

Postpartum amenorrhoea-galactorrhoea associated with hyperprolactinaemia and pituitary enlargement in primary hypothyroidism

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ABSTRACT

We report a 36-year-old woman with primary hypothyroidism revealed by postpartum amenorrhoea-galactorrhoea associated with hyperprolactinaemia and suprasellar pituitary enlargement on magnetic resonance imaging (MRI). On thyroid hormone replacement therapy all clinical, biochemical, radiological and endocrine abnormalities disappeared. Hyperplasia of pituitary thyrotrophs and/or lactotrophs seems to be responsible for the pituitary enlargement seen on MRI.

INTRODUCTION

Amenorrhoea, galactorrhoea and hyperprolactinaemia in a young woman usually suggests a prolactinoma of the anterior pituitary.¹ Hyperprolactinaemia is present in one-third of primary hypothyroid patients.²⁻⁷ Less commonly, galactorrhoea and amenorrhoea is associated with primary hypothyroidism.^{2,5} Rarely, amenorrhoea, galactorrhoea and hyperprolactinaemia in primary hypothyroid patients are associated with an enlarged pituitary gland leading to diagnostic confusion with prolactinomas.⁸⁻¹¹

We report a patient with primary hypothyroidism associated with postpartum galactorrhoea, amenorrhoea and pituitary gland enlargement as well as her clinical course during L-thyroxine replacement therapy.

CASE REPORT

A 36-year-old woman, gravida 2 para 2, was referred to our hospital in 2001 for analysis of amenorrhoea and

galactorrhoea since her last pregnancy in 1997. The patient had a normal pregnancy and delivery in December 1997. After a nursing period of six weeks, secretion of milk persisted associated with amenorrhoea. Serum prolactin concentration (PRL) was 103 µg/l (normal 0-20 µg/l). Thyroid function was not tested at that time. She was treated with conventional doses of bromocriptine for nearly twelve months, leading to cessation of galactorrhoea and normal periods. After discontinuation of therapy all symptoms returned. After a brief period of oral contraceptive therapy, during which periods were regular, the patient discontinued this medication as well and was seen by a gynaecologist in 2001 for amenorrhoea and galactorrhoea. The external and internal genitalia were normal. On examination bilateral galactorrhoea was confirmed. Again prolactin was 103 µg/l. Magnetic resonance imaging (MRI) revealed a 14 x 20 x 12 mm pituitary macroadenoma extending to the suprasellar cisterna without compression of the chiasma (*figure 1*). With this information the patient was sent to the department of endocrinology. Typical clinical signs suggesting hypothyroidism were noticed on physical examination. There was no palpable thyroid tissue. Milk could easily be expressed from the breasts. Thyroid function tests were consistent with primary hypothyroidism. The serum free T₄ (FT₄) was 3.9 pmol/l (normal 10.0-24.0 pmol/l) and thyroid stimulating hormone (TSH) >75 mU/l (normal 0.40-4.00 mU/l). Basal serum prolactin (PRL) was elevated: 103 µg/l (normal 0-20 µg/l). Luteinising hormone (LH) was <1 U/l and oestradiol (E₂) was <0.07 nmol/l. The remaining dynamic tests of the hypothalamic-pituitary axis were normal, including growth hormone and ACTH.



Figure 1
MRI of the pituitary gland in a young woman with primary hypothyroidism before treatment with L-thyroxine showing a 14 x 20 x 12 mm pituitary mass extending to the suprasellar cistern (arrow)

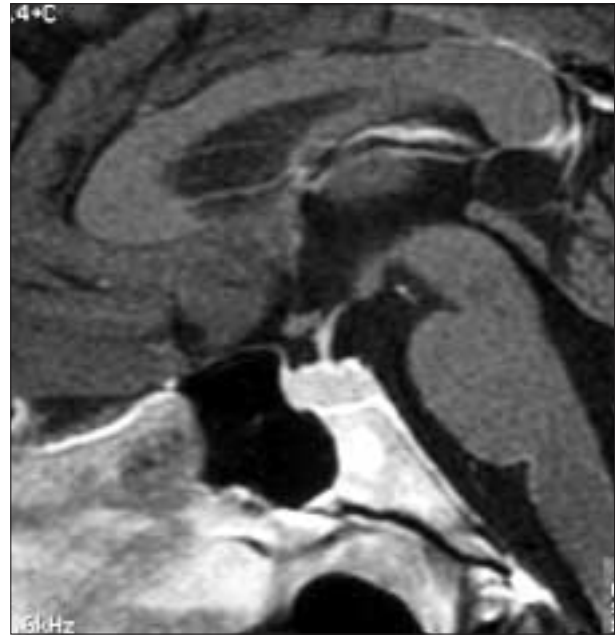


Figure 2
MRI of the pituitary gland in a young woman with primary hypothyroidism after one year of treatment with L-thyroxine showing normal dimensions of the pituitary gland and the bony structures surrounding it

Substitution therapy with L-thyroxine was started, gradually increasing to 125 µg daily. During the next ten months the galactorrhoea resolved and menstrual bleeding resumed. Serum free T₄ concentration became normal at 18.7 pmol/l. TSH and prolactin concentrations returned to normal, at concentrations of 2.5 mU/l and 20 µg/l respectively. LH concentration was 4.5 U/l and E₂ 0.36 nmol/l. MRI of the sellar region was repeated after six months of treatment. MRI demonstrated a marked decrease in the size of the pituitary mass within the sella turcica. After one year of treatment with L-thyroxine repeated MRI showed normal dimensions of the pituitary gland and the bony structures surrounding it (figure 2).

DISCUSSION

This case illustrates that primary hypothyroidism in a female may present by amenorrhoea, galactorrhoea and hyperprolactinaemia. Amenorrhoea appears to be caused by suppression of the hypothalamic GnRH secretion by prolactin leading to low gonadotropin and oestradiol levels.¹² The cause of hyperprolactinaemia in primary hypothyroidism is less clear. Several mechanisms have been proposed. At least four factors may contribute to hyperprolactinaemia in primary hypothyroidism. Firstly, the elevated prolactin could be attributed to increased PRL secretion under the

influence of TRH, which stimulates TSH as well as PRL secretion.^{2,13}

Secondly, prolactin clearance may be decreased in hypothyroid patients.¹⁴ Thirdly, a study by Foord *et al.* demonstrated that cultured anterior pituitary cells from hypothyroid rats have a reduced sensitivity to the inhibitory action of dopamine and dopamine agonists on prolactin production, possibly by a defect at the level of the dopamine receptor or at the post receptor level.^{15,16} Fourthly, thyroid hormone itself may also play an important role in the cause of hyperprolactinaemia. Davis *et al.* noticed that 3,5,3'-triiodothyronine reduces prolactin messenger RNA levels in rodent pituitary cells.¹⁷ Decreased circulating thyroid hormone levels might stimulate prolactin synthesis. The pathophysiological mechanisms in primary hypothyroidism that lead to hyperprolactinaemia might involve factors acting on prolactin receptors as well as on prolactin gene expression.

The pituitary enlargement in primary hypothyroidism may be explained by lactotroph and/or thyrotroph hyperplasia;¹⁸⁻²⁰ severity and duration of hypothyroidism being of influence. In view of the potent negative regulation of dopamine on prolactin cells, compression of the pituitary stalk due to hyperplasia of the pituitary can also lead to a moderate hyperprolactinaemia. In our patient this seems to be unlikely as the other dynamic hypothalamic-pituitary tests were normal.

Table 1

The course of serum FT₄, TSH, PRL, LH and E₂ in a young woman with primary hypothyroidism before and after ten months of treatment with L-thyroxine

	FT ₄ (PMOL/L)	TSH (MU/L)	PRL (μG/L)	LH (U/L)	E ₂ (NMOL/L)
Before	3.9	>75.0	103	<1	<0.07
After	18.7	2.5	20	4.5	0.36

Hypothyroidism and hyperprolactinaemia with pituitary enlargement can cause diagnostic difficulties. Coexistence of primary hypothyroidism and a pituitary macroadenoma as well as primary hypothyroidism associated with hyperprolactinaemia and pituitary enlargement should be taken into account. The resolution of the pituitary enlargement and the resumption of the menstrual cycle after replacement therapy with L-thyroxine strongly argues against the possibility of a coexisting macroadenoma and favours the second possibility.

CONCLUSION

In a female patient with amenorrhoea, galactorrhoea and hyperprolactinaemia associated with enlargement of the pituitary gland, primary hypothyroidism should always be excluded as a possible cause.

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