Myxoedema coma. A report on five successfully treated cases

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Summary

Five consecutive cases of myxoedema coma treated successfully with intravenous triiodothyronine and later oral thyroxine are described. All were hypothermic and had biochemical evidence of advanced myxoedema. Co-existent disease, notably diabetes and anaemia, was common.

Introduction

Myxoedema coma was first described by Ord in 1879, and few subsequent reports followed that of Summers in 1953 until 1963 when Forester reviewed seventy-seven cases. The high mortality rate has been widely reported (Forester, 1963; Blum, 1972). The elderly are often affected (Newmark, Hemathongkam and Share, 1974) and co-existent disease commonly complicates management, occasionally causing coma (Rosenberg, 1968; Royce, 1971).

The rarity of the condition has limited individual experience and differences in management include giving L-thyroxine intravenously (Holvey *et al.*, 1964), triiodothyronine administration either intravenously (Catz and Russell, 1961) or nasogastrically (Hall *et al.*, 1974), in high (Dyson and Wood, 1956) or low dosage (Bayliss, 1966).

Nordquist *et al.* (1960) and Down and Vassallo (1973) were the first to emphasize the hypoventilation and hypercarbia. Sedatives are dangerous as their metabolism is delayed (de Groot, 1971). Administration of hydrocortisone is important both when myxoedema may be secondary (Senior and Burge, 1971), and also because the pituitary is slow to secrete adrenocorticotrophic hormone when advanced myxoedema is corrected (Ivy, 1965). Slow rewarming, the prompt recognition and treatment of arrhythmias and silent infections, are both essential. Hyponatraemia in myxoedema, possibly results, as in other hypo-osmolar states, from the failure of the cell to pump out sodium (Hilton and Patrick, 1974). When severe, it may cause convulsions and coma, and fluid restriction with thyroid hormone replacement correct it.

Holvey *et al.* (1964), remarkably, described seven cases successfully treated with intravenous thyroxine.

However, only two of their patients were hypothermic, one was merely stuporose, and the coma might have been due to other factors.

Cases and methods

Each case is subsequently described in detail. The three tables summarize the clinical features, investigations, and treatment of the five patients.

Serum thyroxine (T_4) was determined by competitive protein binding (Thyopac 4*) and serum triiodothyronine (T_3) by radioimmunoassay (T_3 R.I.A. Kit*). Serum thyrotrophin stimulating hormone (TSH) was estimated by solid phase radioimmunoassay (Phadebas-Pharmacia). Serum cortisol was measured fluorometrically (Spencer-Peet, Daly and Smith, 1975).

E.D.

This 68-year-old lady was the subject of a previous report (Khaleeli, 1976). For eight years she had attended another hospital with myxoedema and varicose veins. She took thyroxine haphazardly and in November 1974 was admitted in a confused state which improved on taking thyroxine.

In November 1975 she was admitted for surgical treatment of extensive bilateral leg ulcers. She was slow mentally and physically, pale, had a hoarse voice and dry skin. The pulse was 60/min, regular, the blood pressure 80/50 mmHg. Her usual thyroxine 0.1 mg twice daily together with ferrous sulphate was prescribed and quinaband dressings applied to her ulcers.

Five days later she became drowsy and then deeply comatose. Her rectal temperature was 32.2°C (90°F), pulse 40/min. Myxoedema coma was diagnosed and confirmed by investigations later (Table 2). Chest X-ray showed basal consolidation and the sputum grew *Staphylococcus aureus*. She was managed with 10 µg/12 hr triiodothyronine, hydrocortisone 100 mg/12 hr, and intramuscular ampicillin and flucloxacillin. She was slowly rewarmed with a space blanket and nursed in an intensive care unit where her heart was monitored.

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TABLE 1. Clinical features of five female patients with myxoedema coma; all recovered

	E.D.	S.F.	F.C.	E.Y.	A.R.
Age (years)	68	85	90	84	84
Previously diagnosed	yes	no	no	no	no
Month of presentation	November	January	February	November	December
Lowest rectal temperature	32°C	35°C	33°C	31°C	35°C
Lowest pulse rate/minute	40	60	52	44	48
Lowest blood pressure (mmHg)	60/20	70/40	90/50	100/70	120/80
Associated diabetes	no	yes*	yes	no	no
Faecal impaction present	yes	yes	yes	no	yes
Associated infection	yes	no	yes	yes	yes
Leg ulcer present	yes	no	yes	no	no

TABLE 2. Investigations of the five patients with myxoedema coma

	E.D.	S.F.	F.C.	E.Y.	A.R.	Normal range
Serum T ₄ (nmol/l)	<10	14	<10	<10	<10	60–160
Serum T ₃ (nmol/l)	<0.5	<0.5	<0.5	<0.5	<0.5	1.4–3.0
Serum TSH (i.u.)	45	45	62	55	31	up to 5.0 (mu./l)
Serum cortisol (nmol/l)	635	950	—	770	570	250–700 (9.00 a.m.) up to 200 (midn't)
Thyroid antibodies (micro-haemagglutination)	+ve	+ve	+ve	—ve	+ve	Up to 40 ²
Blood glucose (mmol/l)-on admission	5	39	12.5	5	5.3	3.0–5.0 (fasting)
Blood urea (mmol/l)	16.5	18.6	9.2	6	6.2	2.5–6.5
Serum creatinine (mg/dl)	2.2	1.6	—	0.9	—	42–130 (μmol/l)
Arterial { PO ₂	114	120	82	81	59	88–155
PCO ₂	19	14	39	38	40	32–48
pH	7.41	7.00	7.44	7.47	7.45	7.36–7.42
Standard bicarbonate	15	3.2	26	30	27	22–26
Small complexes on ECG	yes	yes	no	yes	no	—
Haemoglobin on admission g/dl	9.0	12.2	7.4	14.2	11.2	13.5–18.0 (man) 11.5–16.5 (woman)
Lowest haemoglobin g/dl	6.7	8.8	7.4	6.9	7.9	
Lowest serum sodium (mmol/l)	125	199	133	133	127	13–145
Plasma osmolality (mosmol/l)	268	326	294	262	275	275–305
Urinary osmolality (mosmol/l)	120	—	—	389	—	50–1200

Within 3 days she was able to converse. Haematuria, nose bleeds and purpura on the chest wall, however, were noted and her platelet count fell. Transfusion failed to raise the platelet count, and quinaband was withdrawn with dramatic rise in the platelets and haemoglobin. The patient recovered, but the extensive ulcers were responsible for a protracted stay in hospital, terminated by her death from broncho-pneumonia 9 months later.

S.F.

This 85-year-old lady presented in March 1975 at Surgical Out-Patients with blood loss per rectum, lower abdominal pain, weight loss and urinary frequency. Sigmoidoscopy revealed blood in the rectum and first degree piles. After a barium meal and follow-through showed no abnormality, she failed to reattend.

On the 11th January 1977, she was admitted urgently having been found unconscious. On examination she was comatose, dehydrated, cyanosed, and had Kussmaul respiration. The pulse was 80/min, blood pressure 90/40 mmHg. Abdominal distension due to faeces was noted. Although subacute obstruction was diagnosed, blood gases revealed a severe metabolic acidosis (Table 3). This prompted a blood sugar estimation, which confirmed diabetic ketosis. She was rehydrated, given small hourly doses of soluble insulin intramuscularly, potassium supplements and bicarbonate. Although the blood glucose soon returned to normal, her temperature fell during the night and failed to register on a ward thermometer. She was rewarmed with a space blanket, but as she was still unconscious the next morning, a medical opinion was sought.

TABLE 3. Treatment of the five patients with myxoedema coma

	E.D.	S.F.	F.C.	E.Y.	A.R.
Intravenous triiodothyronine (T ₃)	yes	yes	yes	yes	yes
Initial 24-hr dose of i.v. T ₃	30 µg	20 µg	10 µg	50 µg	20 µg
Total i.v. T ₃ given	100 µg	30 µg	240 µg	140 µg	50 µg
Oral T ₃ used	no	no	no	yes	no
Initial oral thyroxine dosage	0.3 mg	0.1 mg	0.03 mg	0.1 mg	0.1 mg
Eventual maintenance dosage	0.25 mg	0.25 mg	0.2 mg	0.25 mg	0.15 mg
Dosage of hydrocortisone over first 24 hr	200 mg	100 mg	200 mg	200 mg	—

On examination she had a puffy facies, pallor and dry skin. Myxoedema coma was suspected and a serum thyroxine confirmed the diagnosis the same day (Table 3). She was started on i.v. triiodothyronine 10 µg/12 hr, hydrocortisone 100 mg i.v., and half normal saline alternating with 5% dextrose, as her sodium was now high. Within 24 hr, she answered questions reluctantly, and resented interference. She was given L-thyroxine 0.1 mg/day orally, and her diabetes was managed on twice daily soluble insulin and later tolbutamide, and a 120-g carbohydrate 1200 calorie diet. She was mobilized and discharged to an old people's home, and was well at follow-up 9 months later.

F.C.

When this 90-year-old hypertensive lady fell and was admitted in February 1975, her diabetes was incidentally found and managed on an 80-g 800 calorie diet.

During the 3 weeks before admission on the 25th February 1977, she became progressively drowsier. Diabetic precoma was diagnosed and she was admitted as an emergency.

On examination she was hoarse, pale, deaf, drowsy and disorientated, with dry skin and absent eyebrows. Ulcers on the shins and bruises on the thighs were noted. The rectal temperature was 33°C, pulse rate 52/min, blood pressure 130/90 mmHg, and the tendon reflexes slow relaxing.

The blood glucose was 12.5 mmol/l and the drowsiness attributed to advanced myxoedema which was later confirmed (Table 2). Diuretics were stopped when her blood pressure fell to 100/70 mmHg, and only 0.03 mg of oral L-thyroxine prescribed, increasing to 0.05 mg after 2 days.

On the 4th March 1977, she became comatose. As the temperature was 36.9°C, cellulitis was diagnosed and later confirmed when a swab grew *Staph. aureus*. Ampicillin 250 mg 4 times/day was prescribed, together with triiodothyronine 10 µg/day intravenously and hydrocortisone 100 mg/12 hr parenterally. Flucloxacillin was later added, the maintenance dose of triiodothyronine doubled with

an additional 20 µg bolus dose, and the patient improved. An accompanying iron-deficiency anaemia was corrected, the maintenance dose of L-thyroxine gradually increased to 0.2 mg/day, and the parenteral therapy of hydrocortisone and T₃ stopped. The patient is now alert and well, awaiting eventual discharge.

E.Y.

This 84-year-old lady was admitted after falling over twice in the preceding 5 days, and had become drowsy and uncommunicative. Her sister explained that over the past 3 years she had slowed down, felt the cold, and gained weight. On examination she had a puffy face, dry skin and absent eyebrows. The rectal temperature was 31°C, pulse rate 44/min, blood pressure 100/70 mmHg. She was stuporose and deep pain stimuli made her mutter a few words with a croaky hoarse voice. The tendon reflexes were slow to relax.

Advanced myxoedema was suspected and confirmed by investigations (Table 2). Intravenous triiodothyronine 20 µg and hydrocortisone 190 mg were given, she was gradually rewarmed, her heart monitored, and normal saline followed by 5% dextrose infused. Over the next 24 hr 50 µg of T₃ were given and then 10 µg i.v./day until the 6th day of admission when oral T₃ was substituted at the same dosage. Hydrocortisone 200 mg/day was given for 2 days.

Two days after admission nasogastric feeding had been started and 'coffee ground' material aspirated. Investigations revealed a lower oesophageal ulcer proximal to a stricture, and the patient was treated conservatively. Although initially improving, 12 days after admission she deteriorated, becoming febrile, hypotensive, blood pressure 70/30 mmHg, and unresponsive. Gram-negative septicaemia secondary to urinary tract *Escherichia coli* infection was discovered, and gentamicin therapy was started together with 20 µg/12 hr of T₃ and 100 mg/12 hr of hydrocortisone. Within 24 hr she had improved and was able to take 0.1 mg of L-thyroxine orally. Her course was complicated further by heel ulcers for

which surgical debridement was needed, but by the 24th week after admission she was able to return home.

A.R.

An 84-year-old chronic bronchitic with gross osteo-arthritis was admitted with a short history of increasing dyspnoea and expectorating purulent sputum. She had been taking amoxycillin. Her relatives had noted no recent general deterioration.

On examination she was drowsy, sleeping through most of the examination, but was rousable. She had a puffy face, dry skin, absent eyebrows and was cyanosed, confused and unco-operative. The rectal temperature was 35°C, pulse rate 48/min, blood pressure 130/85 mmHg. The respiration was grunting in character and there were basal expiratory crackles. The abdomen was distended and the rectum full of hard faeces. The tendon jerks were slow to relax.

Advanced myxoedema was confirmed (Table 2). The sputum was purulent growing *E. coli*, but the chest X-ray appeared normal. She was treated with intravenous triiodothyronine 10 µg/12 hr for 2 days together with 0.1 mg/day of L-thyroxine orally, physiotherapy, amoxycillin and controlled oxygen therapy. The patient improved, but was excitable, and 4 days after admission was given 25 mg of promethazine i.m. The next day she became deeply unconscious and unrousable, the temperature falling to 35°C. Intravenous triiodothyronine was again given and her L-thyroxine increased to 0.15 mg/day. The patient improved.

Two weeks after admission the haemoglobin had fallen to 7.9 g/dl, but correction of both iron and folate deficiencies caused the haemoglobin to rise. Radiology showed no source of gastro-intestinal blood loss. Her course was further complicated by urinary tract *E. coli* infection responding to cotrimoxazole, but she made a full recovery returning home 38 days after admission.

Discussion

These five cases were typical in that they were all elderly, female, presented in the winter months, and had clinical features of advanced hypothyroidism. The concurrence of diabetes, clinically silent infections, anaemia, leg ulcers and faecal impaction serves to stress that many factors other than thyroid replacement need consideration.

The extremely low circulating thyroid hormone and high TSH emphasize that advanced myxoedema was present. Although four out of five cases showed thyroid antibodies, these may disappear in advanced myxoedema.

All five cases were treated with intravenous triiodothyronine (T_3), together with oral thyroxine

(T_4) when conscious. The rationale for the use of T_3 is that its onset for action is rapid (within 6 hr) compared to L-thyroxine (5 days) and its maximal action occurs within 36 hr as opposed to longer than 2 weeks with L-thyroxine. Low dosage of T_3 was given to the five elderly patients as otherwise the risk of fatal arrhythmias would have been high. In one case, the initial very low dosage (only 10 µg) might explain the slow response and the large total dose. Oral thyroxine was started cautiously in all but one case, where the diagnosis had previously been made.

Survival in all the cases may be attributed to: (1) the use of triiodothyronine intravenously; (2) the low dosage adopted, especially in an elderly age group; (3) the avoidance of sedation and cardiac stimulants; (4) attention to concurrent illness, particularly anaemia, diabetes and infection.

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