

# In the kingdom of “tortelli” (ravioli-like pasta) plant poisoning is still a threat. A case report of near-fatal poisoning from *Digitalis Purpurea* accidentally confused with *Borago Officinalis*

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**Summary.** A 58 years healthy old woman was admitted to the Emergency Department (ED) with cardiac arrest due to ventricular fibrillation (VF). Appropriate cardiopulmonary resuscitation (CPR), multiple DC shocks and oro-tracheal intubation (OTI) were effective to induce recovery of spontaneous circulation (ROSC). After ROSC was achieved, the electrocardiogram (ECG) showed an idio-ventricular rhythm with atrioventricular dissociation. A transcutaneous pacing was hence applied and the patient was administered with isoproterenol. Simultaneously, her husband was evaluated in the ED for gastrointestinal symptoms occurred after assumption of home-made “tortelli” (ravioli-like pasta) stuffed with cheese and leaves of a plant which they supposed to be borage two days before admission. Borage, during the non-flowering seasons, can be easily confused with foxglove (*Digitalis* spp.), and this was the main clue to suspect poisoning. Both patients were given DigiFab<sup>®</sup>, a sheep antibody fragment with high affinity for digoxin. The woman was then admitted in intensive care unit (ICU), where a rapid clinical improvement occurred, thus allowing discharge in a few days. The husband was instead discharged from the ED after clinical observation and ECG monitoring. In both cases, a significant plasma concentration of digoxin could be measured. ([www.actabiomedica.it](http://www.actabiomedica.it))

**Key words:** poisoning, toxicity, digoxin, cardiac glycosides, *Digitalis Purpurea*, *Borago Officinalis*

## Introduction

Poisoning from *Digitalis* spp. represents a relatively rare event, wherein digoxin toxicity is usually due to overdose or drug accumulation in patients receiving digoxin therapy (1). Nevertheless, sporadic cases have been reported worldwide, and many suggestions were put forward to prevent this potentially fatal poisoning (2,3). We describe here the case of near-fatal poisoning by digitalis glycosides in a woman who inadvertently ingested *Digitalis Purpurea*, alongside with the less serious poisoning of her husband.

## Case report

A 58 years old woman with no significant clinical or pharmacological history was brought by ambulance to the Emergency Department (ED) of the University Hospital of Parma on January 1<sup>st</sup> 2016, with cardiac arrest due to ventricular fibrillation (VF). She rapidly underwent cardiopulmonary resuscitation (CPR), multiple DC shocks, and oro-tracheal intubation (OTI) according to ACLS protocol, which were effective to induce a recovery of spontaneous circulation (ROSC). After ROSC was achieved, the electrocardi-

ogram (ECG) showed an idio-ventricular rhythm with atrioventricular dissociation. A transcutaneous pacing was then applied and the patient was administered with isoproterenol. After 15-20 mins. a spontaneous rhythm of atrial fibrillation, with ST-T anomalies suggestive for digital toxicity, developed (Fig. 1).

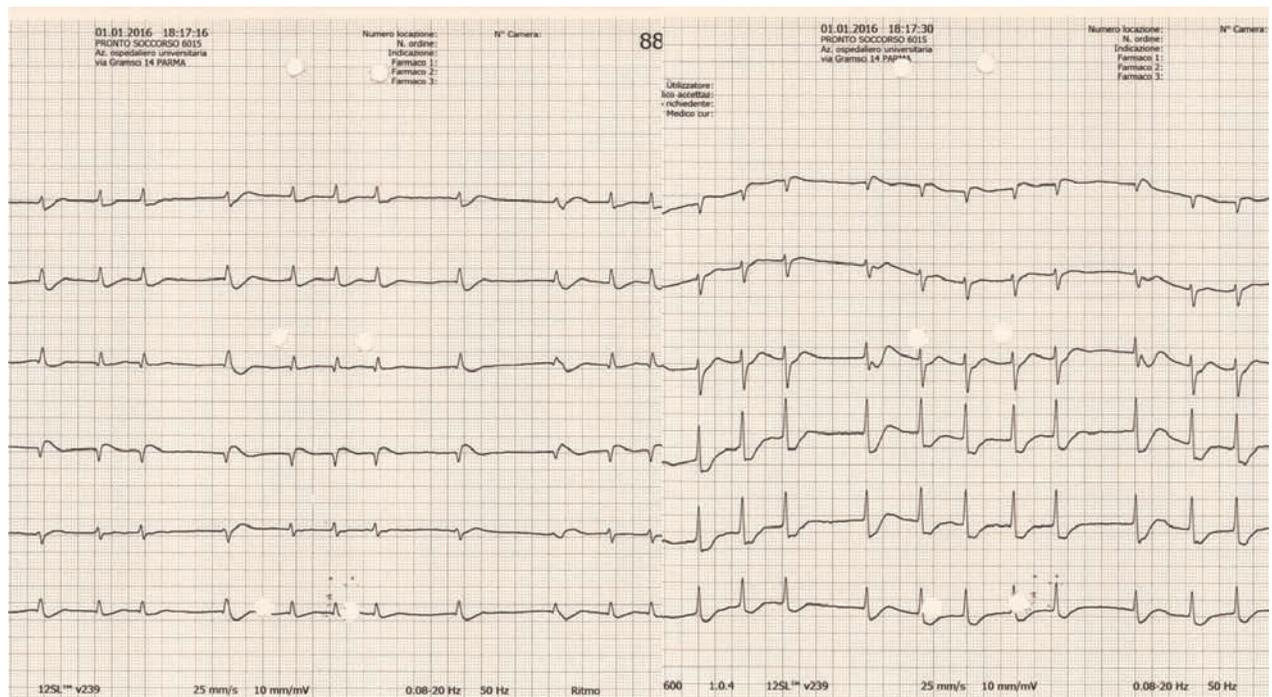
Simultaneously, her husband (65 years old) was evaluated in the same ED for gastrointestinal symptoms (i.e., nausea, vomiting, and diarrhea) occurred after assumption of home-made "tortelli" (i.e., ravioli-like pasta, typical of our regions) stuffed with cheese and leaves of a plant which they supposed to be borage two days before. He also revealed that his wife suffered from identical gastrointestinal symptoms the day before. He denied digoxin assumption.

Due to the aforementioned clinical scenario, and with a strong suspect of digitalis poisoning, the reference Poison Centre was contacted by phone. Blood samples were also collected from both patients and sent to the laboratory for digoxin testing. While waiting for test results, both patients were administered with DigiFab®, a sheep antibody fragment with high affinity for digoxin (4,5).

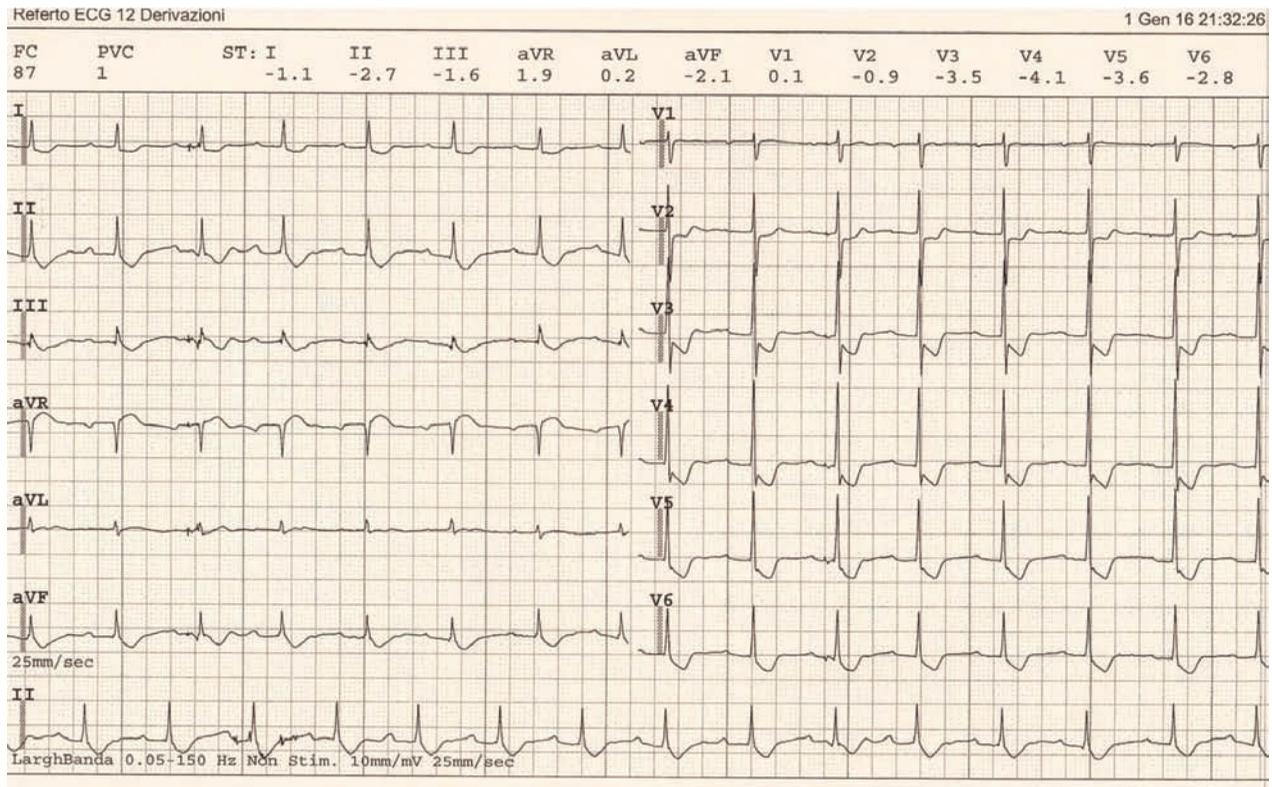
The main results of laboratory testing performed on woman's samples showed increased white blood cells count (WBC: 22.960/ $\mu$ L), hyperkalemia (K<sup>+</sup>: 6.1 mEq/L), detectable troponin I value but still comprised within the 99<sup>th</sup> percentile value of the assay (0.35 ng/mL; upper limit: 0.05 ng/mL) and digoxin concentration of 1.79 ng/mL.

The woman was then admitted to the intensive care unit (ICU), where rapid clinical improvement was observed. She also developed a pneumonia, responsive to antibiotic treatment. Troponin I values displayed an increasing trend during the first day with a peaking of 3.42 ng/ml at 24 hours. The troponin I levels decreased during the following days of hospitalization. The patient was then extubated and the hemodynamic support therapies were withdrawn two days after initial ED admission. The patient was finally transferred in the Internal Medicine ward for further observation, and then discharged with indication of cardiologic follow-up.

The husband, who also had a digoxin plasma level of 1.42 ng/mL, and typical ECG findings (Fig. 2), was hydrated and kept in observation of 12 hours. No clinically significant arrhythmias were recorded.



**Figure 1.** Electrocardiogram recorded few minutes after ROSC



**Figure 2.** Electrocardiogram of the husband of the patient

## Discussion

The toxic mechanism of Digitalis Purpura is attributable to the well-known effect of foxglove glycosides (i.e., digoxin, digitoxin, ouabaine), which induce a Na-K-ATPase pump inhibition and consequent increase of intracellular calcium. The severity of symptoms typically is dose-dependent, but also dependent on the baseline clinical status of the patient. Apart from gastrointestinal (nausea, vomiting, diarrhea), and neurologic (drowsiness, lethargy, dizziness, confusion, hallucinations, snowy vision, photophobia, yellow halos around lights (xanthopsia), scotomata) manifestations, the cardiac toxicity represents the mainstay of this poisoning (6). The most frequent ECG findings are consequence of increased automaticity coupled with concomitant conduction delay, leading to often coexisting dysrhythmias such as frequent premature ventricular beats, 2<sup>nd</sup> and 3<sup>rd</sup> degree atrioventricular block, paroxysmal atrial tachycardia with block, junctional tachycardia, and ventricular tachycardia (7).

The diagnosis of foxglove glycosides poisoning is substantially based on the medical history, clinical findings, ECG and laboratory testing (i.e., assessment of digoxin). Notably, the measurement of digoxin may be misleading, since laboratory assays using specific anti-digoxin monoclonal antibodies may variably react (up to no reactivity) with other cardio-active glycosides. Although in the female patient described in this case report the digoxin concentration (i.e., 1.79 ng/mL) was below the toxicity threshold, the severity of the clinical presentation is strongly suggestive for the presence of others glycosides. An identical consideration can be made for the husband, whose digoxin concentration was 1.42 ng/mL.

In severe cases of foxglove glycosides poisoning, such as those described in this article, the treatment is based on anti-digoxin antibody fragments (Fab), which bind to circulating digoxin with greater affinity than the drug/poison (4,5).

Some other common plants contain cardiac glycosides and are hence potentially dangerous for human

and animal health. Excluding woolly foxglove (*Digitalis lanata*), and strophantus (*Strophantus Gratus*), that are well recognized source of cardiac glycosides, the best known are the oleander (*Nerium Oleander*) which contains the glycoside oleandrine (8,9), and the “lily of the valley” (*Convallaria Majalis*) which contains a mixture of glycosides, mainly convallarin, convallamarin, and convallatoxin (10).

The borage (*Borrago Officinalis*) is a rather common herbal plant in central and northern Italy, the leaves of which are widely used for a variety of culinary preparations. During winter, when the typical flowers are absent, it can be easily confused with foxglove (*Digitalis Purpurea* but also other *Digitalis* spp.) (see Fig. 3 and Fig. 4, respectively). The leaves of the two

plants are not easily distinguishable mainly touching them, due to the most bristly upper and lower surfaces of *Digitalis*.

Another case of poisoning has been recently reported, in which an entire family ingested potato dumplings flavored with leaves of *Borrago officinalis* unconsciously mixed with leaves of *Digitalis purpurea* (3). A favorable clinical evolution was also achieved, thanks to the administration of digoxin-specific antibody Fab fragments.

Notably the patients described in our case report collected the leaves for making “tortelli” during winter-time, when neither borage, nor foxglove carry flowers.

Quite surprisingly, when searching in the web across “natural medicine” sites, *Borrago Officinalis* is



**Figure 3.** Borrago Officinalis: with flowers (left), and leaves only (right)



**Figure 4.** Digitalis Purpurea: with flowers (left), and leaves only (right)

described as a natural remedy for arthritis, various skin problems, upper airways diseases, and, most notably, the plant is suggested as "very healthy for the heart"! Herbal medicines have in fact become a popular form of therapy, since they are often perceived as being natural and therefore harmless. They can, however, cause toxic as well as allergic effects, alongside with drug interactions, and, rarely, mutagenic effects (11).

Due to the widespread use of borage as an edible plant, we conclude suggesting that Emergency Physicians (EPs) should always consider the differential diagnosis with digoxin poisoning, especially in winter-time.

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