THE SYNDROME OF MILD HYPOTHYROIDISM.

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Full blown hypothyroidism is well known and easily recognised as cretinism or myxoedema. It is not so well known, however, that there are a number of cases of hypothyroidism which do not show the full-fledged picture and are missed because the clinician does not think of hypothyroidism. Most of the cases described here were seen by various doctors and hypothyroidism was not suspected.

Dr. Lo Hong Ling (1956) has reported a typical case of myxoedema in which slow cerebration, hoarseness of voice, increase in weight, an enlarged heart in the radiogram, (a low BMR and) a typical electrocardiogram consisting of low voltage of QRS, flat T waves and bradycardia were prominent features. Most of these features were not present in the cases reported in this study.

The most comprehensive description of hypothyroidism is given by Means (1948) and the causes of hypothyroidism according to him are as follows:—

1) Absence of the thyroid—found only in cretinism.
2) Removal of the thyroid by operation.
3) Atrophy of the thyroid which may be
   a) primary
   b) the result of inflamation, or
   c) the result of the administration of anti-thyroid drugs.
4) Endemic goiter.
5) Exophthalmic goiter.
6) Posterior pituitary necrosis.

In athyreosis it takes 80 days for the full effect of removal to be seen and the blood cholesterol is directly proportional to the degree of thyroid deficiency and is therefore a better indication in cretinism than the BMR. In the full-fledged cases the administration of thyroid causes a diuresis and rapid subjective improvement becomes evident within ten days. Means states that hypothyroids are always good tempered, their speech is slow, low-pitched and ill-formed though sometimes they talk incessantly till forced to take a breath, and there may be effusions in any or all the serious sacs. There is myxoedema which does not pit on pressure due to the accumulation of mucin in the tissues (including the skin and the heart) and oedema which pits on pressure due to the accumulation of water. He gives a list of symptoms and signs which have been made the basis of this study. The administration of thyroid gr. 1½ daily causes a diuresis in 48 hours followed by marked subjective improvement and complete recovery in ten days except for the skin, the hair and the anaemia. He further points out that thyroid is a poison in Addison's disease, morphine and digitalis are poisonous in myxoedema and that Diabetes and angina pectoris are favourably influenced by myxoedema. There are according to Means different grades of cretinism but not of myxoedema and while the object of treatment in adult myxoedema should be to produce freedom from symptoms and not to produce a normal BMR it is essential in cases of cretinism and juvenile myxoedema that the BMR must be maintained at normal levels so as to allow for brain development.

Lawrence (1925) on the other hand describes thyroid failure without myxoedema and states that thyroid failure in adult life produces myxoedema, in intra-uterine life it produces cretinism and in adolescents a syndrome characterised by headache, malnutrition, loss of weight, tiredness, a normally moist skin, normal hair, defective hearing, depression, sterility, arteriosclerosis, a low sugar tolerance and a BMR just below minus 20%. These cases are usually diagnosed as neurasthenia. Lee (1925) described a group of young adults with persistent colds for more than three months who had a BMR between minus 5% and minus 20% and who were cured by the administration of thyroid. He considered that they were suffering from temporary hypothyroidism. Ohler and Ullian (1925) considered that mild hypothyroidism was not easy to diagnose and that it was characterised by obesity, general weakness, sensitivity to cold, dryness of the skin, retardation of mental processes and a BMR between minus 5% and minus 20%. Keys et al (1950) found considerable variation in the serum cholesterol of normal persons. Ninety per cent of normal males fell between the ranges given below for the different ages:—

At 18 the serum cholesterol varied from 118 to 219 mg/100 cc.

At 25 the serum cholesterol varied from 128 to 226 mg/100 cc.

At 35 the serum cholesterol varied from 128 to 272 mg/100 cc.

At 45 the serum cholesterol varied from 174 to 297 mg/100 cc.

At 55 the serum cholesterol varied from 180 to 332 mg/100 cc.

At 65 the serum cholesterol varied from 179 to 294 mg/100 cc.

At 75 the serum cholesterol varied from 148 to 276 mg/100 cc.

This would mean, for instance, that only 5% of normal men aged 18 may be expected to have values less than 118 mg per 100 ml. and only 5% of normal men aged 55 may be expected to have values above 332 mg per 100 ml.

Peters et al (1950) found that although the serum cholesterol is raised in outspoken uncomplicated hypothyroidism its concentration is not correlated with the degree of thyroid deficiency. Levitt (1954) described the seven ages of hypothyroidism as follows:—

1) Embryonal—absence of thyroid—genetic.
2) Foetal—Virus—maternal infection (Rubella)
   Sulphonamide and aspirin to mother.
   Thiouracil to mother.
3) Infantile—Congenital endemic cretin—not easily recognised at birth.
   Sporadic cretin is easily recognised at birth—X-Rays show stippled epiphyses of tibia and splintered head of femur.
4) Spontaneous adolescent hypothyroidism—continuation of unrecognised congenital process.
5) Acquired adolescent hypothyroidism—infection, trauma and thyroidectomy.
6) Spontaneous adult hypothyroidism.
7) Acquired adult hypothyroidism.

Asher (1955) has pointed out that myxoedema may present with a crisis and has described the occurrence of coma, psychoses, heart failure, intestinal obstruction, anaemia, and gall-stones. Young (1955) described weariness and absence of sweating. Fraser and Noordin (1955) described a case of myxoedema developing after thyrotoxicosis but the patient had been given methyl throuracil which might account for the myxoedema. Fraser and Garrod (1955) described the occurrence of myxoedema after postpartum shock or haemorrhage without pituitary dysfunction and Pathy (1955) described the occurrence of multiple serous effusions. Summers (1957) described uncommon presentations such as cold sensitivity, menorrhagia, leg pain and numbness, mental disorder and coma. Lloyd (1959) has drawn attention to the fact that the voice in myxoedema is characterised by alterations in quality such as low pitch or a nasal clotted quality, huskiness and harshness and by alterations in diction.

SCOPE OF STUDY AND RESULTS

Ten atypical cases of hypothyroidism have been studied and the results are tabulated below:

A diagnosis of hypothyroidism was made only if five out of the following nine features were present:—

1) Sensitivity to cold.
2) Constipation.
3) Falling out of hair.
4) Dryness of skin.
5) Alteration in pitch of voice.
6) BMR not above minus 10%.
7) ECG showing QRS less than 10 millivolts in each of the standard limb leads.
8) Rapid response to treatment.
9) Cardiothoracic ratio greater than half.

Symptoms	
Gain in weight	8 cases
Impairment of memory	8 cases
Lack of sweating	8 cases
Falling out of hair	7 cases
Lethargy	7 cases
Insomnia	6 cases
Sensitivity to cold	4 cases
Constipation	4 cases
Weakness	4 cases
Menorrhagia	4 cases
Somnolence	2 cases
Alteration in texture of skin	2 cases
Signs	
Oedema of legs	9 cases
Neurosis	9 cases
Dryness of skin	7 cases
Loss of hair	5 cases
Pallor	5 cases
Thickening of skin	4 cases
Slowness of speech	4 cases

Low pitch of voice	3 cases
Mental changes	2 cases
Slurring of speech	1 case

Laboratory findings.

Systolic blood pressure varied from 95 to 180.

Diastolic blood pressure varied from 60 to 120.

Urine—no albumin or sugar was found in any of the 10 cases.

Blood cholesterol varied from 160 to 330 mg per 100 cc.

BMR varied from minus 11% to minus 32%.

Cardiothoracic ratio on the radiogram was less than half in all except in 3 cases.

Electrocardiogram.

Voltage of QRS in the standard limb leads was less than 10 millivolts in all the 10 cases. Voltage of T in the standard limb leads was less than 3 millivolts in all the 10 cases. The T wave was inverted in aVF in 1 case. The T wave was inverted in aVF, V_4, V_5 and V_6 in 1 case.

DISCUSSION

The following interesting features were present in the cases presented here:—

1) The manner of presentation was often atypical and resembled that of an anxiety neurosis, e.g. insomnia, impairment of memory, giddiness, headache and palpitation.

2) Etiological factors.

Severe bleeding shortly preceded the onset of illness in three cases, one from post-partum haemorrhage, one from miscarriage and another from dental extraction, and in two cases thyroidectomy had been performed. In the other five cases, no causative factor could be found. In one case sulphonamides had been used excessively but this patient also had a miscarriage with severe bleeding antedating the illness.

3) Gain in weight.

Two cases had lost weight and treatment brought about an increase in weight.

4) Oedema of the legs with definite pitting on pressure occurred in nine cases. The usual statement that the oedema of myxoedema does not pit is only true in that when the swelling is due solely to the accumulation of mucin in the tissues there is no pitting but often there is accumulation of water in the tissues and pitting is present. In fact one of the earliest and most reliable signs of recovery is a brisk diuresis and the disappearance of pitting oedema.

5) Painful localised swellings in the legs occurred in one case and biopsy showed the swellings to consist of an accumulation of mucin in the tissues.

6) Diarrhoea occurred in one case contrary to the usual history of constipation.

7) Peculiar reaction to drugs occurred in 3 cases (see case reports).

CASE REPORTS

Case 1 (Ref. No. 28715).

A female Ceylonese, aged 50 years, c/o a shivering sensation beginning in the praecordial region and spreading throughout the body for two years and a feeling of general weakness. She had marked pitting oedema of the legs, the blood pressure was 95/60, the blood cholesterol 250 mg. per 100 cc, the BMR minus 21% and the electrocardiogram showed QRS to be not more than 6 millivolts and T wave not more than 2 millivolts in the standard limb leads with T inversion in III. The cardiothoracic ratio on the radiogram was less than 0.5. She was unable to take ordinary thyroid tablets but reacted rapidly to thyroid emplets.

Case 2 (Ref. 25758).

A female Chinese, aged 48 years, had thyroidectomy performed for thyrotoxicosis. One year later she began to have localised swellings in the legs which were red, painful and itchy and recurrent. She was somnolent and had pitting oedema of the legs. She had localised, hard swellings in the legs and feet and the skin was dry and thickened. The blood pressure was 135/90, a twelve lead electrocardiogram was normal except that the QRS voltage was not above 8 millivolts and the voltage of the T wave was not above 1 millivolt in the standard limb leads. The blood cholesterol was 200 mg per 100 cc, the BMR minus 24% and the cardiothoracic ratio less than 0.5. A biopsy of one of the localised swellings showed that it consisted essentially of mucin and was considered by the pathologist to show the changes of circumscribed myxoedema. She responded rapidly to the administration of gr. iii of thyroid daily but the leg swellings did not recede. In fact after a year the swellings suddenly grew worse. It was suspected that the ordinary thyroid tablets had lost their potency and she was put on thyroid emplets gr iii daily with improvement. The leg swellings though they partly receded on thyroid emplets continued to exist and an attempt to raise the dosage of thyroid produced symptoms of thyrotoxicosis.

Case 3 (Ref. No. 25771).

A female Chinese, aged 45 years, complained of giddiness, headache and insomnia for six months. She had loss of weight and impairment of memory, her hair was falling out and she was unduly sensitive to cold. Her blood pressure was 170/100 and the electrocardiogram showed QRS below 8 millivolts and T below 2 millivolts in the standard limb leads. The blood cholesterol was 200 mg per 100 cc, the BMR minus 13% and the cardiothoracic ratio was 0.5. She improved on treatment although the administration of thyroid at first produced diarrhoea.

Case 4 (Ref. No. 26040).

A male Chinese, aged 28 years, had a thyroidectomy done for thyrotoxicosis. Three years later he began to have attacks of praecordial pain lasting 5 to 10 minutes. He also complained of insomnia and impairment of memory. He had oedema of the legs. His blood pressure was 130/80, there was albuminuria and the electrocardiogram showed QRS to be not more than 8 millivolts and T not more than 2 millivolts in the standard limb leads. The blood cholesterol was 250 mg per 100 cc, the BMR minus 17% and the cardiothoracic ratio 0.5. He had a brisk diuresis following the administration of thyroid and the oedema of the legs disappeared but he did not attend for further treatment.

Case 5 (Ref. No. 26075)

A male Indian, aged 48 years, suffered from asthma and other allergic manifestations for 25 years; also palpitation, headache, pain in the legs and nasal obstruction. He had constipation for three years, was deaf, could not stand cold weather, did not sweat at all and was getting bald. He had been gaining weight, had marked impairment of memory and insomnia. His legs were oedematous, the skin was dry and he had early bilateral cataract. The blood pressure was 180/120, the haemoglobin 70%, the blood cholesterol 329 mg per 100 cc, the BMR minus 17% and the electrocardiogram showed QRS to be not more than 9 millivolts and T not more than 2 millivolts in the standard limb leads and there was inversion of T in aVF and III, the QRS complex being mainly upward. The cardiothoracic ratio was less than 0.5 Administration of thyroid brought about a dramatic recovery.

Case 6 (Ref. No. 26078)

A female Chinese, aged 45 years, had recurrent pyelitis for 14 years for which she had received numerous courses of sulphonamides. She had a miscarriage with excessive bleeding seven years previously. She complained of pain in the lumbar region and increasing weight due, she said, to retention of water—she could feel her skin tense. She had noticed increased falling out of her hair and her skin which had been dry since childhood had recently become drier. There was marked pitting oedema of the legs, her blood pressure was 125/80, the electrocardiogram showed QRS to be not more than 8 millivolts and T not more than 3 millivolts, in the standard limb leads, the blood cholesterol was 200 mg per 100 cc and the BMR minus 22%. The administration of thyroid brought about rapid improvement. She was sensitive to many drugs including morphine, anti-tetanic serum and adrenaline.

Case 7 (Ref. No. 26464)

A female Chinese, aged 34 years, complained of palpitation and tiredness for seven years, insomnia, constipation, and loss of weight. She was pale, there was oedema of the legs, the blood pressure was 120/80, the electrocardiogram showed a maximum voltage of QRS of 9.5 millivolts and flat or negative T in the standard limb leads. There was T wave inversion in II, III, aVF, V_4, V_5 and V_6. There was no evidence of any cardiac lesion to account for the electrocardiographic changes. The blood cholesterol was 200 mg. per 100 cc, the BMR minus 11% and the cardiothoracic ratio less than 0.5. She was put on thyroid but unfortunately did not continue treatment so that the effect of thyroid medication is not known.

Case 8 (Ref. No. 26104)

A female Chinese, aged 37 years, had protracted ante-partum haemorrhage. One year later she complained of giddiness. She was pale, she talked very slowly and with deliberation as if it required a great effort, and had menorrhagia. Her voice was low pitched and she had psychotic symptoms for which she had been admitted to a mental hospital. The blood pressure was 110/80, the electrocardiogram showed a maximum voltage of QRS of 5 millivolts and T of 1.5 millivolt in the standard limb leads and T inversion in III. The blood cholesterol was 160 mg per 100 cc, the BMR minus 22% and the cardiothoracic ratio less than 0.5. Administration of thyroid at first brought on diarrhoea but subsequently considerable improvement. Unfortunately she did not continue her treatment.

Case 9 (Ref. No. 17692)

A female Ceylonese, aged 41 years, presented a variety of symptoms which were labelled neurotic for many years until she developed

marked pitting oedema of the legs. The electrocardiogram showed a maximum QRS voltage of 6 millivolts and T of 1 millivolt in the standard limb leads, the haemoglobin was 76% the blood cholesterol 200 mg per 100 cc and the BMR minus 32%. Thyroid administration caused rapid improvement. She collapsed after an injection of ATS with fall in blood pressure and shallow respiration and had to be resuscitated with injections of adrenaline and coramine.

Case 10 (Ref. No. 25098)

A female Chinese, aged 55 years, complained of giddiness, headache, anorexia, constipation, loss of weight, insomnia and feeling unduly cold. Her eyelids were puffy, the skin was dry, the voice was low-pitched, she was pale and had pads of fat in front of the neck. The blood cholesterol was 160 mg per 100 cc, the BMR minus 10% and the cardiothoracic ratio less than half. The blood pressure was 120/80 and the electrocardiogram showed a maximum QRS voltage of 8 millivolts and T of 1.5 millivolt in the standard limb leads. She improved rapidly on thyroid and felt so well that she discontinued treatment but returned two months later with a recurrence of symptoms. She required gr. iii daily to keep well. A peculiar feature of the case was that she felt sick after injections of vitamin B_1 (intravenous) and penicillin (intramuscular) but not after injections of vitamin B_{12}.

SUMMARY

Ten cases of mild hypothyroidism are described. They were difficult to diagnose because they had unusual presenting symptoms and did not follow the typical pattern of myxoedema. Some patients presented with insomnia instead of somnolence, loss of weight instead of gain in weight, diarrhoea instead of constipation; there was pitting oedema in all but one case. the BMR was higher than minus 25% in nine cases, and the electrocardiogram did not show the accepted features of bradycardia, QRS voltage of below 5 millivolts in the standard limb leads and flat or inverted T waves. Because of the unusual manner of presentation the diagnosis was often missed. If the index of suspicion is raised then more such cases will be correctly diagnosed.

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