症例報告：

A Case of Digitalis Intoxication Brought about by Eating Digitalis Leaves by Mistake

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An 78-year-old woman visited our hospital with the chief complaints of abdominal pain, nausea, vomiting and diarrhea. She was operated on for gastric ulcer when she was 56 years old and complained of abdominal discomfort after operation. One day she wished to take Confrey (*Symphytum officinale*), but she took digitalis leaves (*Digitalis purpurea*) by mistake. On admission she was drowsy and the systolic blood pressure was 60 mmHg on palpation. Electrocardiograms showed bradycardia, irregular AV-nodal rhythm and ST depressions and T wave inversions with the shortening of the QT interval. Serum levels were potassium, 6.4 mEq/l; BUN, 34.4 mg/dl; creatinine, 1.5 mg/dl; digoxin, 2.0 ng/ml (therapeutic level, up to 2.0 ng/ml); and digitoxin, 111 ng/ml (therapeutic level, up to 25 ng/ml). Hemodynamic data showed HR, 49 beats/min; CO, 2.8 l/min; CI, 2.3 l/min/m²; SV, 57 ml/beat and SI, 47 ml/beat/m² on administration of dopamine 7 µg/kg/min. So VVI pacing was started at 70 bpm and CO increased to 3.6 l/min after pacing. But unfortunately she died of ventricular fibrillation. The digitalis leaves resemble the Confrey leaves and it is easy to mix up these two plants. Although this is a rare case, digitalis intoxication can be life-threatening. So we should prepared ourselves for the treatment of patients poisoned with digitalis and other poisonous herbs.

① Digitalis purpurea ② Confrey ③ digitalis intoxication ④ ventricular fibrillation

INTRODUCTION

In 1785, after using the medicinal herb for ten years, William Withering introduced *Digitalis purpurea* in An Account of the Foxglove¹⁾. Since then we have gained enormous sophistication in administering digitalis glycosides. In recent years we have come to use manufactured digitalis glycosides as a drug and digitalis leaves are not directly used as a drug. *Digitalis purpurea* is mainly grown as an ornamental plant in Japan.

Confrey (*Symphytum officinale*) is grown as a medicinal herb and often eaten in the agricultural

district. These two plants' leaves resemble and the patient in our case, an 78-year-old woman, ate digitalis leaves by mistake. She visited our hospital with digitalis intoxication and serum levels were digoxin, 2.0 ng/ml (therapeutic level, up to 2.0 ng/ml); and digitoxin, 111 ng/ml (therapeutic level, up to 25 ng/ml). Unfortunately she died of ventricular fibrillation. Although this is a rare case, misuse of these plants is sometimes fatal. So, we must be careful not to misuse these plants.

CASE

The patient, an 78-year-old woman, first visited

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Fig. 1. Electrocardiograms showed bradycardia, irregular AV-nodal rhythm, ST depressions and T wave inversions with shortening of the QT interval

our hospital with the chief complaints of abdominal pain, nausea, vomiting, and diarrhea. There was no particular family history. She was operated on for gastric ulcer at the age of 56 and complained of abdominal discomfort since then. One day, on television she learned that Confrey might be efficacious against abdominal discomfort. She picked three leaves of the foxglove in a neighbor's garden, fried and ate them, believing that they are Confrey leaves. They tasted very bitter. Two hours after eating them, she began to complain nausea and abdominal pain, 4 hours after, vomiting and diarrhea appeared and 19 hours after, she was brought into our hospital in an ambulance. She was a small old person; her height, 145 cm, her weight, 35 kg. On admission she was drowsy and the systolic blood pressure was 60 mmHg on palpation. Her face was very pale. Chest X-ray photographs showed mild

cardiomegaly. Electrocardiograms showed bradycardia, irregular AV-nodal rhythm, ST depressions and T wave inversions with the shortening of the QT interval (Fig. 1). Serum levels were potassium, 6.4 mEq/l; BUN, 34.3 mg/dl and creatinine, 1.5 mg/dl (Table 1). Hemodynamic data showed HR, 49 beats/min; CO (cardiac output), 2.8 l/min; CI (cardiac index), 2.3 l/min/m²; SV (stroke volume), 57 ml/beat; SI (stroke index), 47 ml/beat/m² RVEDP (right ventricular end diastolic pressure), 11 mmHg; mean RA (right atrial pressure), 11 mmHg and AO (aortic blood pressure), 80/40 mmHg on administration of dopamine 7 µg/kg/min. So VVI pacing was started at 70 bpm and CO increased to 3.6 l/min, AO increased to 120/60 mmHg and RVEDP, mean RA decreased after pacing (Table 2). Fig. 2 shows the clinical course of this case. At the beginning, we could not understand digitalis intoxication

Table 1.

RBC	356×10 ⁴ /mm ³	GOT	44 IU/l
WBC	9600/mm ³	GPT	33 IU/l
Hb	12.1 g/dl	LDH	411 IU/l
Ht	34.9%	ALP	224 IU/l
PL	12.6×10 ⁴ /mm ³	γ-GTP	20 IU/l
Na	134 mEq/l	Ch-E	0.58 ΔPH
K	6.4 mEq/l	CPK	36 IU/l
Cl	105 mEq/l	TP	6.7 g/dl
Ca	9.5 mg/dl	Alb	65.5%
P	5.5 mg/dl	α1	2.5%
BUN	34.4 mg/dl	α2	9.2%
Cr	1.5 mg/dl	β	8.0%
UA	7.4 mg/dl	γ	14.8%
pH	7.38		
PCO ₂	41.2 mmHg		
PO ₂	86.6 mmHg		
HCO ₃ ⁻	24.2 mEq/l		
BE	-0.3 mEq/l		
O ₂ SAT	96.4%		

Table 2. Hemodynamic data

(Dopamine 7 μg/kg/min)		(Dopamine 7 μg/kg/min + VVI pacing)	
HR	49 beats/min	HR	70 beats/min
CO	2.8 l/min	CO	3.6 l/min
CI	2.3 l/min/m ²	CI	3.0 l/min/m ²
SV	57 ml/beat	SV	52 ml/beat
SI	47 ml/beat/m ²	SI	43 ml/beat/m ²
RA	11 mmHg	RA	8 mmHg
RV	29/3 mmHg		
RVEDP	11 mmHg		
PA	30/13 mmHg	PA	33/11 mmHg
PCWP	12 mmHg		
AO	80/40 mmHg	AO	120/60 mmHg

completely because it was our first experience in seeing digitalis leaves. But from its chief complaints and ECG change, we guessed that the plant she ate caused similar poisoning effects to those of the foxglove. Serum levels were digoxin, 2.0 ng/ml (therapeutic level, up to 2.0 ng/ml); and digitoxin, 111 ng/ml (therapeutic level, up to 25 ng/ml). But it took two days to determine the serum digitoxin level because in our hospital's laboratory, we could not measure its serum level and we had to ask an outside laboratory to do so. What was worse, she developed acute renal failure perhaps because of low cardiac output. Although cardiac output increased after VVI pacing, one hour urine volume was still low.

Fig. 2. The clinical course of this case.

Because the urine volume did not respond to diuretics and we were afraid of increased accumulation of serum potassium, hemodialysis was done. After hemodialysis serum potassium level decreased to 3.5 mEq/l and fortunately the frequency of ventricular premature beats did not increase at this time²⁻⁴. After that her complaints continued. One day after admission, it suddenly showed ventricular fibrillation on monitor ECG and cardiopulmonary resuscitation was done at once. Intravenous administration of lidocaine and cardioversion was not effective and unfortunately she died of ventricular fibrillation. Fig. 3 shows the course of her electrocardiographic changes. It shows the ECG before digitalis intoxication (a), it shows the ECG at admission (b), it shows the ECG after VVI pacing (c) and it shows the ECG of ventricular fibrillation (d).

Fig. 3. The course of her electrocardiographic changes. (a) The ECG before digitalis intoxication. (b) The ECG at admission. (c) The ECG after VVI pacing. (d) The ECG of ventricular fibrillation.

DISCUSSION

Digitalis purpurea is known as the foxglove and it contains digitoxin, digoxin and digitalin etc.⁵⁾. But its principal element is digitoxin. Although Digitalis purpurea's habitat is originally Europe, it was introduced into Japan in the Edo period. Because it puts forth pretty flowers, we grow it as an ornamental plant in Japan and do not use its leaves in medicine. On the other hand, Confrey (*Symphytum officinale*) is grown as a medicinal herb, but its effect is really doubtful, and often eaten particularly in the agricultural district. These two plants' leaves are exactly alike and it is hard to distinguish between these two plants. In our case, although the patient wished to eat Confrey, she ate Digitalis purpurea by mistake. Fig. 4 shows Digitalis purpurea and Confrey in a neighbor's garden. Fig. 5 shows the discriminating points of these two plants' leaves. (1) Although in the leaf of Digitalis purpurea, the blade lasts to the stem, in the leaf of Confrey, the blade ends before the stem. (2) Although the leaf of Digitalis purpurea has saw-like edges, the leaf of Confrey has smooth edges. (3) Digitalis purpurea tastes very bitter. Digitalis purpurea's principal element is digitoxin. Digitoxin is absorbed from intestinal lumen rapidly and is 97% protein-bound and has a mean serum half-life of 146 hours^{5,6)}. In this case, the dry weight of three sheets of digitalis leaf is 2.4 g and the fetal dose of digitalis leaves is generally 2~3 g^{5,7)}. What was worse, the patient

was a small old person ; her age, 78, her height, 145 cm, her weight, 35 kg. It was assumed that digitalis intoxication must have been too much on her considering her physical condition. The methods of medical treatment of digitalis intoxication are that ; 1. For purposes of impeding absorption washing out the patient's stomach within 8 hours and administration of sickening drugs or laxatives are done. 2. For purposes of impeding the enterohepatic circulation of digitoxin activated charcoal or cholestyramine is administered^{8~10)}. 3. For purposes of removing digitoxin plasmapheresis is done and the clearance of digitoxin by plasmapheresis is much larger than that by hemodialysis¹¹⁾. 4. For purposes of preventing bradycardia cardiac pacing or intravenous injection of atropine is done. 5. For purposes of preventing ventricular arrhythmia correction of serum potassium, intravenous injection of lidocaine or phenytoin are done. 6. Direct-current countershock is used when all other methods have failed in the face of a life-threatening rhythm disturbance. 7. Digoxin-specific antibody is still not used in Japan generally. This time, the patient unfortunately died. Reflecting on the case, we would like to mention the following points: (1) This was a rare case and we could not understand digitalis intoxication completely at first because it was our first experience in seeing digitalis leaves. It took about one day to understand digitalis intoxication completely. (2) In this case, perhaps acute renal failure resulted from digitalis intoxication and we were afraid of in-

Fig. 4. *Digitalis purpurea* and *Confrey* in a neighbor's garden.

Fig. 5. The distinguishing points of these two plants's leaves.

- (1) Although in the leaf of *Digitalis purpurea*, the blade lasts to the stem, in the leaf of *Confrey*, the blade ends before the stem.
- (2) Although the leaf of *Digitalis purpurea* has saw-like edges, the leaf of *Confrey* has smooth edges

creased accumulation of serum potassium, so hemodialysis was done. Because the protein-binding rate of digitoxin was high, the clearance of digitoxin by hemodialysis was little. So plasmapheresis should have been done. (3) It took two days to determine the serum digitoxin level because in our hospital's laboratory, we could not measure its serum level and we had to depend on an outside laboratory for measurement. This time we experienced a case of digitalis intoxication brought about by eating digitalis leaves by mistake. Although this is a rare case, digitalis intoxication can be life-threatening. So we should be prepared for giving similar patients prompt and effective attention.

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ジギタリス葉を誤って食し、ジギタリス中毒となった1例

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症例は78歳女性。テレビにてコンフリーという薬草を食すと胃腸の具合が良くなると聞き、隣人宅に生えていた自生ジギタリスをコンフリーと誤って食した。食後4時間頃より吐気、腹痛出現、その後嘔吐、下痢も出現した。翌日になっても上記症状は消失せず、意識レベルも低下してきたので当院受診した。入院時患者は顔面蒼白で苦悶様、血圧触診で60 mmHg 台、著明な徐脈を呈し、低心拍出量が起因すると思われる急性腎不全像も呈していた。血中ジゴキシン濃度は2.0 ng/ml、血中ジギトキシン濃度は111 ng/ml と著明な高値を示した。患者は第2病日に治療のかいもなく心室細動にて死亡した。自生ジギタリスを誤食した例は比較的珍しく、本例の様に死亡するケースもあり臨床上重要と考えられたので報告した。

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