

Nonfunctional Pituitary Macroadenoma Manifested as Muscular Symptoms

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ABSTRACT

A 75-year-old man with a large pituitary adenoma presented with general muscular weakness, including difficulty in rising in the morning and forceless defecation and urination, and muscular pain, numbness and atrophy in the shoulder, neck and thigh. Testosterone replacement and subsequent resection of the pituitary tumor resulted in resolution of the symptoms. The value of pituitary imaging tests for men with hypogonadotropic hypogonadism is discussed.

Key words: Pituitary adenoma, Muscular symptoms, Hypogonadism

Nonfunctional pituitary adenomas are benign tumors with a predilection for developing in middle-aged or senile males⁵. Usually, because of lack of hormone hypersecretion, these tumors are not diagnosed until they become large enough to compress the optic nerve. Patients therefore frequently present with signs of mass effects, including visual field deficits and disturbance of visual acuity. Here we report a man with hypogonadism who showed marked muscular symptoms due to a large nonfunctional pituitary adenoma, and refer specifically to the value of pituitary imaging tests.

CASE REPORT

The patient was a 75-year-old man who presented with symptoms of general muscle weakness such as difficulty in rising in the morning and forceless defecation and urination, together with muscular pain, numbness and atrophy in the shoulder, neck and thigh over the previous three months. Physical examination including neurological assessment showed no abnormality except for decreased testicular size (6 cc bilaterally). Results of gonadal hormonal tests were testosterone (T) 8 ng/dl (normal 270–1070), luteinizing hormone (LH) 0.43 mIU/ml (normal 1.2–7.0),

follicle-stimulating hormone (FSH) 2.52 mIU/ml (normal 2.0–8.3), and prolactin (PRL) 22.3 ng/ml (normal 3.6–12.8), indicating hypogonadotropic hypogonadism. A single injection of testosterone enanthate (150 mg) to alleviate the castrated level of T dramatically relieved the symptoms for 2 weeks. Brain MRI examination demonstrated a solid sellar mass (26 × 18 × 23 mm) with suprasellar extension, compatible with a pituitary adenoma (Fig. 1). Visual field analysis demonstrated no temporal hemianopia, although there was an area of low sensitivity on the left lower nasal side (Fig. 2). Subsequent hormonal examinations, including tolerance tests, demonstrated panhypopituitarism with both low baseline and peak cortisol levels (Table 1). Oral prednisolone (5 mg/day) was started, and shortly afterwards the patient underwent transsphenoidal resection of the tumor. Pathological examination confirmed the diagnosis of papillary type of pituitary adenoma. Postoperatively, the patient was followed up while receiving oral prednisolone (5 mg/day) for 3 months and levothyroxine sodium (25 µg/day) for 2 months, without testosterone replacement. The muscular symptoms disappeared completely at one month after surgery and beyond. The laboratory data at 3 months after surgery were T 14

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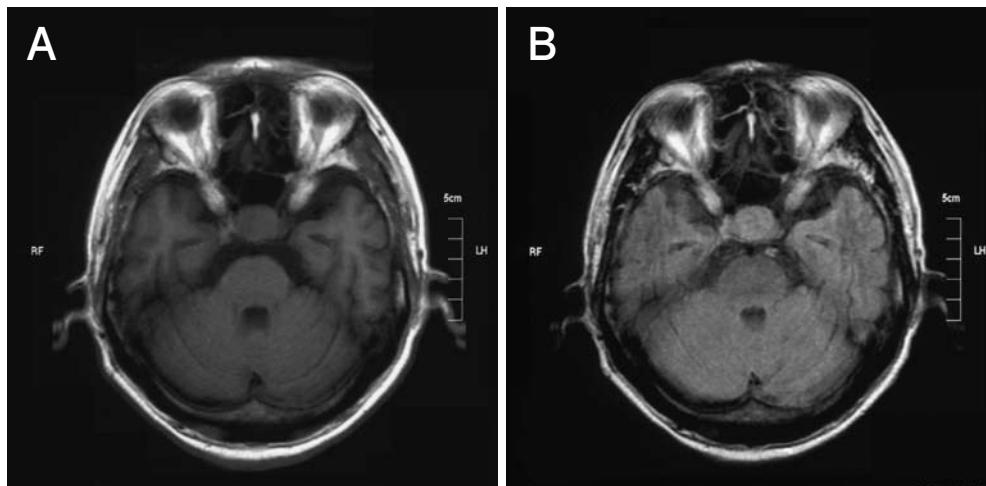


Fig. 1. Brain magnetic resonance imaging (MRI).

A, T1-weighted image. B, T2-enhanced image.

The T1-weighted image shows a smoothly outlined solid sellar tumor with suprasellar extension displaying low intensity, whereas the T2-enhanced image shows an area of high intensity close to that of the cerebral gray matter.

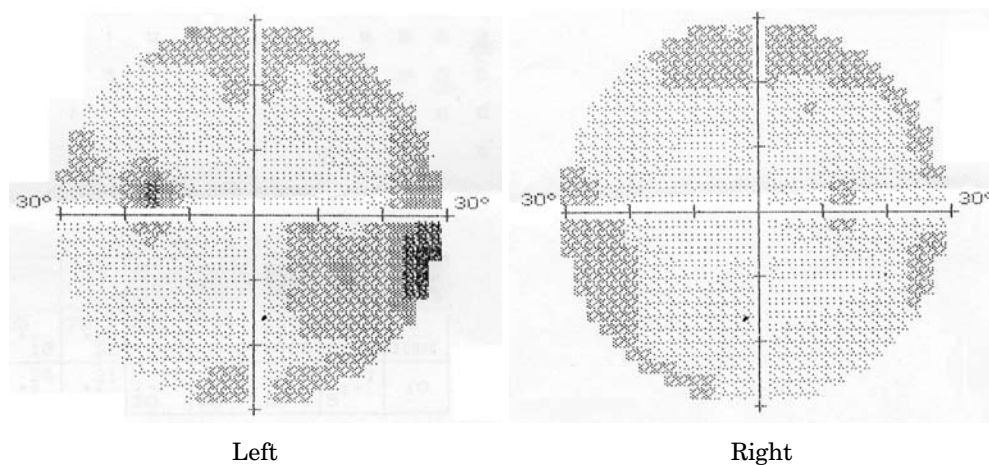


Fig. 2. Static visual field test.

Right, normal. Left, there is a low-sensitivity area on the lower nasal side, but no temporal hemianopia.

Table 1. Results of hormone tolerance tests

	Reference value	Baseline	30 min	60 min	90 min
LH (mIU/ml)	1.2-7.0	0.4	0.9	1.3	
FSH (mIU/ml)	2.0-8.3	2.0	2.4	2.6	
Prolactin (ng/ml)	3.6-12.7	29.1	38.0	31.4	
Testosterone (ng/ml)	2.7-10.7	0.08			
ACTH (pg/ml)	7-56	24.0			
Cortisol (μ g/dl)	4.0-23.3	3.1	4.2	9.3	9.3
TSH (μ IU/ml)	0.49-4.6	3.95			
Free T4 (ng/dl)	0.7-1.8	0.56			
GH (ng/ml)	<1.4	0.46	0.86	0.93	0.54

† Human rapid insulin 7 u., intravenous injection

Luteinizing hormone-releasing hormone (LH-RH) 100 μ g, intramuscular injection

LH, luteinizing hormone; FSH, follicle-stimulating hormone; ACTH, adrenocorticotrophic hormone; TSH, thyroid-stimulating hormone; GH, growth hormone

ng/dl, LH 0.8 mIU/ml, FSH 2.0 mIU/ml, PRL 2.4 ng/ml, free T4 0.80 ng/dl (normal 0.71–1.85), and cortisol 8.7 µg/dl (normal 4.0–23.3) under administration of prednisolone. Repeat measurements conducted 1 year later revealed T 18 ng/dl, free T4 0.73 ng/dl and cortisol 5.7 µg/dl. At this time, testicular size was 8 cc bilaterally.

DISCUSSION

In male patients with large nonfunctional pituitary adenomas, the most frequently observed signs of anterior pituitary insufficiency are hypogonadism typified by erectile dysfunction or decreased libido⁵. The present patient showed predominant muscular symptoms in the form of general muscle weakness, together with muscle pain, numbness and atrophy. The fact that testosterone replacement dramatically alleviated the symptoms indicates that the signs resulted from testosterone deficiency. These muscular symptoms are also significant somatic signs in men with partial androgen deficiency of the aging male (PADAM) or late-onset hypogonadism (LOH)⁴. However, they may be mistaken for signs of muscular disorders, including polymyalgia, when they are unaccompanied by other typical hypoandrogenic symptoms such as impotence. To avoid diagnostic confusion, therefore, it is important to remember that muscular symptoms can be associated with male hypogonadism.

Although nonfunctional pituitary adenomas are most commonly manifested as hypogonadism, the value of pituitary gland imaging tests for men with hypogonadism remains unclear^{1,2,7,8}. While some argue that such imaging rarely yields clinically significant results, others consider that it offers an opportunity to detect a treatable adenoma that might otherwise be missed. Rhoden et al⁸ and Citron et al² have reported that pituitary adenomas were found in 7.8% and 8.5% of men with hypogonadotropic hypogonadism, respectively, using hypothalamohypophyseal MRI or CT. However, the great majority of them were microadenomas with a diameter of less than 10 mm and unknown growth potential, and only 0–2.4% of them were macroadenomas measuring 10 mm or larger and possibly requiring surgical resection. Recently, Hall et al³ observed that 3 of 30 normal men (10%) had MRI-detectable lesions 3 to 6 mm in diameter, suggestive of pituitary adenomas. In a review of 12 autopsy series, Molitch and Russell⁶ estimated a 10–20% prevalence of incidental pituitary or hypothalamic adenoma. Considering this prevalence of incidentaloma, the likelihood of identifying clinically significant pituitary adenomas by MRI appears to be low among men with secondary hypogonadism.

However, the risk of pituitary imaging abnormalities increases considerably when the serum

T level is markedly decreased. Citron et al² found that the serum T levels of men harboring macroadenomas were all less than 100 ng/dl (25–99, mean 63 ng/dl), being apparently lower than those (137–178, mean 157 ng/dl) in men with microadenomas (5–10 mm) or those (13–226, mean 177 ng/dl) in men without abnormality. These findings were compatible with the present patient, whose level of testosterone was equivalent to that of a castrated individual. These data suggest that T levels are a useful predictor for identifying pituitary adenoma. A lower T value indicates a higher likelihood of pituitary adenoma, and therefore pituitary imaging should be considered.

With regard to the postoperative course, the present patient was relieved of his muscular symptoms and required no testosterone replacement after surgery. The T value increased from 8 ng/dl at the time of diagnosis to 18 ng/dl at 1 year after surgery, but this was still within the castrated range. It is therefore uncertain whether or not the improvement of the patient's subjective symptoms was due to the negligible recovery of the T level. However, there is a possibility that as sensitivity to T had been highly increased due to the long-term deficiency of T, even the small recovery of the T level resulted in resolution of the symptoms. To prove this hypothesis, confirmation of whether a low amount of T would resolve the symptoms in the event of future recurrence would be necessary.

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