An unusual case of polyuria in a lithium-treated patient

Introduction

A 60-year-old woman, with a 36-year history of lithium-treated bipolar affective disorder, complained of polyuria. However, after diagnosis and treatment of nephrogenic diabetes insipidus (NDI) and type 2 diabetes mellitus, her polyuria remained a prominent symptom. Routine screening revealed hypercalcaemia secondary to hyperparathyroidism caused by her lithium therapy. This case illustrates the multiple endocrine problems associated with lithium therapy and how they can worsen psychiatric illness. Screening and management guidelines for these conditions are suggested.

Discussion

This case illustrates the many causes of polyuria in a patient taking lithium and several of the endocrine complications of lithium therapy. Some of these endocrine complications worsen psychiatric illness. Others are important as they cause intrusive side-effects. Endocrine complications of lithium therapy include (Salata and Klein, 1987):

- NDI
- Hyperparathyroidism
- Primary hypothyroidism
- Goitre
- Thyrotoxicosis (rare)
- Diabetes mellitus (rare).

Polydipsia and polyuria is a common symptom of lithium treatment. Mostly it reflects an impaired renal concentrating ability as a result of the effect of lithium on the renal tubule. However, only a small percentage of patients with lithium-induced polyuria fulfil endocrinological diagnosis of NDI (Dacso and Tran, 2004). Many have polyuria for other reasons. Often the anti-muscarinic side-effects of concomitant medication cause a dry mouth and provoke polydipsia; sometimes the patient has functional polydipsia. The wide differential of polyuria in lithium-treated patients highlights the importance of performing a water deprivation test to investigate the possible diagnosis of NDI.

The symptoms of NDI can be improved with amiloride or thiazide diuretics, and discontinuation of lithium treatment is not normally necessary. However, lithium cessation usually reverses the problem. (Timmer and Sands, 1999).

Hypercalcaemia and hyperparathyroidism is an under-recognized problem in lithium therapy. It can be a cause of polyuria and polydipsia as well as depression, anorexia, confusion, abdominal pain and tiredness (Ramrakha and Moore, 2004). Hypercalcaemia can be caused by over dosage of lithium, a serum lithium should be measured to exclude this (McHenry and Lee, 1996).

If calcium is elevated 4–6 weeks after initiation of therapy then the hypercalcaemia will probably remain and a parathormone (PTH) level should be checked. If the PTH is elevated then treatment of the hyperparathyroidism should be considered. The way the hyperparathyroidism is treated depends on the efficacy of the lithium on the patient's mental state and is outlined in *Figure 1*.

Conclusions

Polyuric endocrine conditions are often difficult to diagnose as they present with vague non-specific symptoms such as tiredness, weakness or lack of energy. These symptoms can be attributed to a worsening of the patient's mental state. Worsening polyuria is often attributed by the patient and doctor as a side-effect of the lithium and not a sign of an endocrine complication of lithium therapy. Therefore it is prudent to screen for these conditions.

Before embarking on lithium treatment patients should have their calcium and thyroid auto-antibodies levels and thyroid function tests performed. Their calcium levels and thyroid function should be checked 6 weeks after the initiation of treatment and then on an annual basis. Patients complaining of polyuria with nocturia should have a serum calcium and glucose checked and then a water deprivation test if the preceding tests are normal. BJHM

Case Report

A 60-year-old woman, who had been taking lithium for 36 years for bipolar affective disorder, was referred to an endocrinologist by her psychiatrist for investigation of polydipsia and polyuria. Water deprivation did not concentrate her urine, nor did desmopressin, indicating the diagnosis of nephrogenic diabetes insipidus (NDI).

She was started on chlorthalidone, a treatment for NDI, and her symptoms improved dramatically. Her polyuria was well controlled on chlorthalidone for 4 years, until she started feel tired and weak and her polyuria worsened. Initially these symptoms were attributed to her depression and lithium therapy. However, routine blood testing revealed a random blood glucose of 18.5 mmol/litre, thereby confirming the diagnosis of type 2 diabetes, and a corrected calcium of 3.02 mmol/litre (normal range 2.1–2.6 mmol/litre). She was started on a diabetic diet, resulting in good diabetes control (confirmed by haemoglobin A_{1c}) and her symptoms improved.

The patient's chlorthalidone was stopped as thiazide diuretics can cause hypercalcaemia and her calcium was repeated. The repeat value was higher at 3.07 mmol/litre and her parathormone was also elevated at 11.24 pmol/litre, confirming hyperparathyroidism. A parathyroid adenoma was sought but a nuclear medicine scan (Tc99m ssesta-MIBI; technetium 99m-sesta 2-methoxy isobutyl isonitrille) and ultrasound examination of the neck failed to localize an adenoma. It was felt that she had developed parathyroid hyperplasia secondary to chronic lithium therapy (Mallette and Eichhorn, 1986), so her lithium was withdrawn and replaced with sodium valproate. Her NDI and hyperparathyroidism resolved on withdrawal of lithium.

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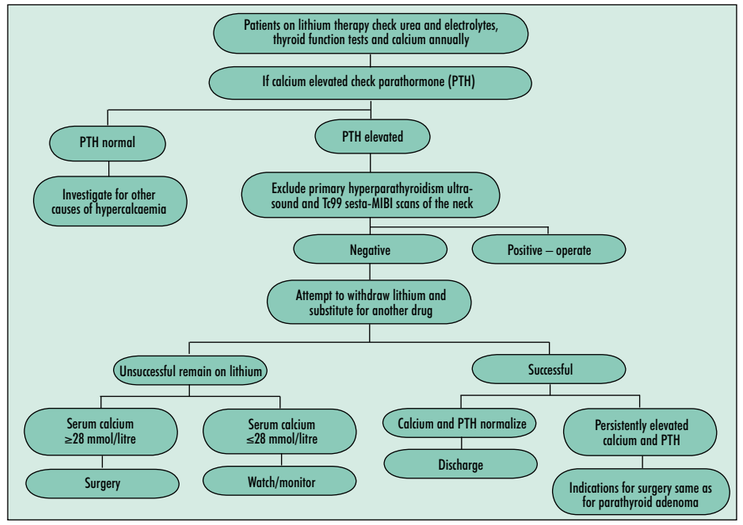
Figure 1. Management algorithm for lithium-induced hypercalcaemia. Tc99m sesta-MIBI = technetium 99m-Sesta 2-methoxy isobutyl isonitrile.



Meat and two veg

Searching through my past columns, I find that cancer is mentioned in 50 of them. Although not always the main theme, cancer makes it into just under one in three, about right for a column telling what is in the public's view and coincidentally the same number who develop cancer in this country. Despite the huge research effort, we still know little of what causes it. We have a fair idea of many associated factors, and more is known of the genetics, but that is all. This doesn't stop strident voices claiming that, for example, breast cancer is a preventable disease and viciously attacking the medical profession for their conniving in the deaths of millions of hapless women. Breast cancer – all cancer – may indeed be preventable, but we don't yet know enough to say so.

Two factors known for a long time are red meat and green vegetables: the first bad, the second good. People who eat more of the first and less of the second are more likely to develop bowel cancer. Some clues in the chain of causation recently made it into the news. While understandable that the media should be interested, the new knowledge does not help the public one bit. The knowledge provides scientific backing for saying don't binge on steak and eat up your greens, but we knew that anyway.

As ever, my argument is not in the facts, but the way they were put across, and especially some of the high-sounding quotes from scientists. This is not entirely fair, of course, because the media don't write what the scientists say but what they wanted the scientists to say. I suspect some of the scientists end up embarrassed.

A team from Washington DC found a compound in broccoli and cabbage that influences DNA repair genes (Sample, 2006), which prompted one of the researchers to comment that, 'There are a lot of supplements out there that claim to help prevent cancer. We can now look at those to see if they upregulate the activity of those genes.' That sounds promising, but it's still probably more fun to eat a bit more cabbage than to take a bottle of pills. Something in soya is especially good at affecting the genes. Showing that there's no such thing as a free lunch, even a veggie one, the same compound disrupts sexual development in mice.

One week earlier, the same newspaper (Hall, 2006) divulged that compounds contained in red meat damage DNA. I am sympathetic with the Meat and Livestock Commission, who admittedly have vested interests, but pointed out that the research on which the report was based had people eating nearly a pound of meat a day.

I do not quite follow the logic of Professor Colin Blakemore, chief executive of the MRC, who claimed that the study was 'an important step towards understanding and potentially preventing' bowel cancer. Would that be by banning red meat? Or by devising chemicals to counter the action of whatever nasties are in it?

Any grand solution to cancer depends on something that we – quite simply – do not yet have a clue about. Meanwhile, continue to eat your greens. BJHM

Hall S (2006) DNA damage from eating red meat linked to cancer. *Guardian* **1 Feb:** 11

Sample I (2006) Broccoli, cabbage, cauliflower: the vegetables that may prevent cancer. *Guardian* **8 Feb:** 9

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