Nephroquiz
(Section Editor: M. G. Zeier)

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Colchicum ad nauseum

A 39-year-old man was admitted to hospital because of vomiting and diarrhoea. He had developed cardiomyopathy of unknown cause a decade earlier that was managed with diuretics and an angiotensin-converting enzyme inhibitor. Two years thereafter, insulin-dependent diabetes mellitus appeared. His HbA1c was controlled at ~7.5%. Two weeks prior to admission, he developed a burning pain in both feet. On the advice of his father-in-law, he ingested tablets hourly to make the pain go away. He continued these instructions despite the development of nausea, vomiting and diarrhoea. After 30 tablets, he became so weakened that he presented to the emergency department. The patient was disoriented in relation to time and place. His blood pressure was 90/50 mmHg, the heart rate was 110/min. The neck veins were flat, the heart was enlarged but no third heart sound was reported. The lungs were clear. The abdomen was soft with tenderness in the right upper quadrant. The liver was enlarged. There was no peripheral oedema. An arterial sample at room air revealed PaO₂ 63, PaCO₂ 32 (mmHg), HCO₃ 21 mmol/l, pH 7.45. The chest roentgenogram showed an enlarged heart with suggestion of congestion. The haemoglobin was 12 g/dl, haematocrit 38 vol%, Na 128, Cl 90, K 5.5, Ca 2.5 (mmol/l). The bilirubin was 81 μmol/l, ALAT 1263, ASAT 537, alkaline phosphatase 400 (U/l). Amylase was 281 U/l, serum creatinine was 330 μmol/l and myoglobin in the urine was 695 μg/l. The urine sodium was 59 mmol/l and the urine potassium was 17 mmol/l. The urinalysis disclosed +1 protein and the urine sediment revealed granular, muddy-coloured casts. The patient was admitted to the intensive care unit. There, an ultrasound examination of the abdomen showed a distended, stone-free gallbladder surrounded by a collection of fluid, consistent with acalculous cholecystitis (Figure 1).

Question
What is your diagnosis?

Fig. 1. The gallbladder with a thickened echogeneous wall shown in two views. Fluid surrounds the organ and no stone can be seen. The wall is prominent. These findings are consistent with acalculous cholecystitis.
Answer to the quiz on the preceding page

In-laws can be problematic, as illustrated by this case. The patient was given colchicine 0.5 mg. He ingested 15 mg over a day. The drug is an alkaloid of *Colchicum autumnale*, a plant first appreciated in Colchis more than 2000 years ago. A schematic sketch is given in Figure 2. Despite being a known poison, the drug was introduced into the medical amamentarium for the treatment of joint afflictions, generally gout. Colchicine binds to microtubular protein and interferes with the function of mitotic spindles. As a result, depolymerization and disappearance of the fibrillar microtubules from granulocytes and other motile cells occur. This effect breaks the cycle that leads to the inflammatory effect in gout. The patient admitted to ingesting colchicine tablets containing 0.5 mg. Thus, he swallowed at least 15 mg of the compound. The colchicine level was measured in this patient, revealing 3.0 ng/ml, although colchicine levels are not generally useful. In our patient, expectant treatment was successful. His acalculous cholecystitis, a previously unreported complication of colchicine poisoning, resolved uneventfully. Our patient proved to have diabetic nephropathy that was responsible for his pain. We found no evidence of gout.

Acute colchicine poisoning has a high mortality rate [1]. Our patient ingested a potentially lethal amount [2]. Acute deaths are due to haemodynamic collapse, cardiac arrhythmias and non-cardiac pulmonary oedema. Our patient survived that stage. Subsequently, rhabdomyolysis, liver damage, bone marrow depression, acute renal failure and infectious complications become prominent. Treatment options are limited. Haemoperfusion is of no value, since the volume of distribution is large. Oral activated charcoal might help since colchicine undergoes an enterohepatic circulation. Baud *et al.* [3] reported on the use of Fab fragments for the treatment of colchicine intoxication. Their patient was seen more acutely and the blood level was 24 ng/ml. The authors administered goat colchicine-specific Fab fragments and achieved a successful result. Their report was not the first for this treatment; a murine model was developed earlier [4].

Colchicine has a good bioavailability. A 0.5 mg dose is clinically appropriate. However, the dose should not exceed 10 mg over 3 days. Our patient ingested 15 mg over 1 day and developed the expected side effects and complications. As little as 7–12 mg is reported to be fatal. The kidneys excrete about half the drug dose. Half is unchanged and half is metabolized. Colchicine is metabolized by CYP 3A4. Thus, an interaction between HMG-CoA reductase inhibitors and colchicine is to be expected and has been reported [5]. Colchicine is an ancient drug that would never pass the requirements of agencies operating today. Nevertheless, given its wide availability, nephrologists must be aware of its toxic potential and the treatment options.

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References


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