Physiological pituitary hyperplasia misinterpreted and treated as lymphocytic hypophysitis

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DESCRIPTION

A 19-year-old nulliparous eumenorrhoeic woman diagnosed with bilateral serous retinal detachment was referred for incidentally detected enlarged pituitary gland, seen on MRI of orbit. A focused MRI documented diffuse, symmetric enlargement of the pituitary gland having a convex superior surface abutting the optic chiasm (11.4 mm in antero-posterior × 16.9 mm in transverse × 9.3 mm in height) with marked homogeneous gadolinium enhancement with a thickened, non-tapering stalk (3.5 mm at infundibulum) and a conspicuous eutopic posterior pituitary bright spot (figure 1). A comprehensive work-up remained unremarkable (table 1). In view of symmetric, enlarged pituitary demonstrating intense homogeneous contrast enhancement and a thickened (>2–3 mm thickness is considered pathological), non-tapering pituitary stalk in this non-pregnant individual, a diagnosis of lymphocytic hypophysitis (LH) was considered, after ruling out the other possible differential diagnosis. Pulse therapy with intravenous methylprednisolone was initiated followed by maintenance therapy with daily prednisolone gradually tapered over 12 weeks. However, serial MRI 4 days following therapy, at 6 months and a year later (figure 2), failed to demonstrate any significant reduction of pituitary or stalk size, necessitating a review of diagnosis.

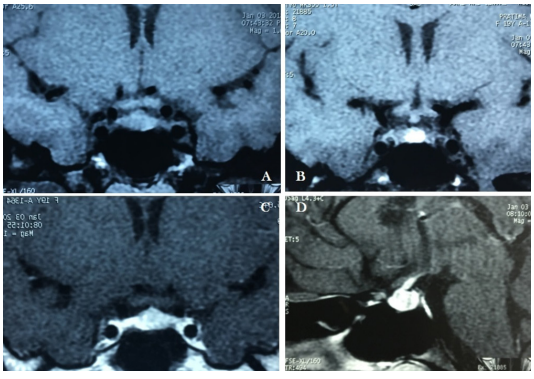

Figure 1 MRI at initial presentation showing diffuse enlargement of pituitary (A), thickened stalk with conspicuous bright spot (B) and intense homogenous contrast enhancement (C, D) of both pituitary and stalk.

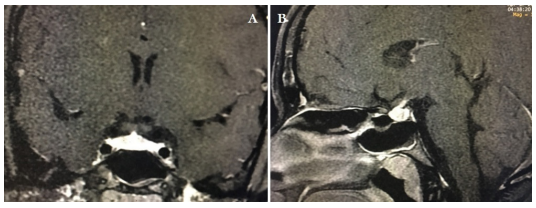

Figure 2 Post-contrast MRI at 1 year follow-up showing enlarged pituitary (A) with intense and homogenous contrast enhancement with a thickened stalk (B). The appearance is unchanged from the initial MRI.

Incidental pituitary enlargement is a frequent cause of referral to endocrinologists. The pituitary gland exhibits wide variations in size and shape across different age, sex and ethnicity cohorts.

Table 1 Summary of investigations

Parameter	At presentation	After 12 months	Reference range
Cortisol (08:00)	15.68	11.6	05–25 µg/dL
Cortisol after overnight 1 mg dexamethasone suppression test	1.2		<1.8 µg/dL
Thyroid-stimulating hormone	0.79	0.9	0.34–4.25 mIU/L
FT4	1.1	1.4	0.7–1.24 ng/dL
T3	102	98	77–135 ng/dL
Prolactin	13.86	15.04	1.9–25 ng/mL
Insulin like growth factor (IGF)1	224		138–442 ng/mL
β human chorionic gonadotropin (HCG)	1.2		<5 mIU/mL
Cerebrospinal fluid (CSF) appearance	Colourless, clear		
CSF cell count	2		0–5 mononuclear cells/µL
CSF protein	30		15–50 mg/dL
CSF angiotensin converting enzyme (ACE)	<0.1		0.0–2.5 U/L
CSF adenosine deaminase (ADA)	0.3		0–1.5 U/L
CSF PCR for *Mycobacterium tuberculosis*	Not detected		
CSF β HCG, quantitative	0.1		0–3 IU/L

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Physiological pituitary hypertrophy (pituitary height ≥9 mm) is observed during puberty and pregnancy, in young women and after menopause.[1] In healthy women between 15 and 30 years of age, the height of the pituitary varied from 3 to 9 mm, as observed in neuroradiological series.[1] A population study from India observed a mean pituitary height of 6.0 (±1.6 SD) mm in females belonging to 11–20 years of age.[2] Pathological pituitary hypertrophy may occur in long-standing untreated end organ insufficiency with loss of negative feedback (primary hypothyroidism, primary hypogonadism), hypothalamic or neuroendocrine tumours secreting excess trophic hormones [growth hormone releasing hormone (GHRH), corticotropin releasing hormone (CRH)] and a number of inflammatory or infiltrative diseases (lymphocytic and granulomatous hypophysitis, sarcoidosis, haemochromatosis, amyloidosis, Langerhans cell histiocytosis, Wegener's granulomatosis), infective (tuberculosis) and neoplastic (germinoma, lymphoma, leukaemia, metastatic carcinoma) disorders. Underlying tuberculosis, sarcoidosis and central nervous system germinoma were excluded with certainty in this woman with appropriate tests. Central serous retinopathy, rarely, has been known to be associated with Cushing's disease. Serous retinal detachment with subretinal fluid accumulation, a variant of central serous retinopathy, along with pituitary enlargement with thickened stalk in this woman, necessitated a thorough evaluation. Since corticosteroids have a beneficial role in early stages of LH,[3] high-dose glucocorticoids were administered. Learning from our errors, we conclude this patient to be a case of physiological hypertrophy of the pituitary gland (PH). Without a pituitary biopsy the diagnosis of PH, although highly likely in this woman, remains presumptive. Since the duration of persistent peripubertal pituitary hyperplasia is unknown and data on epidemiology, diagnosis or management of PH are scarce, and a pituitary biopsy facilitating a tissue diagnosis remains elusive in routine clinical practice, the diagnosis of PH is largely clinico-hormono-radiological. Thus, pituitary enlargement (pituitary height ≥9 mm, or greater than that predicted by age, gender and ethnicity matched values, when available) with a normal hormonal assessment (absence of hyperprolactinaemia or diabetes insipidus in particular) and gland homogeneity on MRI (plain and contrast) with a conspicuous posterior pituitary bright spot should also be considered as normal pituitary hypertrophy to avoid therapeutic misadventures.

Learning points

- Pituitary gland dimensions in normal individuals are largely influenced by age, gender and ethnicity.
- Pituitary height ranging from 3 to 9 mm with anteroposterior and transverse diameter of 10–14 mm is considered normal.
- The pituitary stalk normally is widest superiorly and tapers inferiorly measuring 3.5 mm near median eminence, 2.9 mm near its midpoint and 1.9 mm at its insertion to the pituitary.
- Physiological pituitary hypertrophy is observed during puberty and pregnancy, in young women and after menopause.
- The duration of persistence of physiological hypertrophy following puberty is not known.
- Minimal pituitary enlargement (height ≥ 9 mm, or greater than that predicted by age, gender and ethnicity matched values, when available) with a normal hormonal assessment (absence of hyperprolactinaemia, cortisol deficiency or diabetes insipidus in particular) and gland homogeneity on MRI (plain and contrast) with a conspicuous posterior pituitary bright spot should be considered as normal pituitary hypertrophy.
- Correct identification of pituitary hypertrophy obviates the need of unnecessary therapeutic interventions as it rarely progresses.

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