Acute psychosis caused by hypothyroidism following radioactive iodine treatment of Graves' disease

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This case serves as a poignant reminder that sudden changes in thyroid hormone levels (e.g. acute hypothyroidism) can induce psychosis.

Case history

A 26-year-old woman was seen in the endocrinology clinic originally in September 2010 with symptoms of sweats, headaches, tremor, palpitations and weight loss of approximately 6 kg over the previous 3–4 months. She was clinically and biochemically thyrotoxic. There was a smooth goitre and there were no signs of thyroid eye disease at that stage. She was started on standard treatment with carbimazole 40 mg once daily and propranolol slow release (SR) 80 mg once daily, but she missed clinic appointments in October and December 2010. The endocrinology team wrote to her encouraging her to have a blood test and re-attend, but the next contact from the patient was on 30 March 2011 after a referral was received from her Occupational Health Department.

It transpired that the patient had developed intolerance to carbimazole in October 2010 and had stopped taking all medication shortly after her first clinic visit. When seen in March 2011 her symptoms of excessive heat, tremor and palpitations had worsened, but interestingly her weight was recorded at 52 kg, only 0.5 kg less than September 2010. She had a sinus tachycardia 100 bpm, there was proptosis of the left eye with reduced visual acuity to 6/9 in the left eye and normal acuity in the right eye. Blood investigations showed free thyroxine (fT4) 45 pmol/L (normal range 9–19 pmol/L), free tri-iodothyronine (fT3) 31 pmol/L (normal range 3.5–6.5 pmol/L) and thyroid stimulating hormone (TSH) <0.01 mU/L; TSH receptor antibodies were strongly positive at a level of 12 IU/L (normal < 1.0 IU/L). A diagnosis of Graves' disease was made, on the basis of elevated free thyroid hormone levels, the clinical signs and positive TSH-receptor antibody status. The patient was started on standard second-line treatment with propylthiouracil 200 mg twice per day and propranolol SR 80 mg daily.

At the end of April 2011, her weight had decreased to 50 kg and she remained tachycardic at 120 bpm. She had experienced headaches with propranolol, so this was then switched to verapamil 80 mg thrice daily, and the dose of propylthiouracil was increased to 300 mg twice per day. However, at the end of June 2011, thyrotoxicosis remained uncontrolled with fT4 38 pmol/L, fT3 10 pmol/L and suppressed TSH and the dose of propylthiouracil was increased to 800 mg once daily (once daily to aid compliance). By the end of July 2011 her thyroid hormone levels were unaltered. An urgent thyroidectomy (with appropriate preparation) was recommended but she did not want to have surgery.

The patient was referred for radioactive iodine (I-131) treatment as definitive treatment of thyrotoxicosis and followed standard local protocols for radioiodine dose, propylthiouracil cessation and steroid cover for thyroid eye disease – she received 533 MBq of I-131 on 16 September 2011. Propylthiouracil was stopped five days before radioactive iodine and resumed at a lower dose of 300 mg once per day five days after radioactive iodine treatment. She received three weeks of oral

together wrote the psychiatric aspects of the case history and discussion for the article.

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prednisolone to prevent deterioration of thyroid eye disease which she completed on 7 October 2011. She was reviewed in the endocrinology clinic at the end of October 2011, five weeks after radioactive iodine therapy and two weeks after stopping steroids. She was not anxious and she felt more like her normal self. Her weight had climbed to 56 kg. She was clinically euthyroid. Her thyroid hormone levels had fallen with an fT4 of 20 pmol/L, fT3 4.1 pmol/L and TSH 0.01 mU/L. The propylthiouracil was reduced to 200 mg daily with a plan to repeat blood tests four weeks later, but the patient did not attend for a repeat blood test four weeks later. The next contact was from a Consultant Psychiatrist who had admitted the patient with an acute psychosis on 7 December 2011, nearly three months after radioactive iodine treatment and seven weeks after her last endocrinology outpatient consultation. The patient's family reported that over the previous month, following her return to work, she had become increasingly tired and then in the two weeks preceding psychiatric admission she had developed paranoia, describing broadcasting of thoughts. Her only previous psychiatric history of note was of anxiety while thyrotoxic (she had been referred to a psychiatrist one year earlier by her general practitioner [GP], for an opinion on anxiety) but there was no past history of psychosis. A diagnosis of Acute and Transient Psychotic Disorder was made (ICD10 F23.8) and she was admitted under Section 2 of The Mental Health Act. On admission, she was found to be biochemically hypothyroid: the FT4 level was low at 5.1 pmol/L (normal 9–19 pmol/L) and TSH was elevated at 38 mU/L (normal range 0.35–4.94 mU/L). Propylthiouracil was stopped and levothyroxine 100 μg daily was commenced. On 7 December 2011, she was very agitated. She attempted to abscond and was violent towards staff. The police assisted her to a seclusion room. On 8 December 2011, she took her first dose of levothyroxine 100 μg and lorazepam 2 mg and on reassessment 10 hours later, she was much calmer than the previous day and was more cooperative. On 9 December 2011, as psychotic symptoms were still evident she was started on risperidone 1 mg twice daily and took a three-day course as an inpatient. At this stage, in accordance with the family's wishes she was granted Section 17 leave to her mother's address. According to the family, she never took risperidone after discharge from hospital but continued to take Levothyroxine. She was reviewed on 12 and 22 December when there was evidence of continued progress with reduction in psychomotor agitation, paranoid ideations and thought disorder. She was subsequently discharged from psychiatric review on 22 December 2011.

Subsequently, she missed four endocrinology outpatient appointments, but she continued taking levothyroxine 100 μg daily and was reviewed by her GP in April 2012. At that point she was euthyroid with a TSH of 3.2 mU/L. She was subsequently reviewed in the endocrinology clinic in June 2012: she remained biochemically euthyroid and was maintained on levothyroxine 100 μg once daily. There had been no relapse of psychotic symptoms since discharge from the psychiatric unit. The patient understands the importance of long-term compliance with levothyroxine as she has already demonstrated susceptibility to psychosis while severely hypothyroid and we/she would not want to risk a relapse in future.

Discussion

Hypothyroidism is a common endocrinological disorder, which can present with a variety of symptoms. A well-recognized symptom of hypothyroidism is mood change, ranging from a more commonly mild depression to a rarer state of agitation or psychosis. Asher[1] termed the phrase 'myxoedema madness' for the relationship between hypothyroidism and psychosis in 1949. There is evidence that the onset of psychosis may not be clearly related to the degree of hypothyroidism.[2] The older literature suggests that 5–15% of chronically myxoedematous hypothyroid patients show some form of psychosis,[3] but such severe chronic hypothyroid states are rarely seen today, due to more prompt diagnosis and effective treatment. Although there have been multiple case reports of psychiatric disease associated with both thyrotoxicosis and hypothyroidism, psychosis typically emerges after the onset of physical symptoms and is thought to be more common with a longer duration of disease.[4]

The authors conducted a Medline search of the literature from 1966 to present and found only two

case reports suggesting a link between radioactive iodine treatment and psychosis.[5,6] In both cases, details of thyroid function test results at the time psychosis was diagnosed were unclear or missing. Bethell[5] reported a case of psychosis in 1970 developing in a patient who had received radioactive iodine treatment for thyrotoxicosis three months before presenting with a 'schizophrenic illness'. The case is similar to the patient we describe, although thyroid function test results are not detailed. The case report implies that the patient was hypothyroid at the time she developed psychosis and after she was treated with Thyroxine 100 μg thrice daily 'the response was immediate and spectacular. The restlessness, irritability and suspiciousness all departed'.[5]

A more recent case of radioiodine-associated psychosis was described by Freeman[6] with a patient developing 'paranoid delusions' the day after receiving radioactive iodine for treatment of thyroid cancer (following a partial thyroidectomy). It is unclear whether the patient was hypothyroid when she developed delusions as she had only had a partial thyroidectomy and was noted to have a TSH of 6.7 MU/L (borderline elevation and free thyroxine level not stated) 1–2 months prior to radioiodine treatment.[6] Although the dose of radioiodine given was not stated, the typical dose of radioactive iodine given to ablate the thyroid in thyroid cancer patients is between 2000 and 3000 MBq. Much smaller doses of radioactive iodine are given to treat patients with thyrotoxicosis – our patient featured in this report received 533 MBq. Freeman's case is interesting but very different from the case we describe in terms of the rapidity of onset of psychosis after radioactive iodine, the dose of radioactive iodine given and the lack of thyroid function test data.

Psychosis in our patient was unrelated to corticosteroid use as there was no evidence of psychosis when initiated on steroid treatment prior to radioactive iodine treatment or when she was reviewed in the endocrinology clinic two weeks after stopping corticosteroids. There is a clear temporal relation between onset of hypothyroidism and onset of psychosis, but psychosis induced by use of/withdrawal from prednisolone would have occurred while on steroids or within two weeks of stopping steroids.[7]

Our patient had only exhibited mild anxiety while thyrotoxic prior to radioactive iodine treatment and her psychotic symptoms occurred within six weeks of becoming hypothyroid following radioactive iodine treatment. Poor compliance was a complicating factor, with non-attendance resulting in delayed diagnosis of hypothyroidism, prompt treatment of which may have prevented psychosis developing. There is a history of non-compliance and non-attendance prior to radioactive iodine treatment and in the lead-up to the psychotic episode, but fortunately, although attendance has been intermittent, she has remained compliant with levothyroxine treatment subsequently.

In keeping with previous reported cases of iatrogenic hypothyroidism causing psychosis, when our patient was admitted to the psychiatric unit she was highly agitated, exhibiting thought disorder without hallucinations. Her psychotic symptoms occurred after a short period of hypothyroidism (2–6 weeks) and were severe enough in nature to merit admission under The Mental Heath Act. After commencing levothyroxine treatment her symptoms resolved rapidly. In the past it was claimed that 4–6 weeks was a necessary timescale to see clinical improvements in psychosis following commencement of antipsychotic drugs such as risperidone.[8] However the evidence in recent years suggests improvement in psychosis can be seen within the first week of commencing antipsychotic medication. Some even argue it can be seen within 24 hours.[9] Symptoms of agitation are more readily responsive to drug treatment than more complex signs such as delusions. However in this case, symptoms of agitation and paranoia both improved rapidly within two days of starting levothyroxine (albeit with lorazepam addition). Risperidone may have speeded up recovery,[10] but her rapid improvement is most likely attributable to levothyroxine. As she only took risperidone for three days, it is clear that levothyroxine replacement was the most important factor in resolution of psychosis.

In summary, this is a rare case of transient psychosis induced by iatrogenic hypothyroidism, following radioactive iodine treatment. To our knowledge, this case report represents the first case since 1970 of psychosis secondary to radioactive iodine-induced hypothyroidism, when radioactive iodine was given to treat thyrotoxicosis. We report a rare adverse event of

hypothyroidism secondary to radioactive iodine treatment, illustrating that the rapid development of hypothyroidism (over weeks rather than months) can precipitate psychosis.

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