HYPOTHERMIC MYXOEDEMA COMA

THREE CASE REPORTS

BY

DONALD W. MACDONALD, M.B., Ch.B.

Medical Registrar, Victoria Hospital, Blackpool

Hypothermic myxoedema coma is an uncommon condition in which interest has grown recently (*Lancet*, 1956). Only 15 cases have been reported, and those since 1953. Three further cases are reported, each of interest in itself. Case 1 is the first reported case of hypothermic coma in juvenile myxoedema. Case 2 is the oldest reported case. Case 3 is the second reported case to have survived over three months.

Case 1

A youth aged 19 was admitted to hospital in coma on November 21, 1956. At the age of 12 he developed weakness of his legs, and from that time his walking deteriorated, although he remained mentally alert. During the 12 months before admission he became increasingly lethargic, spending most of his time asleep before the fire. On the day of admission he could not be roused.

On examination he was deeply unconscious. Physically he had the appearance of a boy of 12. His skin was soft, dry, and cold; his lips were thick and a large tongue protruded from his mouth. Axillary and pubic hair were present. His genitalia showed normal development. The rectal temperature was 82° F. (27.8° C.); the apex rate 50 a minute; respiratory rate 2 a minute; B.P. 80/60 mm. Hg.

Investigations.—Hb, 98%; W.B.C., 19,000/c.mm., mainly polymorphs; blood cholesterol, 200 mg./100 ml.; serum sodium, 144 mEq/l.; serum potassium, 6.7 mEq/l.; plasma chlorides, 63 mEq/l.; CO₂ combining power, 41 mm./l.; blood sugar, 100 mg./100 ml. E.C.G. twelve hours after admission showed low-voltage complexes in all leads in sinus rhythm at 100/minute. X-ray examination of the chest was negative.

Treatment was begun immediately: (1) Warmth:—He was immersed in a lukewarm bath until the rectal temperature rose to 89° F. (31.7° C.), and then nursed between electric blankets until his temperature reached 95° F. (35° C.), eight hours after admission. He was then maintained at this level by intermittent heating from the electric blankets. (2) L-thyroxine sodium, 0.02 mg. four-hourly, was given sublingually. (3) Cortisone:—100 mg. of hydrocortisone hemisuccinate was given intravenously over the first 12 hours, then 50 mg. of cortisone acetate intramuscularly six-hourly. (4) Penicillin, 500,000 units, was given twice daily.

Twelve hours after admission the pulse rate rose to 100, respirations to 10, and the B.P. to 110/70. Three hours later he regained consciousness and asked for a cup of tea. His voice was deep and his speech slow. He knew who he was and took an interest in his surroundings. Twenty-eight hours after admission he had an epileptiform fit and became comatose. Respiration ceased, and was maintained by intermittent positive-pressure inflation through a cuffed endotracheal tube via a tracheotomy. He died 78 hours after admission.

Post-mortem Findings

External appearances:—The body was that of an adolescent male with thick lips, low receding forehead, and slanting eyes; there was also a recent tracheotomy wound. In some places the tissues were gelatinous. *Central nervous system:*—The brain weighed 1,280 g.; no significant abnormality was seen. *Trachea and lungs:*—The right lung weighed 280 g. and the left 270 g.; both pleural spaces contained large quantities of straw-coloured fluid; both lungs were congested. *Cardiovascular system:*—The heart weighed 240 g.; the pericardium contained straw-coloured fluid; no significant abnormality was found. *Alimentary*

tract:—The liver weighed 880 g.; no significant abnormality was found in the tract. *Urogenitals:*—The kidneys together weighed 250 g. *Reticulo-endothelial system:*—The spleen weighed 100 g. and showed no significant abnormality. *Endocrine system:*—The adrenals were normal in size and appearance; the testes were in the scrotum and showed no significant abnormality; the thyroid was small and rather firm, probably fibrous; the pituitary was not examined as the sella turcica was removed intact.

Histology.—The thyroid gland was dissected off the trachea and found to weigh 27 g. Histological examination revealed that its weight was in fact considerably less, as much of the tissue weighed was voluntary muscle. This muscle contained localized areas of pale homogenous fibres whose appearance suggested focal degeneration or necrosis. Such thyroid tissue as there was looked fairly normal, although there was definitely some increase in the inter-acinar fibrous tissue. There was a fibrin thrombus in one thyroid artery. In the testis there was no active spermatogenesis. The Leydig cells were very scanty indeed and did not stain characteristically. The pituitary was normal in size and histological appearance.

Case 2

A widow aged 80 was admitted to hospital on November 26, 1957, with a fractured neck of femur. Before operation her condition was good; pulse 60, B.P. 130/70, temperature 97° F. (36.1° C.). Smith-Petersen nailing was carried out under general anaesthesia. Post-operatively she became cold and cyanosed, with a systolic B.P. of 95 mm. Hg. Plasma was given intravenously. Later she lapsed into coma with a pulse rate of 50, respirations 4, and a temperature reported as subnormal.

In retrospect it was realized that this was a case of myxoedema. Further information obtained from her brother showed that for three years she had become increasingly tired, sleeping most of the day and night. Her voice was gruff.

Examination now showed her to be deeply unconscious, with a rectal temperature of 91° F. (32.8° C.). Her skin was dry and coarse, her hair and eyebrows were scanty. No other abnormality was detected. Treatment was commenced: (1) warmth by a bed cradle, the patient protected by a blanket; (2) L-thyroxine sodium, 0.05 mg. sublingually four-hourly; (3) cortisone acetate, 50 mg. intramuscularly four-hourly; (4) penicillin, 500,000 units twice daily.

The patient died within 12 hours without regaining consciousness.

Investigations.—Hb, 60%; W.B.C. 2,600/c.mm., 65% neutrophils; serum cholesterol, 280 mg./100 ml. E.C.G. low-voltage complexes in sinus rhythm at 45/minute.

Post-mortem Findings

The body was that of an obese woman aged about 80 and 5 ft. 3 in. (160 cm.) in height. Rigor mortis was present. An old, sound surgical scar was present in the right inguinal region and a fresh surgical incision over the left hip. There was bruising of the right shoulder, right cheek, and right forehead. The skull was not injured. The brain showed no significant abnormality apart from one or two minor localized subarachnoid haemorrhages. The pituitary was small but of normal appearance. The mouth, tongue, larynx, oesophagus, and trachea were healthy. The thyroid gland was small, pale, firm, and fibrous. The lungs were oedematous and there was bilateral basal bronchopneumonia. The heart was dilated. The myocardium was flabby. There was some coronary atherosclerosis but little in the aorta.

The stomach was empty. The bowel was healthy, although the proximal part of the colon was dilated. The liver showed a minor degree of passive venous congestion. The spleen was of normal size but soft. The kidneys were healthy, as was the bladder. The uterus had a fundal fibroid. The pancreas and adrenals appeared normal. The adrenal glands together weighed 13 g. Histological examination showed no significant abnormality in the adrenal glands or in the ovary, breast, and pituitary. The thyroid

gland, which weighed 17 g., was pale, firm, and fibrous. Histological examination showed it to consist almost entirely of fibrous tissue in which there were a few groups of atrophic thyroid acini, each group being infiltrated by lymphocytes. There were a number of large blood vessels in the fibrous tissue, some of which were calcified.

The appearances were those of a primary failure of the thyroid gland and suggestive of a long-standing case of Hashimoto's disease.

Case 3

A spinster aged 79 was admitted to hospital in coma on December 17, 1957. She had remained well until five months before admission, when she became slowly lethargic and intolerant of cold. On the evening of admission she was found comatose in a chair before a warm fire in a well-ventilated room.

On admission she was unconscious, with no response to noxious stimuli. Her skin was smooth and dry, and had a corpse-like coldness. Her body hair was completely absent, and had been from the age of 18. The rectal temperature was 91° F. (32.8° C.), pulse impalpable, apex rate 60, systolic B.P. 100 mm. Hg.

Investigations.—Hb, 84%; W.B.C., 10,200, normal differential count; blood cholesterol, 200 mg./100 ml.; serum sodium, 152 mEq/l.; serum potassium, 5.1 mEq/l.; plasma chlorides, 69 mEq/l.; C.S.U., a trace of protein only; liver-function tests, within normal limits; Kahn negative; blood urea, 44 mg./100 ml.; urea clearance, 60% of average normal function. E.C.G. showed low-voltage complexes in all leads.

Treatment was begun immediately: (1) Nursed between blankets, no external heat; (2) L-triiodothyronine, 0.08 mg. intravenously on admission, and 0.02 mg. sublingually four-hourly; (3) cortisone acetate, 50 mg. four-hourly intramuscularly; (4) crystalline penicillin, 500,000 units intramuscularly twice daily.

Twelve hours after admission her temperature had risen to 97° F. (36.1° C.). She spoke occasionally in a slow deep voice. A further 0.08 mg. of triiodothyronine was given intravenously. Thirty-six hours after admission her temperature was 100° F. (37.8° C.) and a few crepitations could be heard at the left base. She was then given cortisone, 50 mg. six-hourly orally. Forty-eight hours after admission she relapsed into coma once more, but recovered 12 hours after receiving a further dose of 0.08 mg. of triiodothyronine intravenously. From that time she made an uneventful recovery, at first on oral L-thyroxine sodium and later thyroid B.P.

Although tests on pituitary function could not be carried out owing to lack of co-operation, the fact that the patient gave a further response to intravenous triiodothyronine after lapsing into coma a second time and that she has remained greatly improved on thyroid alone for three months shows this to be a case of true myxoedema and not hypopituitarism.

Sheehan (1956) states that thyroid given alone has no beneficial effect on the symptoms of hypopituitarism.

Discussion

Hypothermic coma is the natural termination of untreated, uncomplicated myxoedema. Its occurrence has been recognized only within the last five years, although a similar picture presenting in hypopituitarism has been known for longer (Sheehan and Summers, 1952).

In addition to these three cases, 15 cases have been reported to date (Le Marquand, Hausmann, and Hemsted, 1953, 1955; Summers, 1953; Malden, 1955; Reid, 1955; Marshall and McCaughey, 1956; Dyson and Wood, 1956; Anderson and Hausmann, 1956). Of these, only one reported in the series of Malden survived. Karhausen and Zylberszac (1955) described a case without hypothermia.

The rarity of this condition is more apparent than real. Including this series, five series account for 16 patients. Once seen and recognized, the clinical picture is never forgotten. The patient is corpse-like in appearance. Occasional respirations indicate that life is still present. The usual features of myxoedema are present.

Sheehan and Summers (1952), in discussing hypopituitary hypothermic coma, state that a major factor causing the failure to recognize a hypothermic state is that the clinical thermometer records only to 95° F. (35° C.), anything lower being recorded only as subnormal. They emphasize that all patients with subnormal temperatures *must* have their temperatures measured by a low-reading thermometer. Hypothermic coma has not been reported previously in juvenile myxoedema.

Precipitating Factors.—*Cold*:—The reported cases show a marked seasonal incidence occurring between October and April. *Trauma*:—Case 2 went into coma following the fracture of her femur and the subsequent operative procedures. It is likely that during periods of stress the requirement of thyroid hormone increases like that of the adrenal corticosteroids.

Treatment

The condition is due directly to lack of thyroid hormone. Treatment is to give this. Although this appears simple, 15 of the 17 patients have died.

1. *Thyroid Hormone.*—3:5:3-L-triiodothyronine is the most active thyroid hormone readily available. Dyson and Wood (1956) gave a dose of 1,200 mg. followed by 1,000 mg. 36 hours later. Anderson and Hausmann (1956) described a case given 50 mg., in which anginal pain and cardiac failure developed. Both patients died. Goolden and Burrell (1957) suggest that 10 mg. 12-hourly be used initially. The third patient in this series received approximately 80 mg. of L-triiodothyronine intravenously per 24 hours. This produced a clinical response without untoward effects in a patient aged 79. It is suggested that thyroid hormone acts as a metabolic catalyst at cellular level. As such it would be less effective at low temperature. Hypothyroid patients with low temperatures probably tolerate thyroid hormone better than those at normal body temperature, the tolerance increasing with the degree of body hypothermia. If this is true, as I believe it is, then one should give an amount of triiodothyronine proportionate to the degree of hypothermia, reducing the amount as the body temperature rises to normal, then slowly increasing to the optimum dosage. A suggested scheme would be to give 100 mg. 12-hourly until the body temperature begins to rise, then reduce to 50 mg. 12-hourly or lower, depending on response of temperature and pulse rate. Maintenance dosage could then be worked up gradually when the patient is able to take the triiodothyronine orally.

2. *Rewarming.*—This can be done by immersion in warm water, by nursing between blankets, or by heat cradle. Care must be taken to avoid cutaneous vasodilatation. Rewarming is illogical and probably dangerous. Hypothermia is only a symptom of the disease state and will improve as the latter responds to treatment. Administered thyroid hormone will produce warmth that is diffuse, gradual, and physiological. No external heat was applied to the third patient in this series, who survived.

3. Intravenous fluids should be restricted on three accounts: (1) the danger of myxoedema heart failure; (2) the occurrence of acute tubular necrosis has been demonstrated secondary to hypothermic muscle damage (Marshall and McCaughey, 1956); and (3) the physiological requirement of fluid is small, as fluid loss is reduced and metabolic need low. Our successful case was given no intravenous fluid.

4. Antibiotic cover must be given.

Two further cases of severe myxoedema with marked hypothermia have come under our care. They have not been included in this series, as coma and death occurred rapidly before treatment could be initiated. In the case which came to necropsy no cause of death other than myxoedema was found. This suggests that hypothermia is an indication to start treatment immediately even when coma does not appear imminent.

Summary

Hypothermic myxoedema is an uncommon condition with a high mortality rate, recognized only in the last

five years. Three further cases are presented; one is the first reported case of coma in juvenile myxoedema, another the second case reported to have survived. This patient is still alive nine months after starting treatment.

The treatment is reviewed and discussed. It is suggested that hypothermia in itself is an indication for immediate treatment, that the application of external warmth is unwarranted, and that thyroid hormone be given in a dosage related to the degree of hypothermia.

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Note.—Since this paper was accepted for publication a further case of myxoedema coma has been reported by S. J. Surtees and S. Ginsberg, *Postgrad. med. J.*, 1958, **36**, 443. Their patient was resuscitated but died of cardiac failure a month later.

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Medical Memorandum

Bilateral Polycystic Disease of Kidney Complicated by Intestinal Obstruction

The following case of bilateral polycystic disease of the kidney developed acute large-gut obstruction two days after admission to hospital. The case is reported because of the development of this unusual complication.

CASE REPORT

A Sea Dyak woman aged 38 was admitted to a small out-station hospital in Sarawak, British Borneo, on July 1, 1957, 17 days after delivery of a stillborn child. She complained of cough with white sputum since delivery and frequency of micturition for two days, urine being voided a countless number of times day and night. For the 24 hours prior to admission she complained of a dull aching pain in the left lower chest, left hypochondrium, and left loin, worse on coughing, and a colicky pain in the left loin. She had haematuria for 24 hours, blood occurring throughout the stream.

On admission she was very ill and toxic, with a temperature of 103° F. (39.4° C.), and pulse 112. There was a hard fixed tender mass with an irregular surface in the left loin extending downwards below the level of the umbilicus. The right kidney was palpable, with a soft smooth mass about the size of an orange comprising the lower pole. Air entry was reduced at the left lung base, and there were fine inspiratory and expiratory rales. Blood: Hb, 45% (Sahli); red cells, 2,600,000; white cells, 8,800 (polymorphs 70%; lymphocytes 28%; eosinophils 1%, large monocytes 1%); E.S.R., 137, Westergren. Urine: acid, albumin ++, over 100 red cells per high-power field. Blood urea was 70 mg. per 100 ml.

A clinical diagnosis of bilateral polycystic kidneys with infection of the left kidney was made. Unfortunately further investigation could not be carried out in a small out-station hospital with limited laboratory and no x-ray facilities.

Procaine penicillin, 500,000 units twice daily, and streptomycin, 0.5 g. twice daily, brought little change in her general condition. Two days after admission she complained of generalized colicky abdominal pain. She had passed a very small stool that morning and no flatus all day.

There was moderate distension of the lower abdomen, most pronounced in the right iliac fossa, with marked visible peristalsis. An enema gave a very poor result.

Operation.—The abdomen was explored through a McBurney incision. The lower ileum, caecum, and ascending and transverse colon were greatly distended. The descending and pelvic colon were collapsed. Through the upper part of the wound the lower pole of the right kidney was seen to be covered with cysts up to 1 in. (2.5 cm.) in diameter, varying from blue to brown in colour. The whole right kidney was felt to be involved. The left kidney was greatly enlarged. Details were obliterated by pericapsular oedema. A caecostomy was performed and a Paul tube inserted.

Post-operatively the patient was put on daily washouts through the caecostomy and was given sulphaguanidine to prepare her for any further operative intervention required.

After operation the pains in her left lower chest, left hypochondrium, and left loin started to subside, and had disappeared by July 6, the third post-operative day. The left kidney was correspondingly smaller, softer, and no longer tender. From admission to operation her temperature had shown daily variations between 103 and 99° F. (39.4 and 37.2° C.). It fell rapidly after operation, and she was apyrexial on July 7. On July 8 the Paul tube fell out and she opened her bowels. She continued to have a normal daily motion until discharge from hospital.

On July 12 the caecostomy was separated from the abdominal parietes and closed. Appendicectomy was carried out to avoid future confusion. The abdomen was closed in layers.

She was discharged from hospital on August 2 feeling very well, having refused further investigation and treatment at a larger hospital. Four months after operation she remained well and symptom-free.

COMMENT

Cleland (1951) reported that Dr. W. A. Giles removed a polycystic kidney (side not stated) causing intestinal obstruction in 1905. No other reference to this complication was found in the literature.

The development of acute intestinal obstruction in this patient gave rise to some diagnostic confusion, occurring as it did in a small out-station hospital where diagnosis mainly rests on history and physical examination. It caused a primary inflammatory lesion of the large bowel to be considered as an alternative diagnosis. In view of the limited surgical facilities available, the formation of a caecostomy was decided upon as the simplest way of relieving the obstruction. The decision was not regretted in view of the beneficial effect it had on the course of the illness.

A possible explanation of the clinical picture described is that ulceration of the splenic flexure occurred secondary to infection of the adjacent polycystic kidney. The passage of faeces over the ulcer perpetuated the renal infection and the colon became obstructed by inflammatory oedema. The renal infection and ulceration of the colon resolved rapidly when the colon was defunctioned by caecostomy.

The case reported does not bear out the statement of Duff (1948) that infection of a polycystic kidney affects the prognosis adversely, at any rate so far as the immediate prognosis is concerned. It is possible that the prognosis in this case may be favourably affected by a diet mainly consisting of rice with little added protein.

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P. W. BEDFORD, M.B., Ch.B., B.Sc.,
 Medical Officer, Simanggang Government Hospital, Sarawak.

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