An endocrine potpourri

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INTRODUCTION

Autoimmune endocrine conditions such as type 1 diabetes, autoimmune thyroid disease and Addison's disease are known to occur concurrently. This article presents a unique patient who presented simultaneously with a variety of unrelated endocrine disorders.

DISCUSSION

This patient has four endocrine conditions: primary hyperparathyroidism, autoimmune hyperthyroidism, acromegaly and adrenocortical failure (secondary). Her primary hyperparathyroidism was unmasked when she presented with a urinary tract infection precipitating an Addisonian crisis. Her cortisol deficiency is a result of her previous surgery and radiotherapy to her pituitary gland. The causes of adrenocortical failure are listed in *Table 1*. Cortisol deficiency contributes to her hypercalcaemia by an increase in calcium resorption from bone and a decrease in urinary calcium excretion (Jorgensen, 1973). Furthermore, this patient's hypercalcaemia would be worsened by hyperthyroidism, dehydration and growth hormone excess (acromegaly). *Table 2* gives causes of hypercalcaemia.

Despite a cortisol day curve which had suggested her cortisol excess she presented very soon after with an Addisonian crisis. Her crisis was precipitated by not only her her urinary

CASE REPORT

A 77-year-old woman presented as an emergency with a 1-week history of increasing lethargy, confusion, drowsiness and anorexia. She was known to have active acromegaly, having undergone a transsphenoidal resection of a pituitary adenoma 6 years previously, and a course of radiotherapy 2 years later. She had subsequently developed post-hypophysectomy hypothyroidism, and her acromegaly was known to be still active: a recent insulin-like growth factor (IGF-1) was 49.2 nmol/litre (normal range (NR) 26–29 nmol/litre). Her current medication comprised thyroxine 100 μg daily, bromocriptine 40 mg daily, co-amilofruse 5/40 one tablet daily and aspirin 75 mg daily.

She had been seen in the endocrinology clinic 1 month previously, where she had been noted to be increasing in weight on a daily regimen of hydrocortisone 10 mg in the morning, 5 mg in the afternoon and 5 mg in the evening. A cortisol day curve was performed which showed a basal early morning cortisol of 323 nmol/litre with 1-hour levels after hydrocortisone ingestion in excess of 1100 nmol/litre. On this evidence the patient was contacted and instructed to discontinue her hydrocortisone therapy, which she did some 10 days before her admission.

On examination she was apyrexial, but was noted to be mildly confused and clinically dehydrated, with a blood pressures of 120/70 mmHg lying and 105/84 mmHg standing. General examination revealed signs of soft tissue swelling compatible with acromegaly, but otherwise was unremarkable with no focal neurology. Initial investigations were unremarkable except for: corrected calcium 3.20 mmol/litre (NR 2.12–2.55 mmol/litre); phosphate 1.66 mmol/litre (NR 0.8–1.4 mmol/litre); 9am cortisol 90 nmol/litre (NR 150–700 nmol/litre); free thyroxine (T4) 44.5 pmol/litre (NR 9.8–23.1pmol/litre); free tri-iodothyronine (T3) 20.8 pmol/litre (NR 3.5–6.5pmol/litre); thyroid-stimulating hormone (TSH) <0.03; thyroid peroxidase antibodies 243 IU/ml (NR 0–60 IU/ml); parathyroid hormone 49.1 ng/litre (NR 12–72ng/litre).

Chest X-ray and electrocardiogram were normal. Mid-stream urine confirmed the presence of a significant coliform urinary tract infection.

She was initially resuscitated with intravenous fluids and hydrocortisone, her thyroxine was discontinued, and she was given trimethoprim for her urinary infection and intravenous pamidronate for her hypercalcaemia. She improved clinically over the course of the next week, in that she became less confused and drowsy, and was able to mobilize out of bed, her electrolytes and calcium levels normalized, and she was moved to a cottage hospital for convalescence.

Two weeks later, she was brought back in to the endocrine ward for further investigation. Her blood pressure and electrolytes were normal, but her serum parathyroid hormone level had risen to 80.6 ng/litre in the face of a normal calcium (2.41 mmol/litre). Twenty-four hour urinary calcium excretion was 1.7 mmol (NR 2.7–7.5 mmol). She remained thyrotoxic, with free T4 measured at 31.8 pmol/litre, free T3 12.3 pmol/litre, and TSH <0.03.

Her ongoing management therefore needed to address several issues. She was referred to the nuclear medicine department for further investigation and treatment of her thyroid problems, where a technetium scan demonstrated increased tracer uptake in both lobes of the thyroid, estimated at 3.1% of the administered dose (normal range up to 3%). She therefore was given a treatment dose of 400 MBq 131-iodine which rendered her euthyroid.

The acromegaly will prove difficult to treat, as she has already undergone surgery and radiotherapy in the past, and long-acting octreotide analogues are unlikely to be of benefit because her growth hormone levels were not suppressed by short-acting octreotide therapy. She remains on bromocriptine.

TABLE 1.
Causes of adrenocortical failure

Primary	Autoimmune adrenalitis
	Tuberculosis
	Metastatic carcinoma
	Fungal infections
	Adrenal haemorrhage
	Opportunistic infections in acquired immunodeficiency syndrome (AIDS) patients
Secondary	Pituitary tumour
	Craniopharyngioma
	Pituitary surgery or radiation
	Empty sella syndrome
	Postpartum pituitary necrosis
	Long-term glucocorticoid treatment

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tract infection, but also by hyperthyroidism. Although it was initially presumed that she may have been confused and may have taken too much thyroxine, further tests revealed a positive thyroid peroxidase antibody and increased technetium uptake, indicating endogenous thyroid hyperactivity. She was consequently rendered euthyroid by an ablative dose of radioactive iodine.

TABLE 2. Causes of hypercalcaemia

Primary and tertiary hyperparathyroidism
Metastatic bone disease
Ectopic parathyroid hormone secretion
Thyrotoxicosis
Granulomatous disease
Milk alkali syndrome
Vitamin D excess
Addison's disease
Phaeochromocytoma
Drugs (thiazides, lithium)
Familial hypocalcaemic hypercalcaemia
Multiple endocrine neoplasia

The patient's history emphasizes the importance of continued monitoring of thyroid function tests despite many years of stable replacement dose. Although acromegalics have a high prevalence of goitres, rarely do they exhibit functional abnormality (Kasagi et al, 1999). Her acromegaly remains active and continues to be a therapeutic challenge since she has failed to undergo remission despite surgical, radiotherapy and conventional medical therapy. She remains at high risk of cardiovascular death because of her excess growth hormone (Orme et al, 1998). Furthermore, primary hyperparathyroidism itself also increases the risk of cardiovascular death (Hedback and Oden, 1998).

CONCLUSION

This unusual case of various endocrine diseases occurring concurrently highlights the importance of regular thyroid function monitoring, treating the underlying causes of hypercalcaemia, the need to carefully monitor a patient after steroid withdrawal and dealing with a therapeutically challenging case of acromegaly. HM

Jorgensen H (1973) Hypercalcaemia in adrenocortical insufficiency. *Acta Med Scand* **193:** 175–9

Hedback G, Oden A (1998) Increased risk of death from primary hyperparathyroidism. *Eur J Clin Invest* **28**(4): 271–6

Kasagi K, Shimatsu A, Miyamoto S et al (1999) Goiter associated with acromegaly. *Thyroid* **9**(8): 791–6

Orme SM, McNally RJ, Cartwright RA, Belchetz PE (1998) Mortality and cancer incidence in acromegaly. *J Clin Endocrinol Metab* **83**(8): 2730–4

IN THE PUBLIC'S VIEW...

The unpredictability of medicine

When I was working for the final FFARCS (now FRCA) in 1979, a lecturer told us about the oxygen-carrying solutions that would become available within the next year or two. Soon, the dangers of blood transfusion would be a thing of the past. We all learned about these fluorocarbons, which were so important in the examination syllabus because of the impending revolution in transfusion practice. Twenty-three years on, the journals still intermittently publish articles predicting that it will 'soon' be unnecessary to use blood. One day, no doubt. In the meantime, we should remember the wise words of Niels Bohr, the Danish physicist. 'Prediction is very difficult,' he said, 'especially about the future.'

Unlike most of these columns, this article has been some years in the preparation. I am an avid hoarder and cataloguer of the medical press. I put interesting journal articles into a computer database, with a summary of each article printed on a 6" by 4" filecard. But I also have a less formal system, mainly for newspaper and magazine articles. At the back of that file is a pocket labelled 'Predictions'. In it I drop articles in which someone, usually a doctor or a medical scientist with a large grant to maintain, tells the world that within just a few years this or that medical revolution will have taken place. In the week that the *Daily Mail* told us that a vaccine would soon eliminate cervical cancer, and thus the need for cervical screening, I tipped the contents of the pocket onto my desk.

'Pigs with human genes will be used as donors for lung-transplant operations within 10 years' (*Independent*, 29 August 1992). 'Gene therapy to treat cystic fibrosis will be in routine use within 5 years' (*Guardian*, 7 September 1994). 'By the year 2000 open surgery will be as uncommon as endoscopic surgery appears today' (*BMA News Review*, February 1995).

Here's one that is partly correct, 'within the next 10 years there will be a dramatic fall in the numbers of women who die from breast cancer' (*Radio Times*, 21–27 March 1992). But it all depends what you mean by dramatic, and the same person also said that sophisticated molecular pathology would mean that: 'By the turn of the century oncologists will be able to tailor treatment to suit individual breast cancer patients' (*Hospital Doctor*, 17 March 1994).

So I think it unlikely that in 2006 I will decide what's for lunch by pressing my hand on my personal diagnostic machine to check my blood pressure, cholesterol and weight:fat ratio to determine my nutritional requirements (*Guardian*, 30 January 1996). Nor do I think that when today's babies die they will be able to download their minds into electronic storage and carry on digitally (*Sunday Times*, 2 January 2000). Those who make predictions should take heed: make sure that neither you nor those who read them are around to find out they've not come true. And remember that the real future will be different because of something unexpected, which no one has yet thought of. HM

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