associated with acromegaly, not only from the axillae but also from the forehead and limbs. It may be particularly useful in those patients who do not respond to bromocriptine.

IAM was supported by a grant from the North-western Regional Health Authority.

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(Accepted 31 July 1979)

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Ionised calcium in fat embolism

Hypocalcaemia has been reported in the fat embolism syndrome, but it is said to be non-specific.¹ We describe here a case where a directly measured low ionised calcium (Ca^{2+}) concentration alerted us to the diagnosis of fat embolism. Subsequent measurements of Ca^{2+} proved to be an accurate index of recurrent embolic episodes.

Case report

A 27-year-old man sustained a displaced fracture of the right tibia and fibula after a road-traffic accident. No other significant injury was sustained. The fracture was manipulated under general anaesthesia and the leg immobilised in full-leg plaster. Two days later the patient complained of sudden retrosternal chest pain radiating to the neck and arms. On examination he had a tachycardia of 120/min with normal blood pressure and respiratory rate of 20/min. An electrocardiogram showed T-wave inversion over the anterolateral leads. The measured Ca^{2+} was 1.06 mmol/l (4.24 mg/100 ml) (Orion SS-20, normal range 1.15–1.30 mmol/l (4.6–5.2 mg/100 ml)) with an arterial pH of 7.42. Fat embolism was considered as a possible cause of the episode of cardiac ischaemia and he was transferred to the intensive care unit. One hour later he became restless and dyspnoeic with a respiratory rate of 30/min. Auscultation showed coarse basal crepitations, and sputum stained positive for fat. Multiple petechial haemorrhages developed over the upper chest and his temperature rose to 37.8°C. Investigations showed: arterial Po_2 6.94 kPa (52 mm Hg), Pco_2 4.4 kPa (33 mm Hg), pH 7.43, forced expiratory volume in 1 second (FEV_1) 2 l/min, FEV_1 : vital capacity 72%, haemoglobin 11.2 g/dl, platelets $160 \times 10^9/\text{l}$. Over the next three days, while the patient was maintained on oxygen alone, two further episodes of clinical deterioration occurred. Firstly, he developed new petechial haemorrhages and increasing dyspnoea and, secondly, he suffered an episode of restlessness and confusion. The figure details the changes in Ca^{2+} , pH,

Fluctuations in ionised calcium over three-day period during which three separate clinical deteriorations occurred (hatched areas). Shaded areas indicate normal limits for ionised total calcium and pH.

Conversion: SI to traditional units—Calcium: 1 mmol/l $\approx$ 4 mg/100 ml.

total calcium, and calcium corrected for albumin during this period. Control values relate to an age- and sex-matched patient confined to bed with a fractured 12th rib.

Comment

The course of the embolism syndrome in this case was uncommon and differed from the usual clinical course of fat embolism. The classic clinical syndrome of respiratory insufficiency, progressive arterial hypoxaemia, disorientation and other cerebral effects, pyrexia, tachycardia, and petechial rash usually begins 12–72 hours after injury. In a recent study² hypocalcaemia was found in eight out of 100 patients with the clinical syndrome of fat embolism and the authors did not list this as of diagnostic significance. The mechanism of hypocalcaemia is not understood but may result from the binding of Ca^{2+} to free fatty acids said to be liberated by local lipolysis, possibly in the lungs. Raised serum lipase values have been reported in 40% of patients with fractures three to five days after trauma³ but may also be non-specific. Fatty acid binding would affect the total calcium only if the fall in Ca^{2+} is substantial. Theoretically the Ca^{2+} as directly measured by the Orion SS-20 should be a much more sensitive index of calcium homeostasis than the measured total calcium. In this patient the ionised calcium was low before other signs of fat embolism became apparent. Furthermore, the Ca^{2+} fell with each subsequent deterioration and seemed to correlate well with a recurrent clinical episode. Total calcium values estimated at the same time were within the normal range.

There is no single laboratory test which can be used to diagnose fat embolism. Those "simple" tests which are available are time consuming⁴ and their results often do not correlate with the clinical severity of the syndrome.² The development of flow through specific ion electrode analysers such as the Orion SS-20 now allows accurate estimations of Ca^{2+} , while being easy to use and within the scope of most laboratories. Although we report only one case the Ca^{2+} (as directly measured) mirrored the clinical state of the patient and warrants further investigation by the centres of major trauma.

We thank Mr G D Stainsby and Professor D N S Kerr for permission to report this case and Dr J Stoddart and Dr J Gill for help and encouragement.

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(Accepted 25 July 1979)

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Severe poisoning with chlormethiazole

Chlormethiazole (Heminevrin) is used in treating alcohol withdrawal symptoms and as a hypnotic in the elderly. We report 16 cases of chlormethiazole poisoning.

Case reports

Thirteen patients were admitted on 16 occasions after overdoses of chlormethiazole. The clinical details are summarised in the table. Four had been prescribed chlormethiazole as a hypnotic and three had taken tablets belonging to relatives. The other six were alcoholics who had taken three to 12 Heminevrin tablets daily for periods varying from two months to six years, although most had continued to drink heavily. No patient was known to have cirrhosis but five had chronic bronchitis. Alcohol had been taken in at least six cases. Three patients had taken other drugs,

which were nitrazepam 30-40 mg (patient 3), digoxin, paracetamol, and aspirin. Eight patients were unconscious (grade 2, 3, or 4¹) on arrival, and on another five occasions consciousness was lost after admission. Patients 1, 2, and 3 had severe respiratory depression and required endotracheal intubation and artificial ventilation for 3, 4, and 18 hours respectively. Patient 4 breathed satisfactorily after intubation. In a further six an oropharyngeal airway was used. Bronchoscopy was performed in two patients (1, 6a) who had apparently aspirated vomit before admission. Three patients (1, 2, 3) were hypothermic and hypotensive (rectal temperatures 31.5-33.5°C, systolic blood pressures 50-70 mm Hg). Another three had systolic blood pressures of only 85-90 mm Hg. The pulse rates on admission ranged from 68-150/min (mean 99). Electrocardiograms in eight unconscious patients showed no unexpected features. The muscle tone and limb reflexes were reduced or absent in deeply unconscious patients. The pupils showed no consistent changes. Bowel sounds were present in all patients. Increased salivation was observed during seven admissions in six patients. Bronchial secretions were increased in patients with chronic bronchitis but appeared normal in the others.

Intensive supportive treatment was given, as for barbiturate poisoning.¹ All patients recovered, although five were unconscious for more than 20 hours and one was in grade 4 coma for 41 hours and unconscious for 92 hours after reaching hospital. Of the six patients who developed pneumonia, four had chronic bronchitis and two had aspirated vomit before admission. Plasma was assayed for alcohol and chlormethiazole by gas-liquid chromatography² and screened for other drugs. The highest plasma chlormethiazole concentration recorded in a conscious patient was 11.5 mg/l. Concentrations in unconscious patients ranged from 7 to 36 mg/l. In 10 cases in which serial concentrations were measured the plasma half-lives ranged from 4 to 15 hours, but in one elderly patient (1) the plasma concentration was about 18 mg/l for 36 hours before falling with a half-life of 17 hours.

Comment

These and other cases^{3,4} show that chlormethiazole can cause severe and sometimes fatal poisoning. Except for increased salivation the clinical features are similar to those of barbiturate overdose,¹ with deep coma, respiratory depression, hypotension, and hypothermia in severe cases. The cause of the increased salivation is not known. Our three hypothermic patients had been lying unconscious for many hours before admission and so were at particular risk of hypothermia. But hypothermia has also been described⁵ after intravenous administration of chlormethiazole, which may have a direct effect on thermoregulatory centres. All our patients survived but the incidence of pneumonia was high. Aspirations of secretions may be more likely in patients unconscious from chlormethiazole overdose who have increased salivation. We did not use charcoal haemoperfusion. Its efficacy in removing chlormethiazole is not known, but it might be helpful in patients with deep, prolonged coma and respiratory complications.

Self-poisoning is common in alcoholics, so the long-term prescription of chlormethiazole for the "treatment" of alcoholism is dangerous⁴ as well as ineffective. The safety of chlormethiazole in elderly patients and in chronic bronchitis is also questionable since it may cause hypothermia and respiratory depression.

We thank Dr A T Proudfoot and Dr L F Prescott for advice and encouragement, Dr J Attley (Astra Chemicals Ltd) for information about chlormethiazole, and Mrs M Strathdee for typing.

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(Accepted 3 August 1979)

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Primary anaerobic peritonitis

Spontaneous peritonitis is a rare condition usually occurring in children and accounting for about 2% of abdominal emergencies in childhood.¹

The incidence of primary peritonitis is increased in patients with ascites due to hepatic or renal disease and primary anaerobic peritonitis may occur in these patients.² There have been no reports of primary anaerobic peritonitis occurring in a patient without ascites. The following case report describes a previously healthy 16-year-old boy who presented with primary anaerobic peritonitis.

Case report

A 16-year-old Negro schoolboy, who had lived all his life in Britain, was admitted to St James's Hospital, Balham, with a 24-hour history of the sudden onset of severe abdominal pain and vomiting. Except for an influenza-like illness one month earlier he had had no relevant medical history. He was dehydrated and toxic, with a pulse rate of 120/min and a temperature of 38.5°C. There was pronounced tenderness, guarding, and rebound tenderness over the whole abdomen and no bowel sounds were heard. The haemoglobin concentration was 11.9 g/dl, the white blood cell count was $27.6 \times 10^9/l$ and the sickle cell test was negative. Serum electrolytes and amylase concentrations were normal, and the serum urea concentration was 15.9 mmol/l (95.4 mg/100 ml). Urine microscopy and subsequent culture showed no evidence of a urinary tract infection.

At laparotomy, performed after resuscitation with intravenous fluids, 650 ml of odourless yellowish pus was found throughout the whole peritoneal cavity. Careful examination of the entire length of the bowel failed to show any abnormalities and the only unusual finding was a slightly enlarged spleen. Peritoneal toilet was performed and the abdomen closed without drainage. An immediate Gram stain performed on a sample of pus showed Gram-negative coccobacilli. A course of gentamicin and penicillin was started and when subsequent culture produced a profuse anaerobic growth metronidazole was added.

The patient made a slow but uneventful recovery. Postoperative liver function tests, upper and lower gastrointestinal barium studies, and an intravenous urogram all gave normal results. Ultrasonography showed a normal liver and enlargement of the spleen by a posterior splenic cyst. The causative organism was eventually identified by the Anaerobic Reference

Clinical features and highest recorded plasma chlormethiazole and alcohol concentrations in 16 cases of chlormethiazole overdose in 13 patients

	Patient No:												
	1	2	3	4	5a	5b	5c	6a	6b	7	8	9	10
Age (years)	84	77	29	22	40			46		35	43	53	70
Sex	F	M	F	M	M			M		M	M	M	M
Stated amount of chlormethiazole*													
Tablets		18	30	25	47	50	35	50		25	40-60	20-40	10-20
Capsules	90								50				
Ingestion-admission interval (hours)	c18	12-15	14	13	2	4	2-4	20	2	c12	1	9	2
Coma grade on admission	4	4	4	4	0	0	0	3	0	3	1	2	2
Deepest coma grade	4	4	4	4	4	2	0	3	2	3	3	2	2
Duration of coma in hospital (hours)	92	34	22	28	29			4	0.5	4	6	6	0.5
Increased salivation	—	+	+	—	+	+	—	+	—	—	—	+	—
Pneumonia	+	+	—	+	—	+	—	+	—	—	—	—	+
Highest plasma chlormethiazole concentration (mg/l)	20.5	36	19	19	16	19	9	(3)†	10.5	12	(10.5)†	15.5	7
Highest plasma alcohol concentration (mg/100 ml)	0	0	0	0	(10)†	100	50	0†	245	190	0†	380	0

*Heminevrin tablets each contain chlormethiazole edisylate 500 mg. Heminevrin capsules contain chlormethiazole base 192 mg in arachis oil.

†Not measured before recovery of consciousness.