A CASE OF MYXOEDEMA COMA SUCCESSFULLY TREATED WITH TRI-iodo-THYRONINE

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Introduction

The termination of myxoedema in coma was described in the Report of the Clinical Society of London (1888) and had been noted even before this (St. Thomas's Hospital Report, 1879). It is an uncommon complication occurring in long-standing untreated cases and hitherto was fatal, with the possible exception of one patient (Malden, 1955), and here the cerebro-spinal fluid protein was markedly raised and on recovery there was a unilateral hyperreflexia suggesting a cerebrovascular accident complicating myxoedema.

This article reports the successful treatment of an undoubted case of myxoedema coma with oral tri-iodo-thyronine.

Case Report

Mrs. E. A., aged 69, was admitted to Walton Hospital at 8.30 p.m. on January 22, 1957, as a case of 'apoplexy.' The casualty officer noted that she was unconscious.

The relatives said that she had felt the cold excessively for many years and her face had become puffy over the last 12 months. For six months she had restricted her activities and been troubled with deafness. During the previous week she was drowsy, had taken to sleeping during the afternoon, and on the day of admission was found to be unrousable in her chair.

The patient had had three normal deliveries, the last 25 years ago, and had menstruated again after the last pregnancy.

On examination the patient was comatose. She had a typical myxoedematous facies, the skin was cold and dry, the axillae were dry and hairless, the vulval hair was absent and the labial hair sparse. She could not talk, but was capable of making croaking noises on painful stimulation.

The pulse rate was 52 per minute and regular, the blood pressure 180/100, and the heart sounds very distant. There was no evidence of neurological abnormality apart from absent ankle jerks, but the ocular fundi could not be adequately

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visualized due to bilateral lenticular opacities. The rectal temperature was 87° F. (after ten minutes' insertion of a laboratory thermometer).

The investigations performed on admission are tabulated.

Treatment

The patient was put in a heat cradle and at midnight 100µg. of 3-5-3'-l-tri-iodo-thyronine was given intragastrically by means of a Ryles tube.

On the morning of January 23 her conscious level was higher in that spontaneous movements were more frequent, but she was still not talking although the rectal temperature had risen (see graph). She was given 40 µg. of tri-iodo-thyronine by the same route at 10 a.m. During the day she became more active, the pulse rate rose to 68 per minute and the rectal temperature to 95° F. She was given a further 40 µg. of tri-

17-KETOSTEROID ESTIMATION BY THE METHOD OF MOXHAM AND NABARRO, 1956

	January 22	January 23	January 24	January 29	February 5	February 14
Serum cholesterol (mg./%) ..	645		565	445	285	
Blood sugar (mg./%) ..	122					
Serum potassium (mEq/l.) ..	4.9	4.7	4.9			
Serum sodium (mEq/l.) ..	126	122	120			
Serum chlorides (as NaCl) (mEq/l.) ..	95	94	93			
17-ketosteroids (mg./24 hours) ..			3.1		7.0	
17-ketogenic steroids (mg./24 hours) ..			2.8		13.6	
CO ₂ combining power (ml./%) ..		65				
Haemoglobin (% M.R.C.) ..		82				75
White cell count (per cm.) ..		4,300				9,100

iodo-thyronine administered in a milk drip commencing at 6 p.m.

The next day (January 24) she could just speak a few words and she was slowly returning to a normal conscious level. The pulse rate was 88 per minute and the rectal temperature 99° F. She was put on 40 µg. of tri-iodo-thyronine daily by mouth.

At 11.30 p.m. on January 25 she had become very restless and was singing in the ward. It was considered that she had become mentally hyperactive following tri-iodo-thyronine therapy and she was sedated with paraldehyde 5 ml. I.M. and the tri-iodo-thyronine suspended until January 27 (when she was started on 20 µg. daily), by which time although still slightly confused and noisy she was more rational.

Over the next two days she made a remarkable recovery, becoming quite rational and able to walk about the ward. Now that she was co-operative a B.M.R. was performed (February 2) and gave a result of minus 25 per cent. An E.E.G. (February 6) was reported by Dr. E. A. Nieman as 'there is a well-developed regular 8 per second alpha rhythm and some slow activity within the theta range,' a picture found in cases of myxoedema. Chest X-ray showed no pulmonary pathology and the heart size was within normal limits.

On February 13 she complained of vomiting and admitted to having not felt well the previous day, but she denied any chest pain. Examination showed her to be in mild congestive heart failure. She was put to bed, digitalized, given mercurial diuretics, a salt-free diet and the tri-iodo-thyronine was discontinued. By February 16 her vomiting had settled, the heart failure improved and she was given cortisone 25 mg. twice daily (because the possibility of a hypopituitary state was entertained) and the tri-iodo-thyronine in a dose of 20 µg. daily recommenced.

On February 18 she complained of palpitations and breathlessness, the pulse rose to 110 per minute, the blood pressure fell to 110/60 (the

rectal temperature was 97.4° F.), and she was found to be in severe congestive heart failure. She collapsed shortly afterwards and died.

Post Mortem

There was oedema of the ankles and about 200 ml. of clear fluid was found in both pleural cavities. The lungs, liver and spleen were congested, but otherwise of normal appearance. There was severe atheroma of the coronary arteries and the right coronary artery contained atheromatous debris on which was superimposed a recent (still red) thrombus for a distance of 2 cm. The myocardium of the posterior wall of the left ventricle and of part of the septum showed a diffuse extensive infarction. There was very advanced atheroma of the aorta and the mesenteric arteries. The uterus and ovaries appeared normal for her age.

On histological examination the thyroid was very small and weighed 3.8 g. It consisted practically entirely of fibrous tissue in which only occasional tiny islets of atrophic thyroid tissue were found.

The adrenals were of normal size (5.8 and 6.2 g.). The cortex contained only a moderate amount of lipid. The zona reticulata appeared slightly atrophic; there were a number of small hyperplastic nodules in the zona glomerulosa. The adrenal medulla contained numerous large Russell bodies and some of the medullary cells in the vicinity had very large nuclei.

The pituitary weighed 1 g. The general structure was normal, but many of the basophil cells contained small vacuoles. The proportion of the different types of cells was normal. The pancreas appeared normal and healthy on naked-eye and microscopic examination. Both ovaries showed senile atrophy with no trace of ova. Only one parathyroid was found. This showed normal histological appearances and had the usual islets of eosinophil cells.

Discussion

This was a case of primary myxoedema which

had progressed to the stage of hypothermic coma and the post-mortem findings were in accord with the clinical diagnosis, showing no evidence of preceding adrenal or pituitary abnormality.

The depression of adreno-cortical function as demonstrated by the 17 ketosteroids and 17 ketogenic steroids estimation on January 25 is a secondary effect (Statland and Lerman, 1950). It is generally accepted that adrenal cortex failure follows thyroid function failure (Hill, Reiss, Forsham and Thorn, 1950; Hubble, 1955) and the rapid elevation to normal levels of this patient's corticoid excretion after substitution therapy would tend to confirm this view and might also suggest that tri-iodo-thyronine is more active than thyroid sicca in restoring adrenal function. The normal serum electrolytes and blood glucose in this case emphasizes that the adrenal hypofunction was minimal; although electrolyte imbalance has been recorded in some cases of myxoedema coma (Summers, 1953; Le Marquand, Hausmann and Hemsted, 1953; Curtis, 1956), treatment with cortisone, thyroxine and heat did not produce a satisfactory response.

The many features of similarity in the clinical pictures of hypopituitary and myxoedema coma may lead to some difficulty in differentiation. In hypopituitary coma there is often a history of severe post-partum haemorrhage followed by amenorrhoea and loss of libido and the icthus is generally preceded by infection or trauma (Caughey and Garrod, 1954). It can also be classified into several relatively well-defined types, namely, hypoglycaemic, hypothermic or electrolyte imbalance/water retaining (Sheehan and Summers, 1952), and the treatment is to correct the pertinent abnormality.

The almost constant finding of hypothermia in myxoedema coma would suggest the application of heat to the patient. A heat cradle was used in this instance, but it has been shown that the elevation of body temperature in itself is insufficient to produce recovery, in contradistinction to its successful use in hypothermic hypopituitary coma (Sheehan and Summers, 1952). It is interesting to note that a case of myxoedema coma has been described in which the patient was febrile (Karhausen and Zylberszac, 1955).

Experience with 3-5-3'-l-tri-iodo-thyronine has demonstrated its potency in myxoedema (Gross, Pitt-Rivers and Trotter, 1952; Asper, Selenkow and Plamondon, 1953; Deltour and Bekaert, 1953; Lerman, 1954) and shown that whereas its short duration of action precludes routine use in hypothyroid patients (Frawley, McClintock, Beebe and Marthy, 1956), its rapidity of action makes it the logical therapy in myxoedema coma. 1,000 µg. of tri-iodo-thyronine given intravenously to a case

of myxoedema (Rawson *et al.*, 1953) was shown to raise the B.M.R. appreciably in seven hours and to exert its maximal effect in 24 hours, whereas l-thyroxine in a dose of 3 mg. I.V. produced a slight rise in the B.M.R. in 24 hours and a maximal effect in 11 days. A comparable rapidity in action has been noted with oral administration (Zondek, Leszynsky and Zondek, 1955).

Two reports of its use in myxoedema coma have appeared in this country and in both cases, despite some improvement, the patient died before attaining a euthyroid state (Dyson and Wood, 1956; Anderson and Hausmann, 1956). However, the efficacy of tri-iodo-thyronine in this condition has been amply shown by the response in this case. It is quite possible that either larger dosages or the use of the intravenous route may produce serious cardiac complications (Frawley *et al.*, 1956), such as auricular fibrillation, angina and congestive heart failure. In this case the cause of death was due to a coronary thrombosis and tri-iodo-thyronine therapy was not considered a contributory factor as the patient had been euthyroid on a maintenance dose of 20 µg. daily for a period of two weeks and post mortem demonstrated a recent thrombosis and infarct. E.C.G.s performed on January 23 and 24 showed a tendency to low complexes although by no means displaying a typical myxoedema record (but the patient had been on treatment for 12 and 36 hours respectively). A repeat record on February 14 showed changes suggestive of lateral infarction and sub-endocardial ischaemia.

In conclusion, it is suggested that cases of myxoedema coma be given tri-iodo-thyronine intragastrically and in relatively small doses. The use of heat may be beneficial. On the rare occasions when there is severe associated endocrine hypofunction as evidenced by electrolyte disturbance or hypoglycaemia the use of cortisone and intravenous glucose and saline would appear to be logical.

Summary

1. A case of myxoedema coma successfully treated with oral tri-iodo-thyronine is described.
2. The question of associated endocrine disturbance is discussed.
3. A regime of treatment for future cases is suggested.

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