CRUSH SYNDROME FOLLOWING SEDATIVE-HYPNOTIC OVERDOSAGE

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SYNOPSIS

A young woman was admitted in coma following an overdosage of butobarbitone (Soneryl). She developed apparent cutaneous manifestations of drug-induced disorders. However features of crush syndrome of a compressed limb were soon noted. She did not develop any renal abnormality but a foot drop of the other limb was noted later. The medical and surgical treatment is discussed.

INTRODUCTION

Crush syndrome of a limb following traumatic injuries is well-known and is not infrequently encountered. However crush syndrome following drug-induced coma has not been reported in Singapore. A series of 11 cases was reported by Schreiber et al in 1972 (1,2). It has also been reported in cases of improperly applied medical anti-shock trousers (MAST) (3). We report a case of crush syndrome of the limb following drug-induced coma.

CASE REPORT

A 35 year old woman was admitted, to Tan Tock Seng Hospital, unconscious and unresponsive to pain. She was found slumped on the dressing table in a sitting position. Both her legs were tucked under her buttocks and she was sitting on her right leg. She was last seen by her husband the day before apparently drowsy and high on sedatives.

Clinically she was in coma and unresponsive to pain. Her pulse rate was 125/min, Blood pressure 100/70 mmHg, and Respiratory rate 24/min. Her pupils were responsive to light and fundoscopy revealed no papilloedema or haemorrhage. On her right leg, was a patch of ecchymosis and blisters postero-medially from lower 1/3 thigh to heel; with oedematous plaques scattered over the leg anteriorly. Blisters were seen over the right ear and left 4th toe. (Fig 1) She was flaccid in all the limbs, reflexes were absent and plantar response was equivocal. Examination of her heart, lungs and abdomen revealed no abnormality.

X-rays of the chest and right tibia were normal. Blood investigations revealed a raised WBC count with a shift to the left. Blood urea was 25 mg/dl, Serum Na 138 mmol/l, Cl 110 mmol/l, K 4.80 mmol/l, Creatinine 1 (Repeat blood urea, electrolytes and creatinine were normal) Phenobarbitone level was 40 mg/l (n = 15-40).

The patient was intubated and blood pressure supported with dopamine infusion. Stomach washout was done followed by Forced Alkaline Diuresis. (FAD) The right leg was noted to be swollen and tense up to the knee. The right foot was cyanosed with early necrosis of the pulp of the 1st and 2nd toes (Fig 2) and absent dorsalis pedis and posterior tibial pulses. (This was about 2 hours after admission and about 20 hours after ingestion of the drug).

An immediate fasciotomy was done on the right leg. All 4 compartments of the leg were found to be very tense. Post-operatively, the toes were pink.

About 36 hours post-ingestion of drug, she began to respond to painful stimuli. 6 cycles of FAD had been completed. Her blood pressure was supported at 90-100 mmHg systolic. A new skin lesion over the right cheek appeared. Though the capillary return was present her right foot was swollen and cold. About 60 hours post-ingestion of drug, (day 3) there was spontaneous respiration and she responded to simple commands. She became conscious, responding to questions on the 4th day of admission. Blood phenobarbitone level had dropped to 2.9 mg/l. There was necrosis of muscles at the fasciotomy wound. Though the posterior tibial pulse was easily palpable and warmth felt to mid-foot, all the toes of the right foot were gangrenous. (Fig 3,4)

Debridement of necrotic muscle was performed several times. The calf, peroneal and anterior tibial muscles progressively necrosed up to the back of the knee even though the circulation to the skin and subcutaneous tissue was good. (Fig 5) Histology of

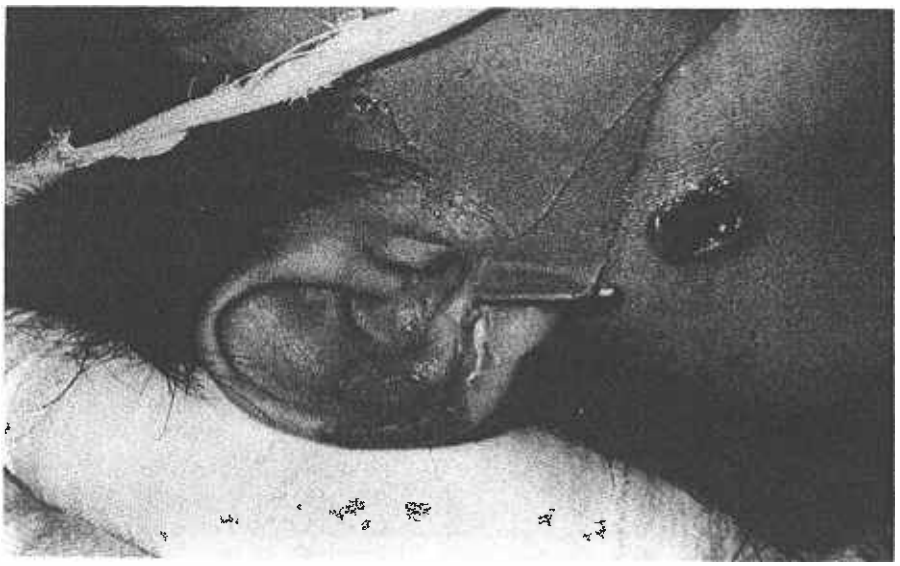

Fig 1 Cutaneous lesions — blisters over right cheek and right ear.

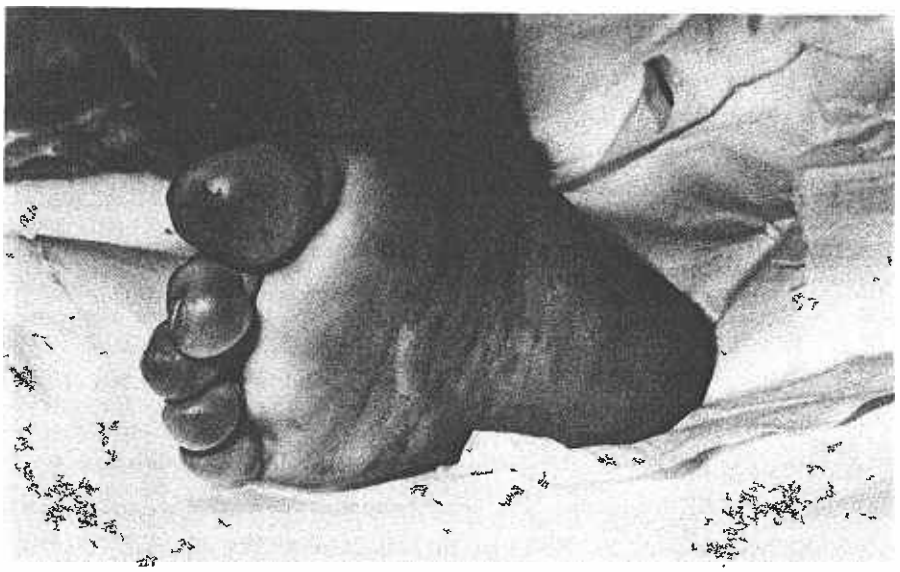

Fig 2 Cyanotic discolouration of toes.

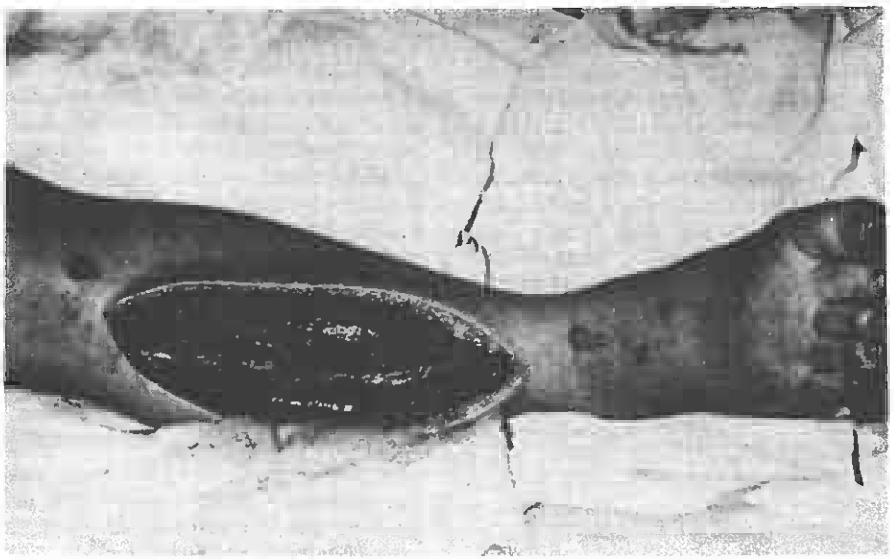

Fig 3 Right leg after fasciotomy: anterior compartment. Note: superficial necrosis of muscles and cyanotic discolouration of toes.

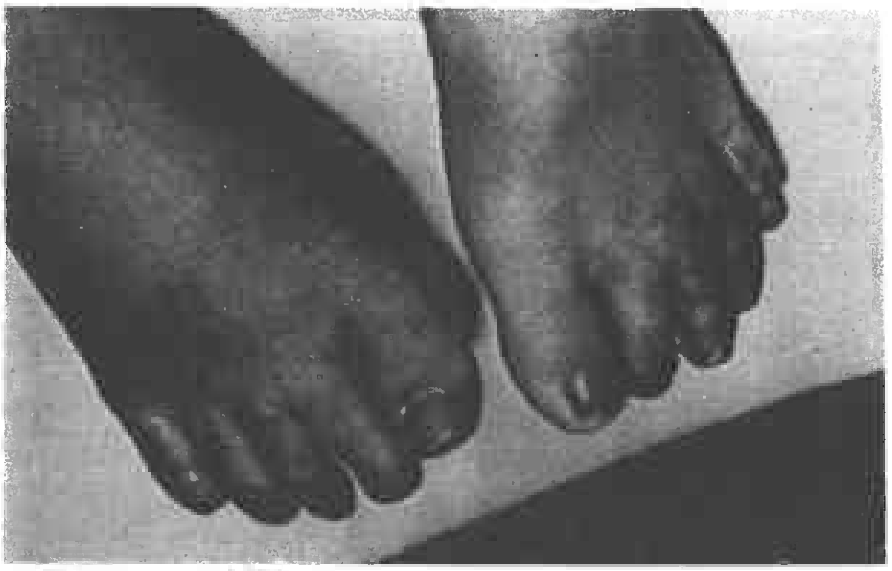

Fig 4 Blisters of toes of left foot and gangrenous toes of right foot.

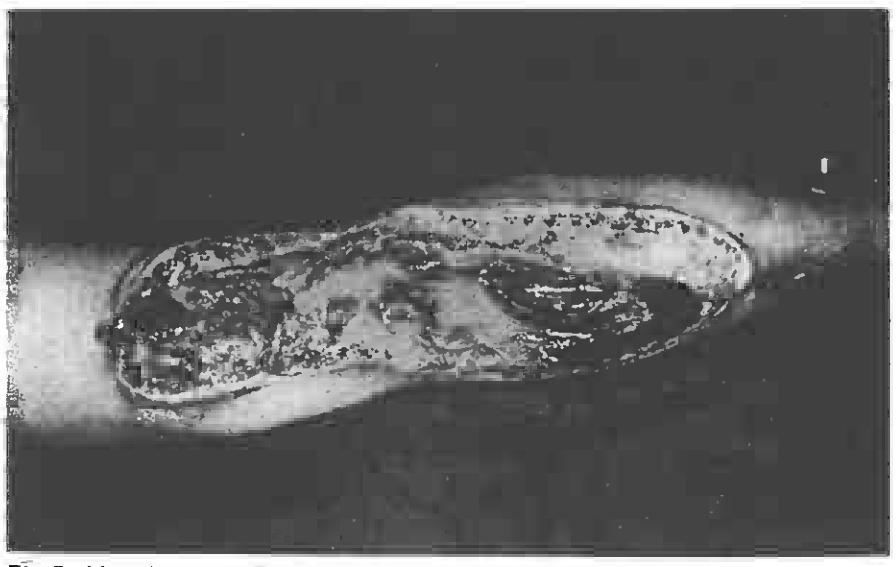

Fig 5 Muscle necrosis and slough extending to lower third back of right thigh.

muscle sample showed features due to pressure necrosis. Foot drop of the opposite leg was noted on day 21 of admission. An electromyelographic study of the left leg showed a completely unexcitable lateral popliteal nerve.

Despite repeated desloughing it was not possible to save the leg and a right below knee amputation was thought necessary. This was done on day 24 of admission. She was discharged on day 56 of admission when she was managing well with balancing and walking exercises.

DISCUSSION

Butobarbitone (Soneryl) is a sedative-hypnotic of intermediate to long duration, marketed as 100 mg tablets. Its peak concentration is attained between 0.6-2 hrs with an average half-life of 37.5 hrs. Up to 54% of a dose is excreted in the urine. Breimer concluded in his study that it is not a suitable drug for treatment of insomnia since the CNS depressant effects are likely to persist into the following day. (4,5)

Various drugs are known to induce disorders affecting the musculoskeletal, connective, skin and neural tissues. Drug-induced rhabdomyolysis have been reported in association with amphetamine, heroin, phencyclidine. (6,7,8,9) Complications following drug overdosage include cutaneous, hepatic, cardiopulmonary and infection problems.

Crush syndrome following drug-induced coma was reported in 1972 by Schreiber et al. Our patient had been unconscious for about 18 hours following ingestion of butobarbitone (Soneryl). The crushing force was due to the weight of the patient's own body. (10,11,12) Areas of erythema, induration and vesicles were seen over the compressed opposing surfaces, the popliteal fossa and leg, and over direct pressure areas i.e. the ear and cheek. She also had a lateral popliteal nerve palsy of the opposite leg.

Renal abnormalities were present in 8 patients in Schreiber's series. Factors that potentiate the effects of myoglobinuria include hypotension, acidosis and volume depletion. Bywaters & Stead showed that myoglobin injection into experimental animals regularly induced acute tubular necrosis provided the urine is concentrated and acid. (13) Our patient did not develop any renal abnormalities. FAD, adequate hydration and maintenance of blood pressure prevented this complication.

Treatment includes medical and surgical measures. General supportive measures are necessary including continuous monitoring of vital parameters with or without assisted ventilation. Gastric lavage is useful if less than 24 hours have elapsed, though little is recovered after 4 hours. Activated charcoal may also be used. Hypovolaemia should be corrected and blood pressure may be supported with Dopamine. Forced alkaline diuresis will hasten the excretion of some barbiturates. In renal failure, haemodialysis is probably more effective in removing long-acting barbiturates because there is less protein binding. Lipid-soluble short-acting barbiturate is removed by the use of lipid containing dialysate or by haemoperfusion through activated charcoal or ion exchange resins.

Elevation and cooling of the crushed limb help to reduce its metabolic needs. Fasciotomy decompression is indicated if there are signs of increasing tension interfering with the circulation, nerve conduction or muscle damage. Early signs include increased tension of the limb, blistering, pain on stretching the muscle and sensory disturbance of the digits. One must not procrastinate till the appearance of advanced signs. These include coolness, loss of peripheral pulses and paralysis. Repeated debridement of devitalised muscle may be necessary and secondary infection must be controlled. The aim of surgical treatment is to save the limb but amputation surgery may be necessary.

CONCLUSION

Blisters (vesicles and bullae) following ingestion of drugs like frusemide, barbiturates, sulphonamides, phenolpthalein, nalidixic acid is well-known. However, they could also occur after prolonged pressure on a limb and may lead to crush syndrome. An awareness of this complication would enable one to institute immediate treatment preventing the progression to the advanced stages of crush syndrome.

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