CASE REPORT

Comfrey herbal remedy causing second-degree heart block: do not be outfoxed by digitalis

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SUMMARY

A previously well woman aged 63 years presents to the emergency department with vomiting, palpitations and 3 presyncopal episodes. She had no previous medical or cardiac history, with the patient stating that she tried a herbal remedy of boiled comfrey leaves for insomnia 18 hours before arrival to the department. Her ECG showed multiple abnormalities, including bradycardia, second-degree atrioventricular node block, Mobitz Type 2, a shortened QT interval, downsloping ST depression and presence of U waves. After viewing the images of comfrey and foxglove, it highlighted the possibility of mistaken ingestion of *Digitalis*, containing the organic forms of cardiac glycosides, such as digoxin and digitoxin. Raised serum digoxin levels confirmed this. The patient was haemodynamically stable, and given digoxin-binding antibodies. After 5 days of cardiac monitoring, her ECG returned to normal rhythm, and she was discharged home.

BACKGROUND

It is not surprising that there are frequent cases of mistaken identity when inexperienced botanists pick their own wild flora herbal remedies. However, it is rare for these mistakes to be life-threatening. Here, we present a case of life-threatening accidental toxic ingestion in an urban environment. It highlights to all clinicians that they must be vigilant against the accidental ingestion of the foxglove plant, containing organic cardiac glycosides, when patients experiment with natural herbal remedies. It is a reminder that any ingestion of novel or uncommon plants should receive comprehensive investigations, such as blood tests and ECG.

CASE PRESENTATION

A woman aged 63 years with no previous medical comorbidities presented to the emergency department with 10 hours of vomiting, palpitations and presyncopal episodes. She had no previous cardiac history or cardiac risk factors, and takes no regular medications. She stated that she had tried a new herbal remedy the night before. Her friend had recommended the herbal drink comfrey (*Symphytum officinale*) to help with her symptoms of insomnia. The patient selected a handful of comfrey leaves from a local market and mixed these with hot water. These symptoms developed several hours after ingestion.

On examination, she was bradycardic with an irregular pulse, but haemodynamically stable. Cardiovascular examination showed normal heart

sounds. Respiratory and abdominal examination was unremarkable, and there was no evidence of focal neurological abnormality.

INVESTIGATIONS

ECG showed a sinus rhythm with second-degree atrioventricular heart block, Mobitz Type 2 with 2:1 conduction and a ventricular rate of 45. Several other abnormalities were seen on the ECG (shown in figure 1), including: (1) a shortened QT interval, (2) downsloping ST segments in II, III, aVF and V3–V6 and (3) U waves in II, III, aVF and V4–V6.

Blood tests showed normal full blood count, inflammatory markers and electrolytes.

The National Poisons Information Service (NPIS) website database Toxbase did not have an entry for comfrey. However, further searching on UpToDate (an international peer-reviewed clinical resource) showed an association with veno-occlusive disease affecting the hepatic circulation, but no documented association with cardiac disease or arrhythmia. After a simple internet image search, there was a suggestion that the comfrey plant closely resembled the foxglove plant (*Digitalis*) whose species contain the organic forms of cardiac glycosides, such as digoxin and digitoxin, frequently used in the treatment of arrhythmia and cardiac failure. When shown both images, the patient was not confident which leaves she had picked from the market stall (figure 2).

The patient's serum digoxin levels were elevated at 5.3 µg/L (range 1.2–2 µg/L), with a serum potassium of 4.6 mmol/L.

DIFFERENTIAL DIAGNOSIS

In view of the ECG findings, the elevated serum digoxin levels and the close resemblance of the comfrey and foxglove plants, the patient was suspected to have an accidental overdose of organic cardiac glycosides.

TREATMENT

The patient was treated with a digoxin-binding antibody, 'Digibind', due to the presence of a second-degree atrioventricular block and symptoms of *Digitalis* toxicity. However, this was delayed due to the limited availability of the antidote in many hospitals, and required emergency delivery from a local hospital. The quantity of digitalis ingested was unknown, and she was given one cycle of 38 mg of Digibind as per the cardiology recommendation. There were no immediate changes in the ECG after 2 hours, but her heart rate remained above 60 bpm and she was haemodynamically stable. After

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Figure 1 ECG changes. The ECG changes seen after ingestion of the herbal remedy. (A) Lead II rhythm strip showing bradycardia with second-degree atrioventricular node heart block with 2:1 conduction (Mobitz Type 2). (B) ST segment depression seen in leads II, III, aVF and V3–V6, a classical sign of digoxin use. (C) U waves present in leads II, III, aVF and V4–V6, also seen in digoxin use.

Figure 2 Spot the difference. The flowers of (A) *Digitalis purpurea* (foxglove) and (B) *Symphytum officinale* (comfrey). This case illustrates the great difficulty in distinguishing between the leaves of (C) foxglove and (D) comfrey. Images from <http://www.seasonalwildflowers.com/>.

12 hours, her second-degree atrioventricular node block had resolved, with some evidence of ST depression persisting.

OUTCOME AND FOLLOW-UP

She remained haemodynamically stable over the course of her 5-day inpatient stay, and on discharge, her ECG showed sinus rhythm and no evidence of *Digitalis* toxicity, and no structural abnormality was visualised on echocardiogram.

The patient was unable to find the original leaves she had purchased in the market, but was advised to contact the seller to inform them of the mistake.

DISCUSSION

Homemade herbal remedies on the surface may seem harmless. However, this case illustrates how limited knowledge of plants can be potentially fatal.

Wild comfrey (*S. officinale*) grows in the UK and throughout Europe. It is frequently used in herbal remedies brewed into a tea, and has throughout history been thought to treat many ailments. It was actually named after its supposed ability to assist in bone healing (Greek symphysis—the growing together of bones). Long-term comfrey ingestion has been associated with hepatic veno-occlusion disease,¹ but no direct cardiotoxic effects have been characterised.

Digitalis, commonly referred to as foxglove, is a genus of plants with over 20 different species, including *Digitalis purpurea* and *Digitalis lanata*. *Digitalis* leaves were known to have antiarrhythmic and positive inotropic cardiac effects, and historically were used for the treatment of congestive cardiac failure. There are multiple cardiac active compounds across different *Digitalis* species, and the purified extracts are used in the cardiac glycosides digoxin (from *D. lanata*) and digitoxin (from *D. purpurea*).²

Unfortunately, during Spring in particular, it is very difficult to distinguish between the thick leaves of comfrey and foxglove. This case illustrates how this subtly can lead to mistaken identity, and near-fatal consequences. Although the exact species and quantity of the *Digitalis* plant accidentally ingested by our patient are not known, cases of *Digitalis* ingestion have been associated with significant cardiac arrhythmias and even death.³ The diagnosis was confirmed with raised serum digoxin levels. The Siemens Advia Centaur assay used in the laboratory has cross reactivity with multiple *Digitalis* compounds in addition to digoxin, including digitoxin (11.5% cross reactivity) and digoxigenin (8.1%). The raised levels in the context of the history and ECG were consistent with the ingestion of *Digitalis*.

Digitalis toxicity can result from ingestion of foxglove plants or treatment with digoxin or digitoxin medication. Toxicity can affect cardiovascular, gastrointestinal and visual systems. Cardiovascular manifestations can include any arrhythmia, with atrioventricular dysfunction most commonly seen. Associated symptoms include palpitations, syncope and dyspnoea. Gastrointestinal presentations include nausea, vomiting and abdominal pains. Patients can also present with yellow-green visual disturbances, decreased photophobia and snowy vision.

Previous cases of mixing up of comfrey and foxglove have been documented. In China, foxglove was mistakenly ingested amongst neighbours sharing comfrey tea on a farm, leading to the hospitalisation of nine patients, each with elevated digoxin levels, with three requiring cardiac pacing.⁴ Two cases of a similar mistake have been reported in UK, both manifesting with cardiac arrhythmia.^{5 6}

There are no current evidence-based guidelines for the treatment of digoxin and digitalis poisoning. General consensus states that indications for therapy include life-threatening tachyarrhythmias/bradyarrhythmias, haemodynamic instability and hyperkalaemia.⁷ It is generally agreed that treatment should not be initiated on the basis of raised serum digoxin levels alone, without symptoms of toxicity. However, without formal randomised control trials, the exact efficacy and cost-effectiveness of antibody treatment remain unclear.

Despite these instances of accidental ingestion, Toxbase does not have an entry for comfrey. However interestingly, the entry

under *Digitalis purpurea* states that it may be confused with comfrey herbal tea. The authors recommend an entry under comfrey itself should present, with the risk of accidental ingestion of *Digitalis*, and have contacted the NPIS with this recommendation.

It is, therefore, important for all acute care doctors to be vigilant of digitalis ingestion in patients presenting with nausea, vomiting and cardiac arrhythmia if they have been using herbal remedies.

Learning points

- ▶ Homemade 'herbal remedies' are not as benign as many believe.
- ▶ The comfrey plant is morphologically similar to *Digitalis* and confusion must always been considered in patients presenting with cardiac abnormality.
- ▶ Ingestion of foxglove can result in *Digitalis* toxicity and cardiac arrhythmia.
- ▶ Digoxin-binding antibodies should be considered in patients with cardiac arrhythmias and haemodynamic instability due to digoxin poisoning.

Contributors MKV and ME saw and treated the patient in accident and emergency. They wrote the case report, and researched the literature around the presentation.

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