Lesson of the Week

Hypothyroidism presenting with hyperprolactinaemia

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Now that there is a specific radioimmunoassay for detecting prolactin¹ hyperprolactinaemia is recognised more frequently in women in whom it usually presents as subfertility, amenorrhoea, or galactorrhoea. It occurs less often in men with impotence and subfertility. Although hyperprolactinaemia is often due to a pituitary tumour that secretes prolactin it also occurs because of conditions such as phenothiazine or other drug therapy, polycystic ovarian disease, and disruption of the hypothalamic-pituitary dopaminergic pathways by inflammatory or neoplastic infiltrates. Thyrotrophin releasing hormone raises the serum prolactin concentration by stimulating pituitary lactotrophs,² and hypothyroidism is yet another cause of hyperprolactinaemia.³ The degree of hyperprolactinaemia seems to be proportional to the severity of hypothyroidism, so that mildly hypothyroid subjects often have a normal serum prolactin concentration.⁴

We report on six patients with hyperprolactinaemia and associated syndromes, who were initially suspected of having a tumour that secreted prolactin but the results of endocrinological tests showed that they had hyperprolactinaemia induced by hypothyroidism.

Case reports

Case 1—A 33 year old woman had had secondary amenorrhoea for 18 months. Her serum prolactin concentration had been raised at 420 mU/l and 590 mU/l (normal range 60-360 mU/l). On examination she was clinically euthyroid but because both her father and sister had hypothyroidism this diagnosis was considered and confirmed by thyroid function testing (table). She was given thyroxine treatment, and her serum prolactin concentration fell to normal soon after. She started to menstruate

Hypothyroidism may mimic syndromes that are attributed to prolactin secreting pituitary tumours

regularly and conceived six months after starting thyroxine treatment.

Case 2—A 25 year old woman was referred as a "classic" case of the galactorrhoea-amenorrhoea syndrome. She had lactated for two years after her last pregnancy, she menstruated infrequently, and her serum prolactin concentration had varied from 800 to 1900 mU/l. Clinical examination and the results of biochemical tests showed that she was hypothyroid, and she was treated with thyroxine. She began to menstruate regularly and the galactorrhoea disappeared. Her serum prolactin concentration was moderately raised (400-700 mU/l) for two years despite high normal concentrations of thyroxine and suppressed serum thyroid stimulating hormone concentrations, but after three years it was normal.

Case 3—A 24 year old woman had been referred to a neurosurgeon because of hyperprolactinaemia (580-1300 mU/l), oligomenorrhoea, and primary infertility. A clinical examination and the results of biochemical tests showed that she was hypothyroid. She was given thyroxine and her menses rapidly became regular. Despite being clinically euthyroid and having high normal serum thyroxine concentrations with suppressed serum thyroid stimulating hormone concentrations her serum prolactin concentration was raised (400-600 mU/l) for one year after treatment, but six months later it was normal though her infertility persisted.

Case 4—A 33 year old woman received thyroxine 0.1 mg/day for hypothyroidism. Because she had a two year history of amenorrhoea, galactorrhoea, and hyperprolactinaemia (900-1360 mU/l) she had been referred to a neurosurgeon. The results of endocrine assessment showed clinical and biochemical under-replacement with thyroxine. Pituitary tomography, cavernous sinogram, and computed tomography of her pituitary fossa suggested that she had an intrasellar pituitary tumour. The thyroxine dosage was increased, and she became euthyroid. A regular menstrual cycle rapidly returned and galactorrhoea disappeared. Over six months her serum prolactin concentration fell to normal, and repeat computed tomography was normal. Eighteen months after referral she conceived and delivered a healthy child after a normal pregnancy.

Case 5—A 40 year old woman who gave an eight year history of galactorrhoea was referred to a neurosurgeon because of hyperprolactinaemia (800-1270 mU/l) and he referred her for endocrine evaluation. She had had a partial thyroidectomy 13 years before for dysmorphogenetic goitre and had been prescribed replacement treatment. Nevertheless, clinical examination and biochemical test results showed that she was

Results of biochemical tests in the six patients with hypothyroidism

Case No	Thyroxine (normal 55-144 nmol/l)	Triiodothyronine (normal 0.9-2.8 nmol/l)	Thyroid stimulating hormone (normal 0-8 mU/l)	Peak prolactin (normal 0-360 mU/l)
1	23	1.5	> 25	590
2	Undetectable	0.7	> 50	1900
3	Undetectable	0.9	> 50	1300
4	69	0.9	> 50	1360
5	27	Undetectable	> 50	1270
6	15	1.1	> 50	3800

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hypothyroid, and she had not taken her treatment. Thus, galactorrhoea and hyperprolactinaemia continued.

Case 6—A 53 year old man, who was known to have congenital hypothyroidism, had his eyesight checked and was found to have bilateral optic atrophy. The results of a detailed ophthalmological assessment confirmed this, showing bitemporal hemianopia. Computed tomography showed a large pituitary tumour with suprasellar extension (figure a). His serum prolactin

Computed tomography of the pituitary in the patient in case 6, showing (a) an enhanced lesion filling the suprasellar cistern; (b) disappearance of the lesion with reduced density in the pituitary fossa, suggesting intrasellar cisternal herniation.

concentration was raised (3800 mU/l); he had not taken replacement treatment for many years. He was of short stature and had dry skin but otherwise seemed clinically euthyroid. Nevertheless, the results of laboratory findings showed hypothyroidism. He was treated with gradually increasing doses of thyroxine, and prolactin concentrations returned to normal. His visual fields improved though optic atrophy persisted. A repeated computed tomographic scan showed that the suprasellar extension had resolved (figure b).

Comment

Although it is well known that menorrhagia is a common feature of hypothyroidism in women during the reproductive years it is less well recognised that hypothyroidism may lead to amenorrhoea or oligomenorrhoea sometimes associated with hyperprolactinaemia. This is clearly shown in the patients in

cases 1 to 4. Our findings do not support the view of Bigo *et al*⁴ that only severe hypothyroidism raises the serum prolactin concentration. The patient in case 1 had hyperprolactinaemia despite being clinically euthyroid, and the patient in case 4 had a raised serum prolactin concentration despite normal concentrations of thyroxine and triiodothyronine.

Now that prolactin secreting pituitary tumours are diagnosed more often and can be successfully managed either by microsurgery or by dopamine agonist treatment there is a danger that failure to recognise hypothyroidism will lead to inappropriate treatment. Hypothyroidism is likely to be overlooked when the radiological appearances (cases 4 and 6) or a visual field defect (case 6) indicate that the patient has an expanding tumour in the region of the sella. Pituitary enlargement in hypothyroidism is probably due to hypertrophy or hyperplasia of the thyrotrophs,^{4,5} or both. It is important to recognise these "feedback tumours" because they are readily reversed⁶ (case 6). Neurosurgery has appreciable risks when performed on a hypothyroid patient.

Despite the rapid correction of thyroid deficiency, the prolactin status of three of our patients (cases 2 to 4) returned only slowly to normal. This suggests either that the pituitary lactotrophs have become unusually sensitive to thyrotrophin releasing hormone or that they have developed a resistance to the usual modulating influences and continue to hypersecrete prolactin for some time after correction of the hypothalamic-pituitary-thyroid axis.

It is essential that thyroid function tests are performed on every patient with hyperprolactinaemia.

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What is the nature of "gippy tummy" and is it avoidable?

Diarrhoea, sometimes with associated constitutional disturbance, may afflict any traveller, but it is commoner in countries with generally lower standards of hygiene where it is known by a variety of affectionate and colourful cognomens apart from gippy tummy—Aden gut, Aztec two step, Basra belly, Delhi belly, Hong Kong dog, Montezuma's revenge, Tokyo trots, turista, etc. In medical publications it is called traveller's diarrhoea and is due to an enteric infection with one of a variety of organisms. Standard enteric pathogens (salmonellae, shigellae, campylobacter, giardia lamblia, or viruses) are sometimes responsible, but in most victims enterotoxigenic *Escherichia coli* is the cause. Some individuals seem more prone to the condition than others, for unknown reasons. Common sense measures to avoid infection seem wise—avoidance of salads, unpeeled fruit, and ice cream and care about sources of water—though no firm evidence

exists to show their value. The liberal use of alcohol to stimulate gastric acid secretion has many enthusiastic proponents but no controlled trial to support it. The use of clioquinol (enterovioform) affords no protection. Antibiotic prophylaxis, however, does diminish the risk. Streptotriad (one tablet twice daily for one week and one tablet daily thereafter)¹ and doxycycline 100 mg daily² both protect travellers against diarrhoea for as long as the drug is taken. Antibiotics are only justified when the likelihood of infection is sufficiently high (Mexico or Asia, for example) or if the inconvenience of an attack would be great—for instance, for a competitor in an international athletic competition.—JOHN R BENNETT, consultant physician, Kingston upon Hull.

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