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Mania Secondary to Thyrotoxicosis

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A case of severe mania due to thyrotoxicosis responded to propranolol and propylthiouracil.
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Pathological mental change in thyrotoxicosis was recognised a long time ago (Whybrow & Prange, 1981). While anxiety symptoms are familiar, the reporting of psychosis and its treatment has been limited.

Case report

A 29-year-old previously normal Chinese housewife presented with a ten-day history of progressive irritability, irrelevant speech and loss of sleep. Apart from a gradual loss of body weight of 10 kg over the past one to two years, no history of other thyrotoxic or psychiatric symptoms was reported. On admission, she was thin (38 kg, 162.5 cm tall), restless, irritable, disinhibited, distractible and overly talkative, with loosening of association and fleeting auditory hallucinations.

She had hyperdynamic circulation, with resting sinus tachycardia (120/min), warm moist hands and a small diffuse goitre. A diagnosis of manic psychosis secondary to thyrotoxicosis was made. Investigations confirmed Graves' hyperthyroidism: sensitive TSH <0.02 mIU/l (normal 0.3–4.0), free T3 >40 pmol/l (normal 3.3–8.2), free T4 >67 pmol/l (normal 7–21.8), and thyroid antibodies were positive and a thyroid ultrasonogram revealed a diffuse toxic gland.

After informed consent was obtained, an 'ABAB' experimental design was used to investigate the patient's response to beta-blockade (days 5–9), its withdrawal (days 10–14), readministration (day 15 onwards) and antithyroid drug treatment. Five-day intervals were chosen in view of the short half-life of propranolol (3–4 hours) and the ethical problems associated with prolonged drug withdrawal. Apart from clinical diagnoses (according to DSM-III-R criteria; American Psychiatric Association, 1987), rating scales were used for assessing her thyrotoxicosis, mania, anxiety, general functioning and ward behaviour rated by nurses (see Table 1). It was found that the use of propranolol (20 mg t.d.s.) alone led to significant improvement of her symptoms over three days (without significant change in thyroid hormone status), while re-emergence of severe manic symptoms soon followed its withdrawal. Readministration again led to remission of mania, although mild anxiety symptoms persisted. With antithyroid drug therapy (propylthiouracil 100 mg t.d.s.) she became clinically and biochemically euthyroid in two months.

Table 1
Patient's response to drug therapy

	Baseline	Propranolol	Off propranolol	Propranolol	Propyl-thiouracil
Day	4	9	14	19	180
HSS[1]	19	7	15	6	0
MRS[2]	38	8	32	4	0
HRSA[3]	28	15	27	14	2
GAS[4]	21	80	15	70	85
NOSIE[5]	33	5	41	1	-
Clinical diagnosis	Mania	Generalised anxiety disorder	Mania	Generalised anxiety disorder	Well

1. HSS: Hyperthyroid Symptom Scale (range 0–40, euthyroid <5), (Klein *et al*, 1988).
2. MRS: Mania Rating Scale (range 0–60) (Young *et al*, 1978).
3. HRSA: Hamilton Rating Scale for Anxiety (range 0–56) (Hamilton, 1959).
4. GAS: Global Assessment Scale (range 0–90) (Endicott *et al*, 1976).
5. NOSIE: Nursing Observation Scale for In-patient Evaluation (range 0–129) (Honigfeld *et al*, 1966).

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No psychotropic medications were used. At nine-months follow-up, when kept on propylthiouracil (50 mg/day), she weighed 50 kg and was well.

Discussion

The evidence for thyroid state playing a role in mood disorders has increased rapidly in recent years. Clinical manifestations of hyperthyroidism are generally believed to be due to a synergistic interaction between increased serum levels of thyroid hormones and excess catecholamine stimulation. Whybrow & Prange (1981) hypothesised that thyroid hormones modulate central adrenergic response to catecholamines in a manner analogous to that in peripheral tissues. Accordingly, hyperthyroidism is believed to augment the ability of beta-adrenergic receptors to receive stimulation by noradrenalin, and predisposes an individual to mania in accordance with the catecholamine theory of mood disorders. This state of supersensitivity may have developed in this patient because of the delay in treatment of her obscure thyroid disorder. The sequence of rapid mental changes suggests central adrenergic blockade by propranolol, which readily penetrates the brain. The presence of residual symptoms which only cleared after antithyroid drug therapy indicates that the therapeutic effect of beta-adrenergic blockade by propranolol was incomplete. Full recovery required the addition of propylthiouracil, which acts more slowly by inhibiting the synthesis of thyroid hormones.

Despite the obvious limitations of a single-case study, this case underscores the clinical importance of carefully excluding hyperthyroidism in psychotic patients. Even though very large doses of propranolol (200–2000 mg) have been suggested for effective antimanic therapy (Whybrow & Prange, 1981), Chinese people may be more sensitive to the drug (Zhou *et al*, 1989), and a relatively low dose may be sufficient for considerable control of symptoms before antithyroid drug therapy takes its full effect. Being lipid-soluble, propranolol may be superior to other beta-blockers which have a selective peripheral action, especially in hyperthyroid patients with conspicuous mental symptoms.

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'Ecstasy' Psychosis and Flashbacks

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We report three cases of flashbacks and one case of recurrent psychosis experienced by three MDMA users. We draw the attention of clinicians to the combination of adverse effects observed with this drug of abuse and to the advisability of prolonged treatment should they occur.
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Methylenedioxymetamphetamine (MDMA) is a derivative of 3,4,methylenedioxyamphetamine (MDA) and classed as a hallucinogenic amphetamine (Gilman *et al*, 1985). As such it is controlled under Class A of the Misuse of Drugs Act 1971. Anecdotal reports of the effects of MDMA in low doses speak

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