

# Empty sella developing during thyroxine therapy in a patient with primary hypothyroidism and hyperprolactinaemia

Fahrettin Kelestimur, Ahmet Selçuklu and Nevzat Özcan

Department of Internal Medicine, Erciyes University Medical School, Kayseri, Turkey

**Summary:** A 35 year old woman presented with severe primary hypothyroidism and galactorrhea. A very high prolactin level was also detected and computerized tomography scan of the sellar region demonstrated an enlarged pituitary gland associated with contrast enhancement. Replacement therapy with thyroxine corrected both biochemical and clinical abnormalities but empty sella developed during this therapy. It is concluded that empty sella may be related to thyroxine-induced shrinkage of lactotroph and/or thyrotroph cell hyperplasia.

## Introduction

Empty sella is characterized by an intrasellar herniation of the suprasellar subarachnoid space. It may be primary or secondary in origin. Secondary empty sella is usually related to surgical treatment or X-ray therapy and it has also been reported after spontaneous infarction of pituitary tumours, Sheehan's syndrome and bromocriptine therapy in patients with prolactinoma and functionless pituitary tumour.<sup>1–5</sup> We present a patient with primary hypothyroidism and hyperprolactinaemia in whom empty sella developed during thyroxine replacement therapy.

## Case report

A 35 year old woman was admitted to hospital complaining of weight gain, cold intolerance, constipation, tiredness and spontaneous galactorrhoea, the last symptom for one year. She denied any menstrual disturbance or drug usage. On physical examination the presence of severe hypothyroidism and galactorrhoea were confirmed. The thyroid gland was not palpable.

Laboratory investigation demonstrated the following results: thyroxine (T4) 0.6 µg/dl (normal range: 4–12.5), triiodothyronine (T3) 42 ng/dl (86–187), thyrotrophin (TSH) 53,805 µU/ml (0.3–4.5), free thyroxine (FT4) 0.01 ng/dl (0.8–

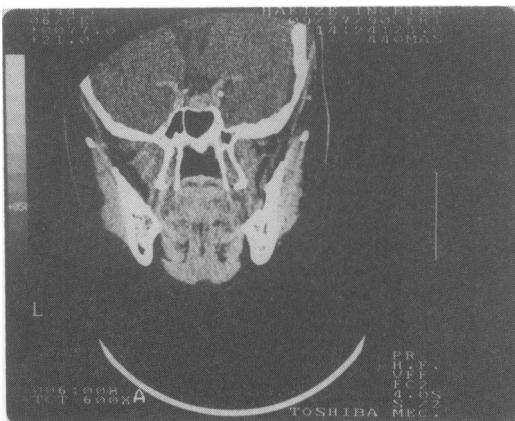
2.0), free triiodothyronine (FT3) 0.82 pg/ml (1.4–4), prolactin (PRL) 3,333.80 ng/ml (0–20), growth hormone (GH) 1.3 ng/ml (0–5), cortisol 17.8 µg/dl (6–27), oestradiol 0.90 nmol/l (0.73–2.08), luteinizing hormone (LH) 1.72 mIU/ml (0–8), follicle-stimulating hormone (FSH) 5.37 mIU/ml (0–20). Antithyroglobulin and antimicrosomal antibodies were negative. Adrenocorticotrophin (ACTH) i.v. stimulation test ruled out adrenal insufficiency. Complete blood cell count, liver and renal function tests were unremarkable. Visual fields examination demonstrated no abnormality. Computed tomographic (CT) scan of the pituitary gland demonstrated contrast enhancement on coronal sections and its height was 9.5 mm (Figure 1). We put the patient on replacement therapy with thyroxine which was gradually increased to 150 µg/day. Hormonal investigations carried out 7 months later showed that T4 was 6.52 µg/dl, T3 99.2 ng/dl, TSH 3.20 µU/ml and PRL 16.6 ng/ml. Repeated CT scan at that time revealed a large empty sella (Figure 2). Galactorrhoea was not present and she denied any complaint.

## Discussion

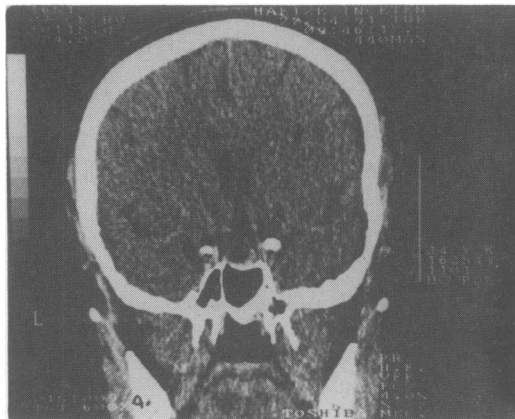
Primary hypothyroidism is invariably associated with increased TSH secretion because of hyper trophy and hyperplasia of the TSH-secreting cells. It may also result in thyrotroph cell adenoma of the pituitary gland as the other end organ failure resulting in pituitary enlargement or tumour.<sup>6</sup> Samaan *et al.* reported two cases with TSH-producing pituitary tumour due to primary hypo-

Correspondence: F. Kelestimur, M.D., Erciyes Üniversitesi Tıp Fakültesi, İç Hastalıkları Kliniği, Kayseri, Turkey.

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**Figure 1** Coronal computed tomography scan demonstrating contrast enhancement and enlargement of the pituitary gland before thyroxine therapy.



**Figure 2** Coronal computed tomography scan taken after seven months of thyroxine therapy, showing a large empty sella.

thyroidism in which PRL levels were normal.<sup>7</sup> Several papers have reported that thyroxine replacement therapy may cause some diminution or disappearance of pituitary enlargement or tumour secondary to primary hypothyroidism.<sup>6,8</sup> PRL level was not detected or within the normal range in the studies mentioned above. There is, however, an increasing number of case reports indicating that primary hypothyroidism may give rise to hyperprolactinaemia and such patients may at presentation have a prolactinoma to suggest a TSH-secreting pituitary tumour.<sup>9-12</sup> Although marked hyperprolactinaemia has been reported in subclinical hypothyroidism, the degree of hyperprolactinaemia has been suggested to be proportional to the severity of hypothyroidism.<sup>13,14</sup>

Katevuo *et al.* suggested that contrast enhancement in patients with primary hypothyroidism reflects increased pituitary circulation associated with the augmented function of the thyrotrophs.<sup>10</sup> However, only one of their patients had marked hyperprolactinaemia which was much less than in our case. Since both TSH and PRL levels are high in some patients with primary hypothyroidism characterized by enlarged pituitary gland, we think that it is not possible to say whether pituitary enlargement or tumour is due to lactotroph and/or thyrotroph cell abnormality in this condition.

Whatever the pituitary abnormality, pituitary enlargement due to primary hypothyroidism may cause suprasellar extension and visual field defects which are reversible with thyroxine therapy.<sup>6,15-17</sup> The incidence of significant hyperprolactinaemia due to primary hypothyroidism varies between 0 and 25%.<sup>10,18</sup> Although the incidence of pituitary enlargement in primary hypothyroidism associated with hyperprolactinaemia is not known, we think that severe hypothyroidism may rarely be associated with hyperprolactinaemia and an enlarged pituitary gland. The mechanism of hyperprolactinaemia in primary hypothyroidism is not understood. We previously postulated that there may be a close relation between prolactin secretion and peripheral thyroid hormone levels in relation to observations in a patient with Sheehan's syndrome presenting with hyperprolactinaemia.<sup>19</sup>

CT scan of the pituitary gland taken when the patient's PRL and TSH levels were normal revealed a large empty sella. Thyroxine replacement therapy brought TSH level within the normal range and prolactin came down simultaneously. In other words, lactotrophs and/or thyrotrophs shrunk significantly in a short time as a result of the removed overstimulation on the pituitary gland. Empty sella has not been reported in the case reports mentioned above. Jawada *et al.* reported a patient with primary hypothyroidism characterized by high PRL and TSH levels and an enlarged pituitary gland.<sup>20</sup> In this patient, thyroid replacement therapy resulted in regression of the enlarged pituitary and also a partially empty sella demonstrated by pneumonencephalogram.<sup>20</sup> In another patient with primary hypothyroidism whose PRL and TSH levels were above normal intrasellar cisternal herniation demonstrated by CT scan developed after thyroxine therapy.<sup>21</sup>

Since only a few patients with primary hypothyroidism and hyperprolactinaemia develop an empty sella after thyroxine therapy, it can be speculated that this occurs only in patients having an abnormal diaphragma sella. We conclude that thyroxine replacement therapy will result in normalization of the high PRL and TSH levels and shrinkage of the pituitary gland and very rarely an empty sella may develop.

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