# Occult (Masked) Thyrotoxicosis with Supraventricular Arrhythmia and Hypertension

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The clinical diagnosis of hyperthyroidism is not always obvious in elderly patients in which supraventricular arrhythmia especially atrial fibrillation may be dominant feature in the absence of goitre, classical eye signs and other signs of thyroid hormone excess.

Clinican may find some clues such as proximal myopathy, palmar erythema, failure of diagoxin to slow the ventricular rate without the addition of beta blocker. The interpretation of confirming biochemical test of thyroid function may present difficulties if we rely solely on measurement of the serum total triiodothyronine (T3) and thyroxin (T4).

Many other illnesses: Cardiac failure or pneumonia and drugs e.g. betablockers, anticonvulsant, antirheumatic agent may produce a fall in the total thyroid hormone concentrations and in patients with mild hyperthyroidism, reduction of these concentrations may amount to normal limit. In susceptible person thyroid hormone in normal range, may be sufficient to trigger the onset of supraventricular arrhythmia: Paroxysmal tachycardia or atrial fibrillation. The relative frequency of hyperthyroidism should be kept in mind affecting 10% of the population and may coexist with ischaemic and rheumatic heart disease (Tunbridge et al 1971) and Hypertension (Bisgard 1939). Lone atrial fibrillation develops in 10-15% with overt hyperthyroidism and is the most common in those aged over 60 (Sandler & Wilson 1959).

## CASE REPORTS

### Case – 1.

An employee aged 59 a known hypertensive (BP 160/100) was seen on 14-12-1980 at the PSPC Medical Centre with the complaint of loss of weight with good appetite, warm limbs and felt less cold in Winter, Sweating with fine tremors of outstreteched fingers since past many years.

On examination pulse rate was 150 p.m. regular rhythm. B.P. 180/80 mm Hg. warm limbs, moist palm with tremors on outstretched fingers without thyroid goitre or eye signs. In winter season he did not use blanket and felt less cold and enjoyed winter in cotton clothes.

INVESTIGATIONS :

T4=10.2 ug.% (normal 3.4 – 9.7 ug%) cholesterol 185 mg%, Triglycerides 95 mg%, random blood sugar 130 mg., routine urine and routine bloodtests were normal. X-ray chest was within the normal limit.

Masked thyrotoxicosis was diagnosed and was put on antithyroid drug neomercazole tablets 5 mg. three times a day. He was evaluated on 22-12-22-12-1980. The pulse was 130 p.m., B.P. 170/80 mm. Hg. and felt little better in tremors and warm feeling. On 27-12-1980 his BP was 160/80 mm. Hg. and pulse was 80 p.m. Propranolol 40 mg. twice a day was added to control hypertension. On 4-1-1981 his BP was 140/80 mm. Hg. and felt much better: body heat, warm limbs and tremors subsided.

He defaulted treatment of hypertension and antithyroid drugs and reappeared on 12-5-1980 with complaint of pain right lower chest and right hypochondrium. X-ray chest showed right pleural effusion. On examination the liver was tender and enlarged – Amoebic hepatitis was diagnosed and he was put on Metronidazole 400 mg. three times a day for 10 days.

As his B.P. was 160/100 he was put again on Propronolol 40 mg. T.D.S. and Neomercazole tablets 5 mg. three times a day. On 31-5-1981 X-ray chest was normal.

He defaulted regular antithyroid treatment and was seen on 5-7-1981 with relapse of thyrotoxic signs and symptoms: palpitation, tremors and heat in body – His pulse was 150 p.m. and

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B.P. was 170/80 mm. Hg. He was put again on Neomercazole and Propronolol regime. On 19-8-1981 his BP was 130/80. His thyrotoxicosis and B.P. were well controlled and his propranolol was reduced to 10 mg. twice a day and Neomercazole was discontinued. He was untraceable for further follow up as he was retired and went up to north country on 18-10-1981.

COMMENTS :

The case had masked thyrotoxicosis and the brunt of the disease felt on the heart, presenting with supraventricular arrhythmia. The clinical signs and symptoms responded well to antithyroid drugs and relapsed after defaulting treatment by the patient and was controlled again with the antithyroid drugs.

The association of systolic hypertension is a coincidence and not related to thyrotoxicosis because in the state of controlled thyrotoxic symptoms his blood pressure was still high which was controlled on addition of Propronolol. In some group of cases systolic and diastolic hypertension is associated but there is little evidence of any direct relation between two diseases and blood pressure does not fall after thyroidectomy (Bisgurd 1939). In this case blood pressure was high even before the onset of thyrotoxic symptoms.

Case – 2.

One of the cases of thyroid disease aged 30 years was seen on 18-2-1964 at the thyroid disease cell of this centre, who was found suffering from acute thyrotoxic adenoma with cardiovascular symptoms: pulse 140 p.m. B.P. 140/6-. Radioactive: iodine $T^{131}$ uptake confirmed the diagnosis of thyrotoxicosis (Courtesy JPGMC Radioisotope Unit). He was put on Neomercazole, 5 mg. T.D.S. on 25-2-1964 and stopped on 31-8-1964 as he was under remission. His signs and symptoms abated and pulse was 80 p.m.

On 18-9-1964 follow-up examination showed signs and symptoms of recurrence with marked tachycardia and was referred to JPGMC radioisotope Unit for $T^{131}$ therapy. On 3-10-1964 he was given a safe and effective dose of radioiodine. He was well again and the thyroid gland regressed with remission of signs and symptoms and remained euthyroid till 14th October 1965 when he showed a second relapse of the disease state. Now $T^{131}$ uptake test and JPGMC showed euthyroid state on 3-4-1966. Tachycardia up to 140 p.m. and signs and symptoms of hormone excess in blood were present. Wait and watch policy was observed as there was no improvement, eventually, on 1-5-1966 he was put again on Neomercazole 5 mg. T.D.S. in spite of euthyroid gland on $I^{131}$ uptake with clinical signs of relapse.

He responded to the second course of Neomercazole and his disease was well controlled on 4-1-1967 and the drug was continued for further 6 months. He had no further relapse till 1984 during long follow up of nearly 20 years. There was no evidence of carcinoma and indefinite follow up is necessary for evaluation. For assessment of hypothroidism, on 11-8-1984, T3 and T4 was estimated and laboratory findings showed T4=2.0 ug/100 ml and T3=0.65 ng/dl suggestive of hypothroidism and he was put on thyroxin regime.

Addition of thyrotrophin releasing hormone test to T3, T4, more cases of masked thyrotoxic can be diagnosed with confidence.

COMMENTS :

The clinical sequence of events in this case suggest that when radioactive iodine therapy is considered, this treatment should be delayed untill several months after antithyroid therapy is begun to allow depletion of thyroid hormone in the gland. This will prevent post $T^{131}$ therapy release of large amount of hormone in the blood. Thus avoiding a serious insult to the already maligned heart. Now this principle is being observed all over the radioisotope and cardiac units.

One can assume that in this case the post-Neomercazole and radio iodine therapy relapse may be due to insufficient dose of Neomercazole (15 mg daily) for a insufficient period.

Case – 3.

An employee aged 35 was seen on 22-7-1984 with complaints of loss of weight with good appetite, paroxysmal rapid beating of the heart, warm limbs and heat in the body since past over 12 months.

On examination he had mild retraction of eye lids with staring look, fine tremors of outstretched fingers, warm limbs and no thyroid gland enlargemen in the neck.

His resting and sleeping pulse was 130 p.m. ECG showed no abnormalities. B.P. 130/70 and

systemic examination was within normal limit.

## INVESTIGATION .

Blood and electrolytes profile was normal. Random blood sugar 100 mg./100 ml. X-ray chest and urine analysis revealed no abnormalities special tests (a) Tri-iodo 12.0 ug/100 ml. (N-11.5 ug/100 ml) (b) Thyroid microsomal antibodies test was positive.

In view of the above clinical and laboratory findings and raised thyroid autoantibodies masked thyrotoxicosis with supraventricular tachycardia was diagnosed and he was put on Carbimazole (Neomercazole) 15 mg. three times a day.

On 13-9-1984 review examination showed appreciable improvement in his cardiac status with pulse fallen to 80 p.m. B.P. 130/80, eye signs improved and felt less heat in the body. Repeat thyroid Miscrosomal thyroid antibodies test was negative.

Follow up review examinatin on 27-9-1984 showed normal cardiac rhythm but lids retraction were still there. Biochemistry showed tri-iodothyronine T3 0.4 ng/dl, (N:0.8-1.6 ng/dl) and thyroxin T4 2.0 ug/100 ml: (N=5-11.5 ug/100 ml) confirmed that carbamizole had suppressed serum T3 and T4. He was put on regular follow-up adjusting dose according to the clinical and biochemical findings.

## COMMENTS :

Presence of thyroid autoantibodies and associated supraventricular tachycardia with other thyrotoxic clinical manifestations even without thyroid gland enlargement suggested thyrotoxicosis. An interesting observation that will be discussed later was a fall in the antibody fibre in this case.

## DISCUSSION :

The diagnosis of hyperthyroidism is difficult in elderly cases in absence of goitre, eye signs and other clinical manifestation of hormone excess. In the presented cases some signs of hormone excess were present. In some cases thyroid hormone within high normal range may be sufficient to trigger the onset of cardiac arrhythmia in susceptable persons. In such cases hyperthyroidism should not be excluded as a cause and so in unexplained or "lone" atrial fibrillation or tachyarrythmia without thyrotrophin releasing hormone test (in absence of hypopituitarism a blunt response of serum thyroid stimulating hormone after intravenous administration of 200 ug thyrotrophin — releasing hormone).

Recently serum angiotensin-converting enzyme levels as an index of thyroid hormone function in severe systemic illness have been evaluated by Brent, Jerome and Hershman et. al 1984. Their study revealed that angiotension-converting enzyme levels was elevated in hyperthyroid patient (37.3+3.2 U/ml) compared with normal control (17.9+1.4 U/ml). Previous workers = Yotsumoto et al (1982) and smallridge et (1982) had also shown that levels of serum angiotensinconverting enzyme are increased in hyperthroidism, parallel thyroid activity in hyperthyroid patients after treatment and are normal to low in hypothyroidism (Nakamura et al 1982, Smallridge et al 1982). The most profound depression was found in patients with adult respiratory distress syndrome with sepsis (Case et al 1981) because of damage to the vascular endothelial cells, that contain enzyme, decreased values have been found (Casey et al 1981, Bedrossian et al 1978). These studies support angiotensin-converting enzyme level as an index of thyroid function. The sick low-thyroxin group had serum angiotensin enzyme level significantly below those in the normal group and hypothyroid group and suggest that thyroid hormone activity at tissue level is reduced in severe systemic illness (Brent et al 1984).

Throid hormones have positive chronotropic and inotropic effects on the heart with the result in rise of heart rate and cardiac output. The maximum velocity of fibre shortening (Merrillon et al 1981) and myocarial excitability increases (Freedberg et al 1970), circulating blood volume expands (Gibson et al 1939) and pulse pressure widens (Degroot et al 1970). Recent view is that heart in hyperthyroidism has an increased density of adrenoceptors (Ciaraldi 1977) and the concept of increased circulating catecholamine concentration or increased sensitivity of the heart to catecholamine induced by thyroxin is no longer considered (Levy 1971) as a mechanism.

The only satisfactory way of restoring myocardial function is to restore raised serum hormone concentration normal as quickly as possible with anti thyroid drugs, surgery or radioiodine as appropriate to patient age, size of the goitre and cardiac state. Treatment with beta blocker alone is not satisfactory and seldom provides complete

control of symptoms and has low remission rate and fails to influence myocardial contractivity (Forfar et. al. 1979 & 1982).

Atrial fibrillation develops in 10-15% case of hyperthyroidism in those aged over 60 and is thought to be due to shortened duration of action potential which increases the electrical excitability within the atria and predisposes to arrhythmia (Freedberg et al 1970). Patients who fail to revert early to sinus rhythm with treatment, careful consideration should be given to the use of anticoagulants, as risk of thromboembolism is reportedly great in hyperthyroid atrial fibrillation.

Recent observations suggest that antithyroid drugs have a direct action on auto antibodies — Thyroid microsomal antibodies levels during treatment fall with carbimazole, while serum thyroxin and thyrotrophin levels did not change (McGregor & Peterson et al 1980). The recent studies suggest (McGregor & Ibertson et al 1980 and Mukhtar et al 1975) that Carbimazole may act directly on autoantibody synthesizing lymphocytes localised in the thyroid glands or indirect effect of antithyroid drugs on the autoimmune process (Pinchera et al 1969). McGregor and Ibertson et al (1980) have demonstrated that serum microsomal antibody level fell in nine of 10 patients with Hashimoto's thyroiditis with carbimazole 45 mg. daily. The fall was maximal after 9 weeks while serum thyroxin and thyrotrophin — hormone levels did not change although 2 patients showed two fold increase in serum thyrotrophin levels after 9 weeks treatment with carbimazole. There was an increase of the antibodies level after discontinuation of carbimazole in three patients and the level remained unchanged in six and decreased in one.

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