CASE REPORTS

Self-poisoning with colchicine

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ALTHOUGH colchicine poisoning by accident and therapeutic misadventure is well documented, ingestion for suicidal purposes has been recorded on relatively few occasions. This paper adds two further cases to the literature.

Case reports

Case 1

Having frequently threatened to kill herself, a 16-year-old girl ate more than a dozen flowers of *Colchicum autumnale* (meadow saffron) at about midday on 3 September 1967. A few hours later she developed profuse vomiting and diarrhoea, which continued throughout the night.

At 10.00 a.m. the following morning she was admitted to hospital in a state of profound shock. She complained of intense thirst and abdominal pain and appeared severely dehydrated. Her heart rate was 132/min and systolic blood pressure 40 mm Hg. She was hypothermic (35°C) and all tendon reflexes were depressed.

Investigations: Hb 17.2 g/100 ml, PCV 57%, WBC 40,800/mm³, platelets 152,000/mm³, blood urea 64 mg/100 ml, capillary blood pH 7.28, std. bicarbonate 18.0 mEq/l, base excess -7 mEq/l, Pco₂ 40 mm Hg.

Urethral catheterization produced a small quantity of urine of SG 1.020. There was heavy albuminuria.

Intravenous fluids were given and the acidosis corrected with sodium bicarbonate. Metaraminol and noradrenaline were infused to maintain a systolic blood pressure of 90-95 mm Hg. Gastric lavage was not performed.

Despite therapy, which included atropine, vomiting and diarrhoea continued and by 4.00 p.m. she had passed only 10 ml urine, of SG 1.010. The blood urea had risen to 84 mg/100 ml, but the urine urea concentration was only 120 mg/100 ml. Her respiratory rate was now 50/min, with a minute volume

of 12 l. Capillary blood pH 7.28, Pco₂ 54 mm Hg. Her blood pressure became increasingly difficult to maintain.

Haemodialysis was commenced, but her condition steadily deteriorated and by 10.00 p.m. respiration had clearly become inadequate. Positive pressure respiration was instituted but shortly afterwards she convulsed and died.

Necropsy: Engorged oedematous lungs and a few subpericardial petechial haemorrhages. There was slight gastric mucosal engorgement. The liver showed some fatty infiltration and centrilobular necrosis.

Analysis showed 196 mg colchicine still in the stomach. The mean tissue concentration was 1.2 mg/100 g from which it was calculated that the total amount ingested was probably about 270 mg.

Case 2

A 35-year-old woman was admitted to hospital at midday on 5 May, 1968, having ingested 50-60 colchicine tablets, each of 0.5 mg, some 3 hr previously. On admission she was symptom free, with a blood pressure of 145/100 mm Hg. Gastric lavage was performed but no tablets were recovered.

Two hours later she developed vomiting and diarrhoea and complained of intense thirst and cramps in both thighs. Intravenous fluids were given to replace gastro-intestinal loss, with morphine to relieve the muscle cramps. A 4 l exchange transfusion was commenced at 9.00 p.m. in the hope of facilitating removal of the drug.

By the following morning her blood pressure had fallen to 60/40 mm Hg. Fluid replacement was intensified and metaraminol given intermittently to maintain a systolic blood pressure of 95-100 mm Hg. Her blood urea rose to 44 mg/100 ml, but her urine output remained satisfactory. There was occult haematuria.

Thrombocytopenia was noted within 24 hr of admission, and by the third day her platelet count

had fallen to 10,000/mm³. Anaemia (Hb 10.0 g/100 ml) and leucopaenia (WBC 2000/mm³) were most marked on the fourth day. A transient leucocytosis occurred at the end of the first week and her blood picture thereafter returned to normal.

Hypocalcaemia (serum calcium 7.0 mg/100 ml) was noted 2 days after admission and persisted for a fortnight. Serum bilirubin was 1.7 mg/100 ml on 10 May and the alkaline phosphatase reached a maximum of 27 K.A. units 3 days later.

Diffuse alopecia was first observed 11 days after admission and over the following week she lost about 70% of her scalp hair. Regrowth was negligible and when last seen (in September 1968) she was still wearing a wig.

Discussion

The alkaloid colchicine is found in all parts of the meadow saffron, whose pale purple flowers contain approximately 0.1% colchicine (Wildman, 1960), together with a number of minor alkaloids constructed on the colchicine pattern and having similar toxic effects (Santavy, Lang & Malinsky, 1950). The drug is a potent mitotic poison.

The fatal human dose appears to be in the region of 20 mg (Prescott & Webster, 1923). There is considerable individual variation, however, and death has followed as little as 7.0 mg taken by mouth over a 4 day period (Macleod & Phillips, 1947). By contrast, Major (1874) reported recovery in a 35-year-old man reputed to have drunk 11 ounces of colchicine seed wine, containing approximately 20–25 mg/ounce.

In acute poisoning, there is a delay of 1–6 hr between ingestion and the development of toxic symptoms. Profuse vomiting and diarrhoea then mark the onset of severe haemorrhagic gastroenteritis, with intense thirst, pharyngeal burning, abdominal colic, and rectal and vesical tenesmus. Fluid depletion and vascular damage rapidly lead to prostration, with tachycardia, tachypnoea, hypotension and oliguria. In severe cases, death ensues in 24–48 hr, but may be delayed up to 2 weeks. Twitching, convulsions and delirium may occur, but consciousness is retained to the end. Death is commonly attributed to respiratory paralysis (Ferguson & Theodore, 1952).

Neurological changes include muscle weakness, loss of sphincter tone, depressed reflexes and myelin degeneration of peripheral nerves (Brown & Seed, 1945). Layani, Aschkenasy and Mouzon (1947) observed a reversible myelitis with extensor plantar responses between the second and fourth weeks. Hypothermia as in Case 1 carries a grave prognosis (Ferguson & Theodore, 1952).

Bone marrow depression is usually observed within 48 hr of administration, and gives way to a

'rebound' leucocytosis at the end of the first week (Layani *et al.*, 1947). Alopecia is well documented. Liver damage may be associated with abnormal serum enzymes (Carr, 1965; Bruns, 1968), whilst hypocalcaemia as in Case 2 may reflect depressed parathormone production due to disordered protein synthesis (Dent, 1968, personal communication).

There is no good evidence that colchicine exerts a specific toxic effect on the kidneys. Oliguria and azotaemia can be explained in terms of inadequate renal perfusion, whilst haematuria may result from capillary haemorrhage (Santavy *et al.*, 1950).

Blood levels, when measured, have been extremely low (Walaszek *et al.*, 1960; Ertel, Omokoku & Wallace, 1969). Brues (1951) showed that colchicine rapidly leaves the bloodstream for the tissue spaces so that the volume of distribution exceeds that of the total body water within 30 min of injection. Radioactive studies suggest that 16–47% of an administered dose is excreted unchanged in the urine (Walaszek *et al.*, 1960).

The large amount of colchicine found in the stomach of Case 1 at necropsy clearly indicates that gastric lavage is mandatory, even after the development of toxic symptoms.

Shock is probably due largely to fluid and electrolyte depletion, which must be corrected immediately, and an attempt to maintain adequate tissue perfusion. In experimental animals colchicine stimulates rather than depresses the vasomotor centre (Ferguson & Theodore, 1952). Calcium, magnesium and potassium supplements may be necessary. In view of the substantial urinary excretion, it would seem desirable to establish a diuresis as rapidly as possible.

No data are available on the role of haemodialysis or exchange transfusion, but the wide tissue distribution and low blood levels would militate against the success of either procedure.

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References

- BROWN, W.O. & SEED, L. (1945) Effect of colchicine on human tissues. *American Journal of Clinical Pathology*, **15**, 189.
- BRUES, A.M. (1951) Discussion on paper by M. Levine: The action of colchicine on cell division in human cancer, animal and plant tissues. *Annals of the New York Academy of Sciences*, **51**, 1406.
- BRUNS, B.J. (1968) Colchicine toxicity. *Australasian Annals of Medicine*, **17**, 341.
- CARR, A.A. (1965) Colchicine toxicity. *Archives of Internal Medicine*, **115**, 29.
- ERTEL, N., OMOKOKU, B. & WALLACE, S.L. (1969) Colchicine concentration in leucocytes. *Arthritis and Rheumatism*, **12**, 293.

- FERGUSON, F. & THEODORE, P. (1952) Colchicine. 1. General pharmacology, *Journal of Pharmacology and Experimental Therapeutics*, **106**, 261.
- LAYANI, F., ASCHKENASY, A. & MOUZON, M. (1947) Intoxication aigue par la colchicine—Importantes alterations de la leucopoïese. *Bulletin et Memoires de la Société médicale des hôpitaux de Paris*, **63**, 10.
- MACLEOD, J.G. & PHILLIPS, L. (1947) Hypersensitivity to colchicine. *Annals of the Rheumatic Diseases*, **6**, 224.
- MAJOR, G.W. (1874) Series of cases of poisoning by *Vinum colchici* recently occurring in Montreal. *Canada Medical and Surgical Journal*, **2**, 241.
- PRESCOTT, A. & WEBSTER, R. (1923) In: *Legal Medicine and Toxicology* (Ed. by F. Peterson, W. Haines and R Webster), 2nd edn., vol. 2, p. 478. Saunders, Philadelphia and London.
- SANTAVY, F., LANG, B. & MALINSKY, J. (1950) L'action mitotique et la toxicité des nouvelles substances isolées due Colchique (*Colchicum autumnale* L.). *Archives internationales de Pharmacodynamie et de Therapie*, **84**, 257.
- WALASZEK, E.J., KOCIS, J.J., LEROY, G.V. & GEILING, E.M.K. (1960) Studies on the excretion of radio-active colchicine. *Archives internationales de Pharmacodynamie et de Therapie*, **125**, 371.
- WILDMAN, W.C. (1960) In: *The Alkaloids* (Ed. by R. H. F. Manske), vol. 6, p. 247. Academic Press, New York and London.

Tension pneumoperitoneum as a postoperative complication of multiple abdominal injuries

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TENSION pneumoperitoneum as the presenting sign of a perforated viscus is very rare (Singer, 1932; Addison, 1959) and is even more uncommon as a postoperative complication (Millar, 1962; Hughes, Cuthbertson & Buntine, 1964). A unique case of tension pneumoperitoneum presenting in the post-operative period but not directly related to the original operation is presented.

Case report

A 9-year-old boy was admitted on 29 August 1969, after a crushing injury of his abdomen. He was moderately shocked and tender on the left side of his abdomen and flank. X-ray of the chest (Fig. 1) showed a large gas bubble filling the left pleural cavity. A provisional diagnosis of a ruptured left diaphragm was made.

At laparotomy (K.C.) the injuries were as follows:

1. There was a 10 cm tear on the lateral side of the left diaphragm. The stomach and spleen had herniated into the chest but were intact. The diaphragm was repaired with continuous linen thread sutures.

2. The small bowel was torn across 7.5 cm from the duodeno-jejunal junction. The proximal 15 cm of the distal part were devascularized. This part was resected and the two ends anastomosed.

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Fig. 1. Radiograph on admission showing stomach lying in left pleural cavity.