

Hepatic Cytolysis Induced by Percutaneous Application of *Atractylis Gummifera*: About a Case

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Abstract

Object: The thistle is an herbaceous plant known for its toxicity; it contains two diterpenic heterosides the Atractyloside and the carboxyatractyloside, which are mitochondrial poisons, disrupting cellular respiration. The clinical manifestations of thistle poisoning are digestive, neurological and hematological disorders. But there are also mild forms of poisoning. We report the case of a 9 month old female infant with no personal and family medical pathological history, admitted to the PII service in a table of jet vomiting associated with consciousness disorders and hypoglycaemia, the biochemical assessment found hepatic cytolysis. The history revealed the notion of local administration of thistle in powder form on diaper rash of the infant. The outcome was favorable with symptomatic treatment based on N-acetyl cysteine.

Conclusion: The use of phytotherapy can induce very significant toxic incidents. Prevention and public awareness remains one of the most effective ways to address this great problem.

Keywords: *Atractylis Gummifera* • Hepatic tropism • Mitochondrial poisons

Introduction

Atractylis gummifera is a poisonous plant of the Asteraceae family known as slimy thistle, in Arabic Addâd or Chouk el-eulk.

The genus *Atractylis* includes about thirty species located on the Mediterranean rim and islands, from Morocco to the Middle East. In Europe, it is frequent in Spain, Italy (mainly in Sicily and Sardinia). At least sixteen species are present in Algeria where *Atractylis gummifera*, widespread, often constitutes dense stands; it is very common in scrub, pastures and forests from the Tellian zone to the High Plateaux.

In Morocco, it is found in all regions except Marrakech, the Anti-Atlas and desert or arid areas (Figure 1). Frequently found in the wild, it is also sold over the counter at all herbalists and in the souks [1].

It is an herbaceous perennial plant with a large, spiny and fragrant root, whose lanceolate leaves form a rosette at ground level. The pink colored flowers gathered in capitules and surrounded by bracts, appear in summer. After fruiting, a yellowish-white latex exudes from the bracts, which agglomerates in the form of glue (Figure 2). The underground parts are characterized by a swivelling and voluminous root accompanied by a flexible rhizome (Figure 3).

Poisonings from glue thistle are often due to confusion of the root with other edible plants such as wild artichoke or Spanish thistle [2].

The toxic principles are distributed throughout all parts of the plant with

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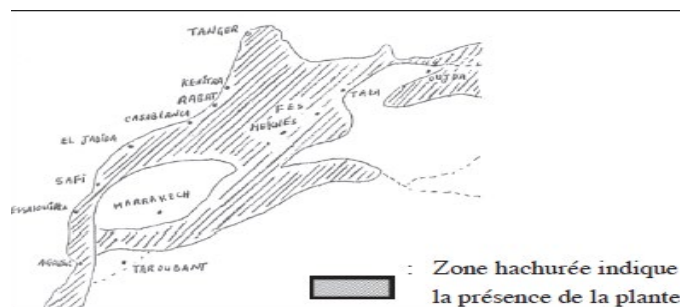


Figure 1. Geographical distribution of *Atractylis gummifera* in Morocco [5].



Figure 2. The aerial parts of *Atractylis gummifera* [1].

decreasing concentrations from the root to the leaves, with the aerial parts being the least toxic.

The ingestion of glue thistle leads to intoxications characterized by hepatorenal attacks, preceded by digestive signs, the evolution of which is most often fatal in the absence of treatment, but its toxicity by local route is observed in very rare cases in approximately 2% of the cases according to a study made in the national center of toxicology in Morocco [3].

We report on a clinical case of intoxication by glue thistle not by ingestion but following a percutaneous passage of the plant.

Case Presentation

The patient was a 9-month-old infant, female, with no notable personal or family pathological history. She was admitted to the general pediatrics department of the Ibn Sina Hospital in Rabat with a history of jet vomiting associated with consciousness disorders.

The clinical examination on admission revealed a hypotonic, reactive, apyretic infant with a soft abdomen, with no purpuric spots, rales or murmurs on auscultation.

The diagnosis of meningitis, initially evoked, was ruled out after a cerebral CT scan and a lumbar puncture, which did not reveal any anomaly.

The diagnosis of viral hepatitis was ruled out after serological tests were performed on D2 of admission

A complementary history, carried out thereafter, revealed the notion of local administration of powdered thistle on the infant's diaper rash.

The biological workup showed: a hematocrit of 33.3%, a PT of 59%, an APTT of 30.8sec with evidence of hepatic cytolysis in the biochemical workup, with (Table 1).

The presence of the toxicant or metabolites in urine or blood was not specified.

After reporting to the Poison Control Center, it was agreed to administer a loading dose of 140mg/kg N-acetylcysteine, followed by 70mg/kg/4h for 3 days orally. With monitoring of liver and kidney functions by ionogram every third day.

The N-acetylcysteine antidote to paracetamol is recommended in this intoxication because of the homology of the mechanisms of action of the two toxic lesions, both of which cause mitochondrial and cytosolic depletion of reduced glutathione, the most efficient detoxifying agent in the human body.

The evolution was favorable marked by a clear improvement of the liver function, with discharge of the patient after 10 days of hospitalization.

Discussion

In Morocco, Glue Thistle is widely used in traditional medicine and is easily found in herbalists in the form of dried fragments of rhizome and root.



Figure 3. Rhizome of *Atractylis gummifera* [1].

Table 1. Biological check-up on day 1 of admission.

Analysis	Value	Standard
Uric Acid	80.00 mg/L	(20-55)
ASAT	>913.00 UI/L	(5-34)
ALAT	>942.00 UI/L	(0-55)
Alkaline Phosphatase	539 UI/L	---
Gamma Glutamyl Transferase	250 U/L	---

The root extract can be used locally as a poultice on infectious or inflammatory lesions, for the treatment of psoriasis, acne pimples and syphilitic ulcers. In internal use the root is used for its antihemorrhagic and emetic effect. In high doses it is used for its abortifacient effect by women in rural areas, which causes serious accidents due to the high toxicity of the plant. In fumigations it treats colds, dizziness, headaches and paralysis. It is known for its oxytocic properties; in fact, pregnant women who inhale thistle smoke have an easier delivery.

The latex of the plant is chewed in rural areas by children as chewing gum, which causes serious poisoning. The flowers are used in the form of infusions for the treatment of convulsions and epilepsy.

When used for criminal purposes, the powdered root is administered alone or in combination with other toxins such as henbane and arsenic for its antiemetic properties preventing the victim from rejecting the poison in vomit.

Most of the poisonings with glue thistle are accidental and occur especially in rural areas among children who confuse the aerial part with other edible plants such as wild artichoke, or the rhizome which has the appearance of a large edible turnip with a sweet taste [4]. As well as they have been observed in the use of thistle as a medicinal plant for its antipyretic, emetic, abortive and diuretic properties [5].

The toxicity of *Atractylis gummifera* is mainly due to atractyloside, carboxyatractyloside and gummiferin which are potent inhibitors of mitochondrial oxidative phosphorylation and the Krebs cycle. Atractyloside acts at the level of ADP/ATP translocase, the enzyme responsible for the transfer of ADP to ATP, by binding to the latter and competing with ADP, which prevents it from entering the mitochondrial matrix and being transformed into ATP.

Carboxyatractyloside has more affinity for the transporter than atractyloside, due to the presence of an additional carboxyl group, interacting with the amino acids at the binding site.

Potassium atractylate could also induce hepatocyte apoptosis by increasing the permeability of the mitochondrial membrane by creating transport pores.

The clinical picture of glue thistle poisoning depends on the age of the patient, the dose and the mode of administration. In the initial stage, digestive signs are the most frequent, represented by diarrhea, vomiting and epigastric pain. Signs of hypoglycemia such as profuse sweating, general malaise and hypotension may be present.

The state phase is characterized by cardiovascular complications (tachycardia, blood pressure irregularities), neurological disorders such as convulsions, headaches and dizziness, followed by respiratory disorders (polypnea, tracheobronchial congestion, cyanosis and swallowing disorders), liver and kidney complications. Death usually occurs 4 to 6 days after intoxication in a fulminant hepatitis picture.

Biologically, there was an increase in transaminases (50 times normal), lactate dehydrogenases, creatine kinase and urea. The hematological examination revealed a decrease in the prothrombin rate with blood hypocoagulability. Proteinuria and positive hematuria indicate renal damage.

The detection of the toxin (Atractyloside) on urine samples or gastric lavage is done by thin layer chromatography (TLC) on silica gel plates and the revelation is done by a UV light examination. Currently, the analytical determination of toxins is done by solid phase extraction and high performance liquid chromatography coupled with mass spectrometry (tandem) [6].

The treatment of intoxication is primarily symptomatic and evacuative. The evacuation treatment must be carried out as soon as possible by a gastric lavage. Symptomatic treatment consists of infusions of hypertonic glucose serum to correct hypoglycemia, isotonic serum to counteract dehydration, vitamin K supplementation to compensate for blood hypocoagulability, assisted ventilation to prevent respiratory complications and the administration of barbiturates for convulsive seizures. The Moroccan poison control center recommends treatment with N-acetyl cysteine to prevent liver damage, as satisfactory results have been reported with this treatment [7].

In Morocco, poisonous plants are the cause of 5.1% of reported poisonings, with glue thistle, the most poisonous plant, predominating at the top of the list, accounting for more than half of the cases of death by plants, thus constituting a real public health problem for the child population. A study conducted at the University Hospital of Fez reported a case of collective intoxication by ingestion of glue thistle in nine children of the same family whose age varied between 8 and 12 years and whose symptomatology was of variable severity, two of whom died in a fulminant hepatitis picture with hepatocellular necrosis [8]. Another fatal case of a 13-year-old child admitted to the pediatric intensive care unit for accidental ingestion of thistle was reported at the University Hospital of Marrakech in 2013 [9].

All cases of intoxication reported in the literature are due to accidental or voluntary ingestion of the plant, except for a single case of hepatorenal lesion, reported in 2010, having been induced by cutaneous application of *Atractylis gummifera* [10]. Our observation testifies to the possibility of intoxication by another route, namely the local route, hence the interest of a rational use of this plant especially in the pediatric population.

Conclusion

The intoxication of the thistle in Morocco is mainly accidental affecting especially the children in rural environment and causing a very important lethality. Hepatotoxicity remains the most frequent damage given the hepatic tropism of the plant.

Our observation allowed highlighting another way of intoxication with *Atractylis gummifera* other than the oral way, namely the local way.

The high frequency of these intoxications could be considerably reduced by a better sensitization of parents and children on the gravity of the plants found in their environment, as well as by the implication of the media through the diffusion of educational messages. In addition, the creation of a legislative framework regulating the activity of herbalists.

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