* 2004; **22**: 299–313, vii.
10 Beaver KM, Gavin TJ. Treatment of acute anticholinergic poisoning with physostigmine. *Am J Emerg Med* 1998; **16**: 505–7.
11 Vale JA. Position statement: gastric lavage. American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. *J Toxicol Clin Toxicol* 1997; **35**: 711–9.
12 Chyka PA, Seger D. Position statement: single-dose activated charcoal. American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. *J Toxicol Clin Toxicol* 1997; **35**: 721–41.
13 Ellenhorn MJ, Schonwald S, Ordog G, Wasserberger J. *Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning*, 2nd edn. Baltimore, MD: Williams & Wilkins 1997.
14 Goldfrank LR, Flomenbaum NE, Lewin NA, Howland MA, Hoffman RS, eds. *Goldfrank's Toxicology Emergencies*, 7th edn. New York, NY: McGraw-Hill Co, 2002.
15 Burns MJ, Linden CH, Graudins A, Brown RM, Fletcher KE. A comparison of physostigmine and benzodiazepines for the treatment of anticholinergic poisoning. *Ann Emerg Med* 2000; **35**: 374–81.

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