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Graves' disease presenting with hypomania and paranoia to the acute psychiatry service

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SUMMARY

This manuscript describes the case of a young woman, with no prior psychiatric history, who developed hypomania and paranoia as the principal presenting features of Graves' disease. After starting treatment with carbimazole and propranolol, symptoms resolved without the use of antipsychotic drugs. Close liaison between psychiatry and endocrinology services was essential. This demonstrates that treating underlying thyrotoxicosis in patients presenting with psychiatric symptoms may lead to recovery without the use of antipsychotic medication. While agitation, irritability and mood lability are well-recognised thyrotoxic symptoms, psychosis is a rare presenting feature of Graves' disease. All patients with agitation, delirium or psychiatric symptoms should have thyroid function checked as part of initial tests screening for organic disease. In new or relapsing psychiatric conditions, it is important to ask patients, their carers or relatives about symptoms of hypothyroidism or thyrotoxicosis.

BACKGROUND

The link between psychiatric disturbance and thyrotoxicosis was first described by von Basedow in the 19th century.¹ Although overt psychotic features are not often seen in patients with thyrotoxicosis, it is important to recognise the phenomenon. It is very rare for psychosis to be the presenting symptom of Graves' disease.² The estimated incidence of psychosis as the presenting feature of Graves' is 1% according to a New Zealand-based case series.³ Equally it is rare for thyrotoxicosis to be the underlying cause of a new psychiatric presentation.

Initiation of thionamides plus beta-blockade to treat agitation, anxiety and sympathomimetic symptoms is of paramount importance. While patients presenting with hypomania often receive treatment with antipsychotic medications, when thyrotoxicosis is the cause of mental health deterioration, treatment with thionamides with or without beta-blockers may be all that is required.⁴ Those patients who have antipsychotics administered as primary treatment may be misdiagnosed or left on long-term antipsychotic medication inappropriately.⁵ Nevertheless, there will be situations where management of psychosis requires a combination of antipsychotic therapy and thionamide drugs.⁶

CASE PRESENTATION

A 32-year-old woman was brought to the accident and emergency (A&E) department by her husband in June 2019, as she had demonstrated increasingly erratic behaviour over the previous 6 months.

In the 4 months prior to presentation, she had been sleeping for only 2–3 hours per night on the family sofa and eating only one meal per day. She had lost 15 kg in weight and had developed palpitations. Her thoughts were racing, and while she spent long hours working, she was unfocused and less productive than normal. She had developed paranoid ideas, reporting to her husband that she was receiving messages from her mobile telephone directly into her brain, despite it being turned off. She had been feeling increasingly anxious, which was attributed to 'stress' and financial difficulties. She was finding it more difficult to look after her 16-month-old child; at the peak of her symptoms, her husband found her wandering around the kitchen and placing spoons in the fridge. She was previously fit, never smoked and was not on any regular medication. There was no family history of thyroid disease. She works as an inclusion manager in a primary school, with responsibility for children with special educational needs.

The situation reached a crisis point 3 days prior to attendance, when she was asked to leave work. Her husband arranged an appointment with their general practitioner the next day. The patient was suspicious of her husband's insistence that she see a doctor and asked him to wait outside during her consultation with the general practitioner (GP). Symptoms were initially diagnosed as 'anxiety', but as symptoms progressed she was referred to acute psychiatry services and was seen in the A&E department. When assessed by the liaison psychiatry nurse, the patient was easily distracted, with intermittent eye contact and was agitated, pacing around the room. There was pressure of speech, but no hallucinations or thoughts of self-harm. The patient expressed paranoid ideas, but these were not held with delusional intensity. Blood tests were performed to help exclude biological causes of acute psychosis: she was referred to the medical team on call as blood tests revealed that she was markedly thyrotoxic.

When she was assessed by the medical team, routine observations found her to be apyrexial at 36.7°C, and tachycardic at 120 beats per minute. She was hypertensive with blood pressure 162/85 mm Hg and had a slightly elevated respiratory rate of 23 breaths per minute. She had a visible and palpable smooth goitre; there was no tremor and she had lid lag but no evidence of thyroid eye disease, nail disease or skin changes of Graves' disease.

INVESTIGATIONS

Blood tests in the A&E department showed no abnormality apart from thyrotoxicosis with thyroid



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stimulating hormone (TSH) <0.01 mU/L (reference range 0.3–4.2 mU/L); free thyroxine (T4) 97.5 pmol/L (reference range 12–22 pmol/L) and the free triiodothyronine (T3) level was 32.3 pmol/L (reference range 3.1–6.8 pmol/L). Full blood count, C reactive protein, urea and electrolytes and liver function tests were normal.

Three days after discharge, a thyroid Technetium-99m uptake scan demonstrated scintigraphic findings consistent with Graves' disease, with uptake of 18.1% (reference range 1.6%–2.2%). There was uniform increased tracer uptake in the thyroid gland. TSH receptor antibody results came back 2 weeks after the A&E attendance and were positive at 5.6 IU/L (normal value <0.9 IU/L), confirming the diagnosis of Graves' disease.

DIFFERENTIAL DIAGNOSIS

Graves' disease with onset 10-month postpartum was the most likely diagnosis given her age, the length of the history, a non-tender goitre and a normal raised C reactive protein. The differential diagnosis prior to the technetium scan and antibody results being available included a transient 'thyroiditis' and solitary toxic thyroid nodule. A thyroiditis was unlikely in the context of a normal C reactive protein and such a long history of symptoms. Solitary toxic thyroid nodules are usually palpable and are less common than Graves' disease. A toxic multinodular goitre usually occurs in older patients. There was no history of an iodine load as a cause of thyrotoxicosis.

After the technetium scan, which often distinguishes Graves' from the other causes of thyrotoxicosis, the diagnosis was not in doubt. The finding of raised TSH receptor antibodies gave final confirmation of the diagnosis of Graves' disease.

TREATMENT

She was initiated on carbimazole 40 mg once daily and propranolol 40 mg three times per day. As she had a supportive family, she was discharged from the A&E department after review by the medical team on call. The opinion of the psychiatry team was that she did not require antipsychotic therapy or anxiolytics (apart from a beta-blocker which was prescribed by the medical team). As she had a young child, the community psychiatry crisis team kept her under close review.

After 4 weeks, carbimazole was reduced to 20 mg once daily as free T4 and free T3 levels had fallen into the normal range, measuring 13.4 pmol/L and 4.4 pmol/L, respectively. Propranolol was reduced to be taken 'as required' if she was feeling anxious or experiencing palpitations. Eight weeks after the initial diagnosis, thyroid function was stable with free thyroid hormones in the normal range and carbimazole was reduced to 10 mg once daily.

After resolution of thyrotoxicosis, in view of the severity of the presenting symptoms, the option of primary definitive treatment was discussed: radioiodine was contraindicated as she had a young child; thyroidectomy was offered but she preferred to remain on medical treatment. When thyroid levels stabilised, she was switched from carbimazole to propylthiouracil as she was planning to conceive again.

OUTCOME AND FOLLOW-UP

Physical symptoms of thyrotoxicosis, along with paranoid ideation and anxiety, gradually dissipated over the first 8 weeks of carbimazole treatment. At clinic review, 8 weeks after starting carbimazole, she was both biochemically and clinically euthyroid: she reported a complete return to her normal mental state, which was corroborated by her partner. At that stage, the

community psychiatry crisis team discharged her from their care and she was assessed by an occupational health physician. She began a phased return to work 3 months after the initial attendance.

Thyroid function was stable on propylthiouracil 100 mg once daily—9 months after the initial diagnosis, propylthiouracil was reduced to 50 mg once daily but, 1 month later, she developed subclinical thyrotoxicosis and propylthiouracil was increased back to 100 mg once daily and maintained at that level. At the time of writing, 15 months after the initial diagnosis of Graves' disease, she remained well and was in the first trimester of a planned pregnancy.

DISCUSSION

The prevalence of thyrotoxicosis within the UK is 0.2% for men and 2% for women.⁷ The peak age range for the development of Graves' disease is between 20 and 39 years of age; 90% of cases are in women, with an incidence in the UK of 0.8 per 1000 women per annum.⁸ Therefore, a typical district hospital with a catchment of 500 000 would typically see 200 new cases of thyrotoxicosis per annum.

Although symptoms of irritability, insomnia, mood swings and anxiety are common presenting features of thyrotoxicosis, acute psychiatric symptoms as an initial presentation of thyrotoxicosis are rare. One retrospective study from Christchurch, New Zealand, suggested that 1% of all patients with thyrotoxicosis diagnosed over a 20-year period required psychiatric treatment—the majority of these were treated with antipsychotic medication as well as thionamides.³

Before there were effective treatments for Graves' disease, thyrotoxicosis was associated with the development of 'Basedow's psychosis',^{1 9} which was first described in the 19th century. Although psychosis is now a rare presenting feature of thyrotoxicosis, thyroid disorders are common in psychiatric patients: in one centre, review of the records of 230 patients with either schizophrenia or bipolar disorder showed that 3% of these patients had thyrotoxicosis and 23% were hypothyroid.¹⁰ The prevalence of newly diagnosed thyroid disorders among all inpatients with psychiatric disorders is low (0.5%).¹¹ However, the prevalence of thyrotoxicosis (or hypothyroidism) in newly presenting psychiatric disorders (as opposed to all inpatients with a psychiatric diagnosis) is not clearly established. Screening for thyroid disease in patients presenting with a first episode of psychosis or delirium is routine practice locally (Barnet, Enfield and Haringey Mental Health Trust), as part of the battery of blood tests carried out to assess these patients. With modern autoanalysers, there is minimal additional cost to the inclusion of thyroid function tests as part of a biochemical screen. The cost to the patient of misdiagnosing a psychiatric condition is immeasurable. Although these symptoms are not specific to thyrotoxicosis, we recommend questions regarding palpitations, weight loss, trembling and sweating are included in the assessment of psychoses that are either newly presenting or relapsing.

The association of hypothyroidism with psychiatric illness was recognised in the 19th century and was later described as 'myxoedema madness' by Asher in 1949.^{12 13} The rapid onset of hypothyroidism after radioactive iodine treatment has been reported to result in acute psychosis.¹⁴ The same has been observed with resolution of thyrotoxicosis following treatment.¹⁵ Symptoms of depression are more frequently associated with hypothyroidism, with a potential mechanism being the 'monoamine hypothesis' whereby centrally acting T3 increases release of the neurotransmitters serotonin and norepinephrine. Animal studies show that

thyroid hormone has dopaminergic action and this may be one mechanism whereby thyrotoxicosis leads to the development of psychosis.¹⁶ Increased levels of dopamine, serotonin and norepinephrine in response to centrally acting thyroid hormone may explain the development of anxiety and, more rarely, psychosis in patients with thyrotoxicosis. A parallel observation is that an acute rise or fall in cortisol levels can be associated with the onset of psychiatric symptoms.¹⁷

In the UK, there is no national guidance on the management of psychosis in patients with thyrotoxicosis. Previous reviews of case series suggest that antithyroid drugs combined with beta-blockers are the treatments of choice for hyperthyroidism presenting with psychotic symptoms; antipsychotic drugs are

Patient's perspective

Before being diagnosed with Graves' disease

When I was thyrotoxic, I felt very hot and in the end, my heart rate would be racing and I was suffering with chest pains. I felt like I had endless amounts of energy and became fixated on my work and getting tasks completed. I was not able to sleep and would be completing work on my laptop until the early hours of the morning, falling asleep for 3–4 hours before waking up at 6:00. My mind would be racing and I could not focus properly on a given task. I would start something and then move on to something else, so I had lots of unfinished tasks and this would make me increasingly anxious. I would talk very quickly and at my worst, did not make much sense. I became very paranoid and anxious when I was signed off work for 7 weeks. I could not sit still and had to find something to do, for example, cleaning and dancing. My husband observed me becoming aggressive towards him and I would have mood swings. I would become emotional and tearful for no reason. I would also become agitated and I could not understand why family members were fussing as I did not feel 'ill'. I was confused about what was wrong with me and at one point, I was convinced that I had diabetes. I felt very on edge and according to my husband, I was convinced that the police were after me if I heard a police siren.

After being diagnosed with Graves' disease

I would read the medication leaflets/read about thyrotoxicosis online and I was convinced that my hair would fall out and that my eye sight had got worse (I am shortsighted) when it had not. I had a lot of paranoid ideology and was not listening to constant reassurances from my husband or family members. At one point, I did not feel I needed to take the medication prescribed. I felt quite low and not myself. I did not feel that I could go out anywhere for fear of being seen by someone I might know from work. I was worried about letting colleagues down by not being at work.

After resolution of thyrotoxicosis

After treatment, I felt much calmer and less anxious. I felt as though I was able to focus on things properly as opposed to starting lots of tasks and struggling to get them completed. This reduced my anxiety. My mind had stopped racing and I felt that I had slowed down in terms of my thoughts. Consequently, my speech was less rushed. I was also able to fall asleep at night (usually between 22:00 and 23:00) and I was no longer awake doing work on my laptop in the middle of the night. Most importantly, I no longer felt like my heart was racing all the time and the chest pains I experienced prior to treatment had disappeared.

Learning points

- ▶ Psychosis can occur as a significant or presenting feature in both thyrotoxicosis and hypothyroidism.
- ▶ In the assessment of patients with either a newly diagnosed psychosis or relapse of a psychiatric condition, ask about symptoms of thyrotoxicosis or hypothyroidism.
- ▶ When screening patients with agitation, delirium or psychotic symptoms for organic disease, always include a thyroid function test.
- ▶ Patients with psychiatric complications of thyrotoxicosis may be managed without antipsychotic medication. Treatment with a thionamide and beta-blocker may be sufficient, but this needs careful assessment on a case-by-case basis in close liaison with the psychiatry team.

indicated where psychotic symptoms remain when thyrotoxicosis has resolved.^{2,4} The emergence of atypical antipsychotics prompted interest in the treatment of thyrotoxic psychosis; one review article concluded that risperidone should be the first-line antipsychotic considered.⁶ There will be situations where the severity of psychotic symptoms requires the use of antipsychotics as a first-line adjunct to antithyroid drug therapy.^{6,18}

This case confirms that acute psychiatric symptoms in patients with thyrotoxicosis can resolve without the introduction of antipsychotic drugs. However, we recommend psychiatric review to determine whether temporary treatment with antipsychotics is indicated in individual cases. In the assessment of patients with either a newly diagnosed psychosis or relapse of a psychiatric condition, questions about symptoms of thyrotoxicosis or hypothyroidism should be included in the assessment. Screening for thyroid dysfunction in patients with acute psychosis and no previous diagnosis of a psychiatric disorder has minimal cost—far outweighed by the risk of misdiagnosing a psychiatric problem, thereby avoiding unnecessary and potentially long-term antipsychotic therapy. Our case report offers an important message for the general physician, general practitioner or psychiatrist managing patients with agitation, delirium or psychosis, who may not have other symptoms of thyrotoxicosis.

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