

Dome-Shaped Pituitary Enlargement in Primary Hypothyroidism: Avoiding Neurosurgical Interventions

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Abstract

We describe three cases of primary hypothyroidism which presented initially to neurosurgery department with pituitary hyperplasia. We have found a novel pattern of 'dome-shaped' enlargement of pituitary in MRI of these patients. Out of these 3 patients, in two of them, the planned surgery was deferred when endocrinologists were consulted and the pituitary hyperplasia completely resolved with levothyroxine treatment. In the third case, pituitary surgery was already performed before endocrinology consultation and histopathology revealed thyrotroph hyperplasia.

The hyperplastic lesions described typically have a homogenous symmetrical 'dome' shaped architecture unlike the non-functioning pituitary adenoma (NFPA), which usually might often be of varying shapes and homogeneity. Analysis of pituitary images from similar case reports published in literature, also showed this typical 'dome' shaped pituitary enlargement. This imaging characteristic can be a clue to look for underlying hormone deficiency, especially in primary hypothyroidism. Therefore, a thorough endocrine evaluation especially looking for primary hypothyroidism in such dome-shaped pituitary lesions are mandatory to prevent unwarranted neuro-surgical intervention as treatment of primary hypothyroidism may result in resolution of the abnormal enlargement.

Key words: pituitary adenomas, pituitary hyperplasia, dome-shaped enlargement, case report

INTRODUCTION

Pituitary adenomas constitute around 2.7% of supratentorial tumours in childhood and 3.5%-6% of surgically resected tumours.¹ Craniopharyngiomas constitute 80%-90% of the neoplasms arising from pituitary origin.¹ The neoplasms present with visual disturbances but at times with growth failure, delayed puberty, secondary adrenal and thyroid insufficiency.¹ Non-specific headache might also accompany in certain cases.¹ Imaging usually clinches the diagnosis and surgery is the treatment of choice in craniopharyngiomas and many selected cases of non-functional pituitary adenomas. However, pituitary hyperplasia is also seen in end organ insufficiency from primary gonadal insufficiency, primary adrenal insufficiency, and primary hypothyroidism.² Pituitary hyperplasia in untreated overt primary hypothyroidism is more common than previously thought.² Until 2019, there are 105 cases of pituitary hyperplasia in untreated hypothyroidism that have been reported.² Such hyperplasia may take the shape of a dome-shaped elevation and might compress the optic chiasma necessitating neuro-surgical opinion which may result in unnecessary pituitary surgery as was carried out in one of our cases below.²

Unwarranted surgical excision especially in children and adolescent females may result in life-long risk of multiple pituitary hormone deficiency and the need for

life long treatment. We report three such cases of pituitary lesions arising secondarily because of untreated primary hypothyroidism, which simulated an adenoma with a common uniqueness in imaging. This however, resolved spontaneously after levothyroxine supplementation.

CASE 1

A 16-year-old female patient was referred to our institute for consideration of pituitary surgery as the magnetic resonance imaging (MRI) revealed a pituitary tumour. The MRI was done at a peripheral clinic because of a history of primary amenorrhea and short stature. She complained of a minor headache and some eye pain but no visual disturbance. There was no history to suggest any malabsorption. She was the only child of her parents.

Her height was 124 cm (less than 3rd percentile for her age) and a body mass index (BMI) of 21.4 kg/m². Sexual maturity rating revealed that she was in stage 3 for breast development and stage 2 for pubic hair as per Tanner scale. Physical examination was otherwise unremarkable. Laboratory investigation showed haemoglobin 12 g/dL, serum TSH 119.20 µIU/mL, free T4 4.14 pmol/L, prolactin of 36 µg/mL. Further hormonal testing was refused by the parents because of cost issues. The cranial Magnetic Resonance Imaging (MRI) showed pituitary space occupying lesion (SOL) with a size of 15x10x22 mm

abutting the optic chiasma with minimal para-sellar extension into the cavernous sinus inferiorly (Figure 1A). Visual field on confrontation was unremarkable. In view of the grossly raised TSH, it was thought that it could merely be a thyrotroph secreting pituitary hyperplasia rather than a true adenoma. The patient was treated with levothyroxine supplementation at a dose of 75 µgm. The patient attained a height of 131 cm in 6 months. The corresponding thyroid profile was serum TSH 3.36 µIU/mL, free T4 12.4 pmol/L. Follow-up MRI after 6 months revealed complete resolution of the hyperplastic pituitary (Figure 1B).

CASE 2

As in the 1st case, a 15-year-old female patient was referred from primary health care to a neurosurgeon because of

short stature and a possible pituitary tumour on the basis of a MRI performed at the centre suggesting a pituitary macroadenoma. The patient had attained menarche at the age of 13 years but had oligomenorrhea with less than 5 cycles per year. The patient did not have any overt symptoms of hypothyroidism other than easy fatigability. She, however, was a 6th standard drop-out. There were no symptoms suggestive of malabsorption. Physical examination revealed a Tanner stage 4 for breast and pubic hair and had a height of 140 cm which was just less than 3rd centile for her age. Physical examination was otherwise non-contributory. Laboratory investigation showed haemoglobin 11.5 g/dL, TSH >100 µIU/mL, free T4 5.8 pmol/L, prolactin 57.78 µg/L. The MRI (Figure 2) was similar to patient 1 with a dome-shaped superior protrusion of the pituitary gland almost abutting the optic chiasma.

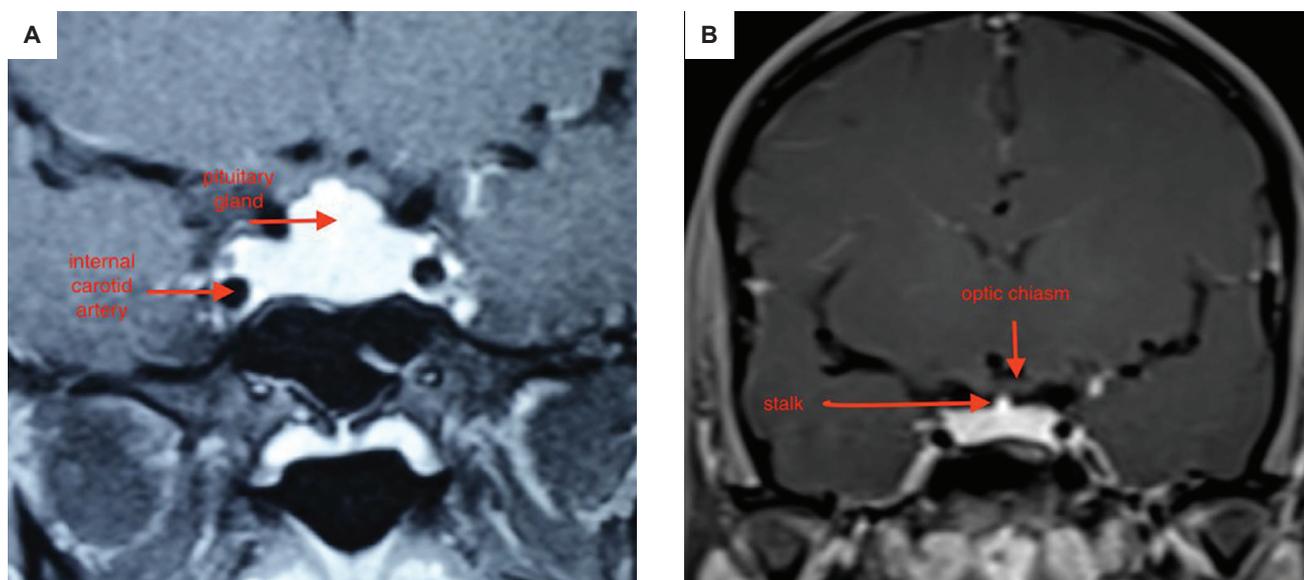


Figure 1. (A) Coronal post contrast T1-weighted image showing pituitary enlargement with dome-shaped convexity. **(B)** Coronal post contrast T1-weighted image showing lesion disappearing 6 months after levothyroxine supplementation.

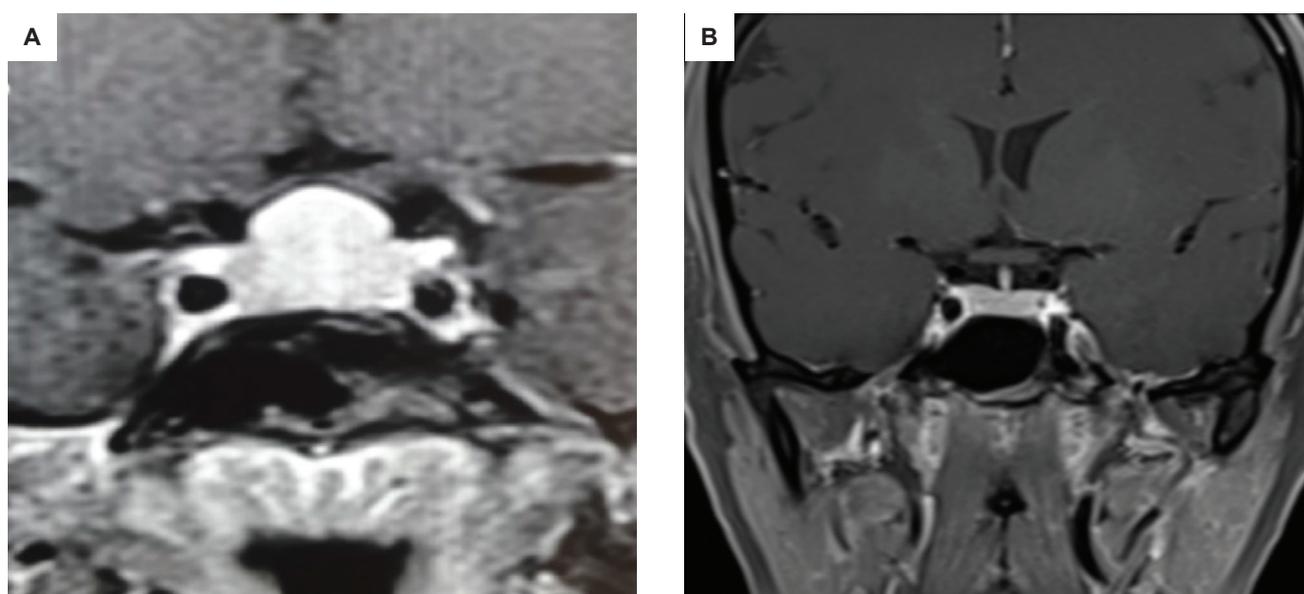


Figure 2. (A) Coronal post contrast T1-weighted image showing dome-shaped superior convexity of the pituitary prior to starting levothyroxine therapy. **(B)** Post coronal T1-weighted image showing post-levothyroxine therapy depicting total resolution of the thyrotroph hyperplasia and obliteration of the “dome.”

Treatment with 75 µgm of levothyroxine was initiated and at the end of 6 months, her TSH was 2.3 µIU/ml and prolactin was 8 µgm/L. The patient had a height of 143 cms and had 4 regular cycles in the preceding 4 months prior to follow-up. A repeat MRI at 6 months revealed complete resolution of the hyperplastic pituitary, previously presumed to be a tumour.

CASE 3

In the aforementioned two cases, an unnecessary Neuro-Surgical intervention was averted not only by Endocrine evaluation but also by the Neuro-Radiologist's insistence of a symmetric, homogenous "Dome-Shaped" pituitary enlargement which was common to both cases which suggested a hyperplasia rather than a tumorous growth. Our third case supplements our 1st two cases where a similar thyrotroph hyperplasia with high TSH levels and a typical "Dome-Shaped," symmetric, homogenous pituitary enlargement was missed due to lack of pre-operative endocrinological intervention and radiological supervision.

A 24-year-old female was referred for endocrine consultation but this time it was on the first post-operative day after pituitary surgery. She was referred in the post-operative period for diabetes insipidus; however, initially sent to the neurosurgical team for a pituitary macroadenoma (Figure 3). She had a history of irregular menstrual cycles for a year followed by secondary amenorrhea for 6 months duration and intermittent headache and a one-month history of blurry vision. The MRI revealed a pituitary macroadenoma with a dome-shaped protrusion towards the optic chiasma of size 13x10x21 cm. This is similar to the above two cases, which we believe is also thyrotroph hyperplasia as evidenced by the typical "Dome sign"

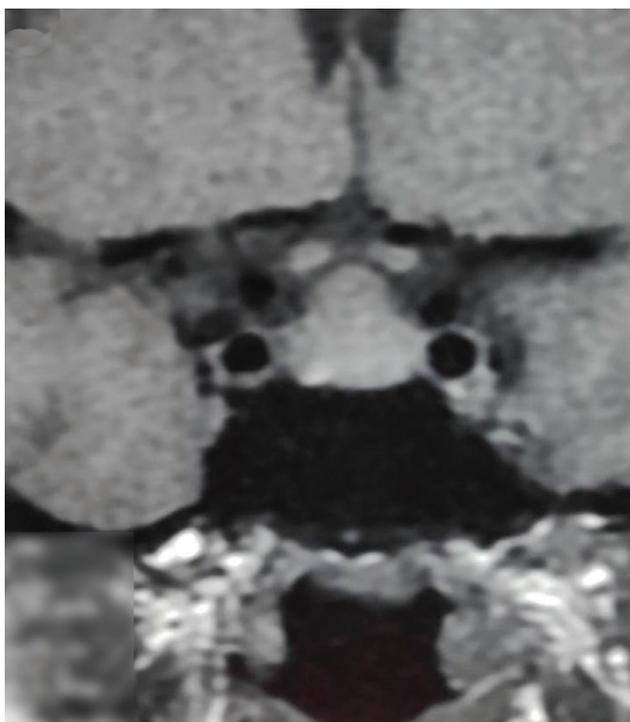


Figure 3. Preoperative coronal T1-weighted image depicting similar pituitary enlargement as in Figures 1 and 2.

and homogenous symmetric architecture. Visual field on perimetry testing was marred by poor comprehension of the patient.

She was seen by an endocrinologist on the first post-operative day for diabetes insipidus as she had a urine output of 3500 ml/24 hrs. Her sodium was 154 mmol/L. On evaluation of the pre-operative hormonal profile it was found that she had a TSH of >100 micro IU/ml. The diabetes insipidus was managed by increase in free fluid intake and it subsided by day 5, when she had a sodium of 136 mmol/L. She was started on a dose of levothyroxine 100 µg post-operatively. The young female fortunately did not have any Post-operative Neuro-hormonal deficits and her regular cycles resumed from the third month post-operative. Post-operative hormonal evaluation performed at 6 weeks revealed a free T4 level of 13.8 pmol/L, 8 am S. cortisol of 9.8 µg/dl, FSH- 5.38 mIU/ml, LH-6.4 mIU/ml and IGF-1 – 213 ng/ml which was normal for her age.

DISCUSSION

The above case reports reveal few unique areas in patients with long-standing hypothyroidism that are of particular clinical relevance. Untreated long-standing hypothyroidism in adolescent females might present with certain symptoms like short stature, amenorrhea (primary or secondary), delayed or precocious puberty, non-specific headache and visual disturbances usually due to benign intra-cranial hypertension, which may closely simulate the features of pituitary adenoma.³ Untreated long standing hypothyroidism results in thyrotroph hyperplasia not only because of lack of feedback inhibition of thyroid hormones on pituitary thyrotrophs but also due to unopposed stimulation by high levels of Thyrotrophin Releasing Hormone (TRH).⁴ Sellar imaging may reveal adenoma which may lead to surgical management. Neuro-surgical initiatives in these cases are not only unnecessary but may also expose the patients to developing multiple pituitary hormonal deficits which require life-long supplementation, and may result in problems with fertility, which fortunately our third patient did not have. A pre-operative endocrine and neuro-radiological evaluation is therefore mandatory in all cases of pituitary adenomas, to avoid unnecessary neurosurgical intervention.

In our series, we also found that there were certain similarities in the imaging characteristics of all three patients. All their lesions had an almost symmetrical dome-shaped architecture i.e., diffuse enlargement of the gland with an upward protrusion. A detailed review of the previous case-reports did show similar architecture. Ahmed et al., put forward the nipple sign based upon CT findings of 5 cases in 1989.⁵ In our series of 3 cases, the MRI revealed enlargement of the pituitary with superior convex margins and extension in suprasellar region with a symmetrical dome shape. This typical morphology with homogeneous signal intensity and contrast enhancement and lack of necrosis/ cystic change/ haemorrhage indicates hyperplasia.

Sarlis et al., demonstrated similar configuration as ours which completely regressed after levothyroxine therapy within 1 month (Figure 4).⁶ Passeri et al., and Franceschi et al., in 2011 reported similar cases with characteristic

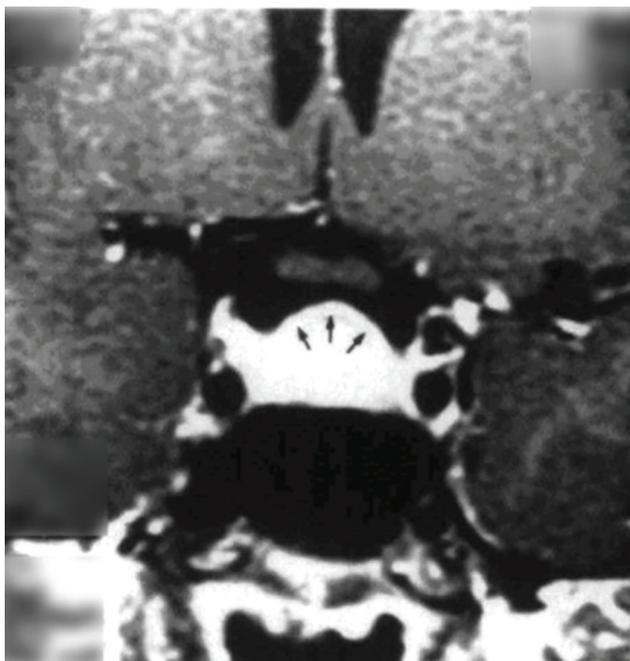


Figure 4. Coronal post contrast T1-weighted image depicting pituitary enlargement with characteristic dome shape (arrows) (used with permission).⁶

similarity as our cases which regressed even within 1 week of levothyroxine therapy (Figure 5 and 6).^{7,8} The MRI of Cao et al., reported in 2018 also did bear the characteristic similarity of the dome-shaped convex homogenous architecture (Figure 7).⁹

Finally, in 2019 Shukla et al., in their detailed review also reported similar findings.² The anatomical location of the thyrotrophs in the midline has been depicted by Ben-Shlomo et al., (Figure 8) which makes it imperative that any hyperplasia in the aforementioned region will cause similar “dome-shaped” imaging characteristic which can alert primary care physicians, gynaecologists

or neurosurgeons to ask for full endocrine evaluation before any surgical intervention is planned.¹⁰

Our cases reveal few aspects of the common problem of untreated hypothyroidism. Firstly, the initial symptoms and signs of hypothyroidism might be subtle enough to remain unnoticed and undetected for a significant time period. Thyrotroph hyperplasia is the usual result. Secondly, the symptoms, particularly in adolescents with short stature, headaches and menstrual disturbances in females, might simulate the features of an NFPA. This often results in imaging studies by primary care physicians or gynaecologists, with or without hormonal evaluation, because in a real world scenario, most cases will consult them initially and not with an endocrinologist.

As soon as an imaging suggestive of pituitary enlargement is found, a Neurosurgical evaluation should follow, which at times may complicate the entire picture as what happened in Case 3. In this context, Du et al., reported two cases of primary hypothyroidism in which pituitary surgery was performed before normalisation of thyroid function (TSH and thyroid hormones) although levothyroxine therapy was started before surgery.¹¹ It is worth mentioning that none of the cases had any obvious neurologic deficit before or after treatment. Thirdly, an expert neuro-radiological evaluation of the MR images depicting the “dome” sign, together with hormonal evaluation will lead to the correct diagnosis, that of primary hypothyroidism, and prevent unnecessary neuro-surgical intervention.

CONCLUSIONS

Untreated hypothyroidism leading to the development of thyrotroph hyperplasia is still a common entity, not only in developing but also in the developed world. Neuro-surgical initiatives in these cases is not only unnecessary, but also can cause patients to have multiple pituitary hormonal deficits which require life-long supplementation, lead to problems with fertility and finally, loss of bone mineral density which adds on to the morbidity.

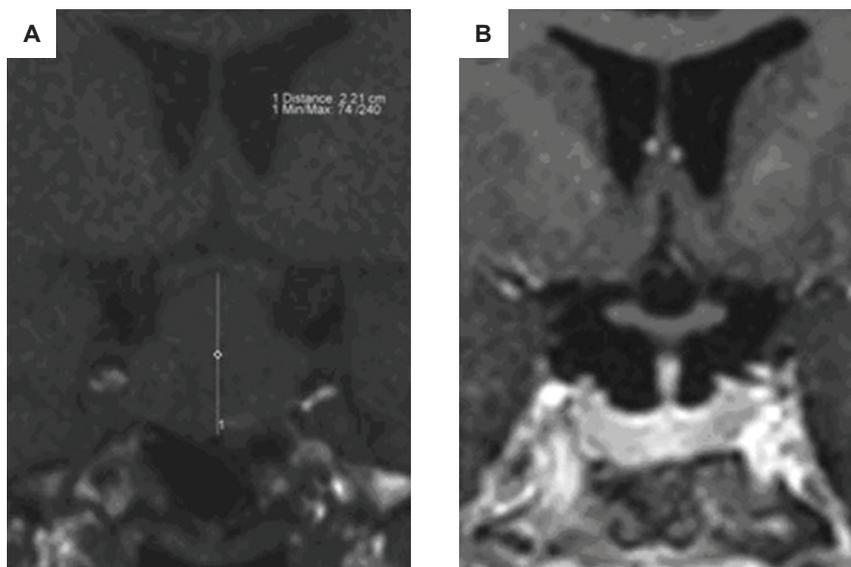


Figure 5. (A) Coronal T1 image showing pituitary enlargement which **(B)** regressed subsequently on Levothyroxine supplementation (used with permission).⁷

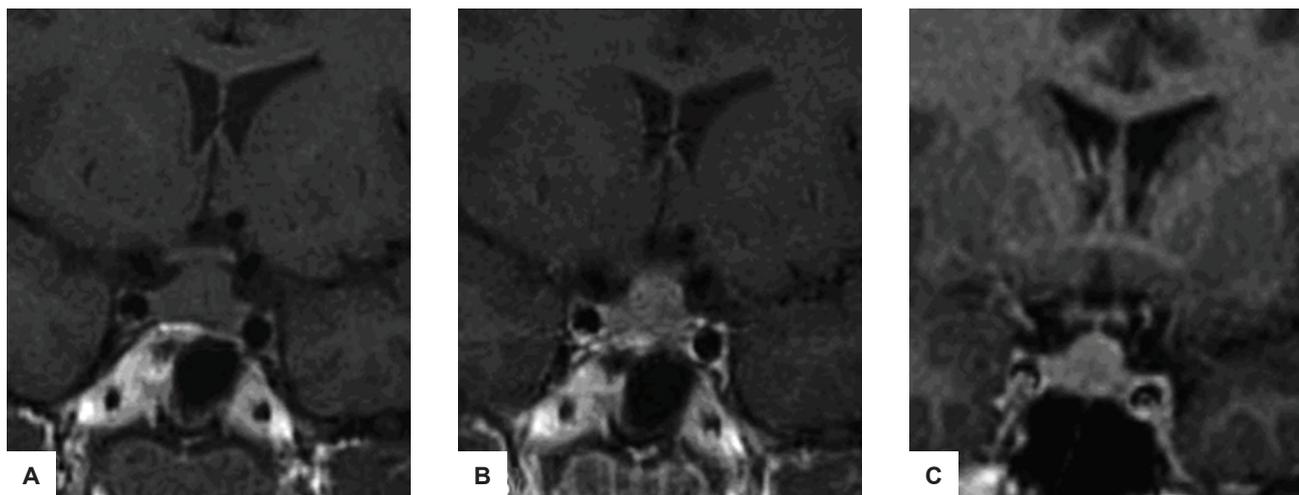


Figure 6. Coronal (A) pre and (B) post contrast T1 image showing characteristic dome-shaped pituitary which shows (C) resolution on follow up image (used with permission).⁸



Figure 7. Coronal post contrast T1-weighted image showing homogeneously enhancing pituitary gland with superior convexity reaching up to optic chiasm (used with permission).⁹

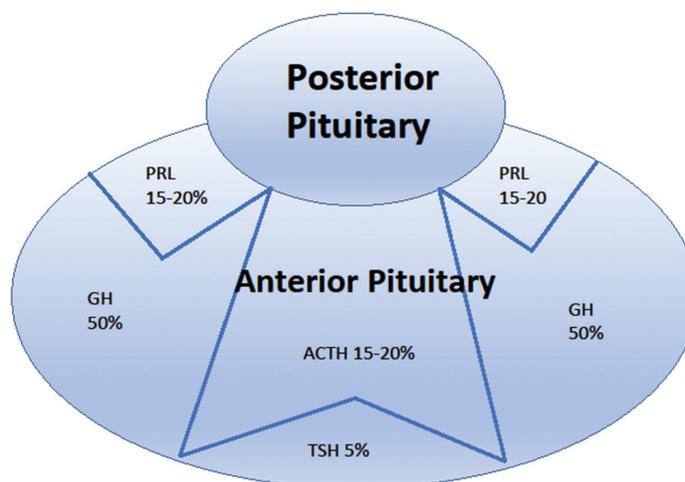


Figure 8. Anatomical location of the thyrotrophs (adapted).¹⁰

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Our discussion not only adds to the already established necessity of endocrine evaluation prior to all pituitary surgeries, but also recommends that the presence of a “DOME sign” on MRI of the pituitary along with an elevated TSH, suggests thyrotroph hyperplasia due to primary hypothyroidism rather than a true pituitary adenoma and therefore, patients can be treated medically by levothyroxine supplementation with the expectation of complete regression of the hyperplastic growth.

Ethical Considerations

Patients’ consent were obtained before submission of the manuscript.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

All authors declared no conflicts of interest.

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