

## Follicle stimulating hormone secreting pituitary macroadenoma in males: A rare entity

Sir,

A follicle stimulating hormone (FSH) secreting pituitary adenoma is a rare entity. It can present with features of optic chiasmal compression, with other symptoms of local expansion or can affect sexual and reproductive function. Classically, pituitary tumors are divided into functional (or secreting), and nonfunctional (endocrinologically inactive). Nonsecreting tumors usually do not manifest themselves until they attain a sufficient size to cause neurologic deficits by their mass effect. Nonfunctioning pituitary adenomas are the most common type of adenomas and are usually macroadenomas at the time of diagnosis. Gonadotropin-suppressing pituitary tumors are not rare, accounting for approximately 25% of all pituitary tumors.<sup>[1]</sup> These adenomas secrete low levels of FSH, luteinizing hormone (LH), or only the biologically inert alpha or beta subunits of these hormones. Therefore, most pituitary adenomas are endocrinologically silent and patients usually present with visual field defects and neurological deficits due to the mass effect. FSH-secreting pituitary adenomas are, therefore, extremely rare.

A 40-year-old married male, the father of two children, presented with complaints of loss of libido and erectile dysfunction accompanied by decreased volume of ejaculation for the last 3 years. He also had complaints of visual disturbances and headache for 2 years, and generalized tonic-clonic seizures for the last 7 months. The physical examination was unremarkable. Fundoscopy revealed bilateral temporal disc pallor. Perimetry showed a bitemporal hemianopia with left superior nasal quadrantanopia. His psychosexual evaluation was normal.

Magnetic resonance imaging (MRI) revealed a solid-cystic space occupying lesion in the sellar-suprasellar region, which was extending until the third ventricle as well as the left cavernous sinus. It had encased the left supraclinoid internal carotid artery, proximal left anterior cerebral artery, and middle cerebral artery and also had a left subtemporal extension. The lesion was compressing the optic chiasma and was causing localized destruction of the sellar floor. A portion of the lesion showed gadolinium contrast enhancement [Figures 1 and 2].

The hormonal assay in blood revealed a normal prolactin (PRL) level of 19.6ng/ml (4.6–21.4ng/ml), a raised serum FSH level of 195mIU/ml (1.55–9.74mIU/ml) with a normal thyroid stimulating hormone (TSH) level of 3.71mIU/ml (0.27–4.2mIU/ml), a normal LH of 2.2mIU/ml, a normal growth hormone (GH) level of 2.4ng/ml (0.0–4.0ng/ml), and there was decreased serum testosterone (T) level of 2.78nmol/L (4.56–28.2nmol/L). The seminal fluid report of the patient before his operation supported the diagnosis of oligoasthenozoospermia [Table 1]. The gonadal hormone levels before the operation are shown in Table 2. In view of the raised FSH and low testosterone, a diagnosis of secondary infertility due to pituitary adenoma was considered.

The patient was evaluated by an endocrinologist and medical treatment was given to treat the symptoms but there was no response. An elective surgery was performed with near total tumor decompression performed via the transcranial route.

The postoperative pathology revealed a pituitary adenoma. Immunohistochemistry of the tumor cells showed cytoplasmic positivity for FSH [Figure 3], GH, and PRL.

The patient has a good recovery and resumed his normal sexual activity after 3 months of the operation. His semen study improved, as evident in semen analysis done 3 months after the operation [Table 1]. The concentrations of FSH and testosterone had also improved 3 months after the operation [Table 2].

Pituitary tumors are common lesions believed to account for 10 to 15% of all primary brain tumors.<sup>[2]</sup> More precise estimates on their incidence and prevalence vary to some degree, depending on the means utilized to survey them, the population studied, and the period of the study. Data from academic medical centers suggest that pituitary tumors represent as many as 20% of the surgically resected primary brain tumors. Epidemiologic estimates indicate an annual incidence of 8.2 to 14.7 cases per 100,000 people.<sup>[2]</sup>

Approximately 30% of pituitary adenomas are clinically nonfunctional, as defined by the absence of excessive hormone secretion found by various endocrinological or routine histological examinations. The simplest approach to classifying pituitary adenomas, one favored by clinicians, is the functional classification. This classification broadly distinguishes tumors as functional or non-functional, based on their secretory activity *in vivo*. Functional adenomas are those that secrete PRL, GH, TSH, or adrenocorticotrophic

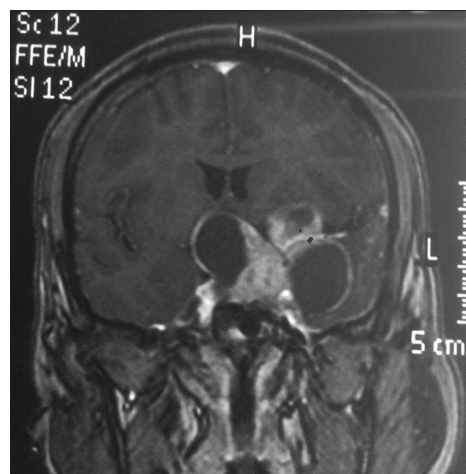


Figure 1: Magnetic resonance imaging, coronal section, showing a solid-cystic space occupying the lesion in the sellar-suprasellar region with left subtemporal extension. The solid part and the wall of the cystic part were showing contrast enhancement

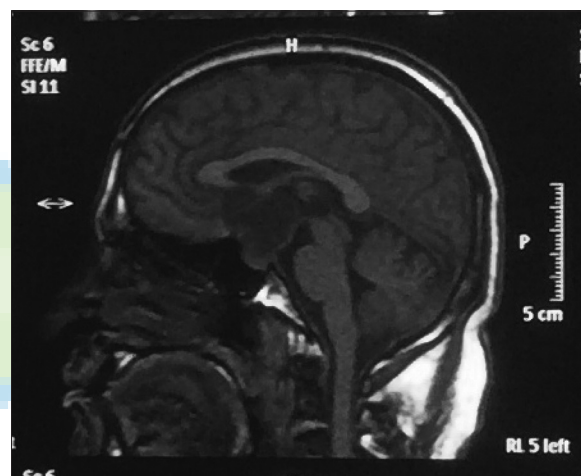


Figure 2: Magnetic resonance imaging, T1-weighted sagittal image, showing the sellar-suprasellar lesion extending until the third ventricle

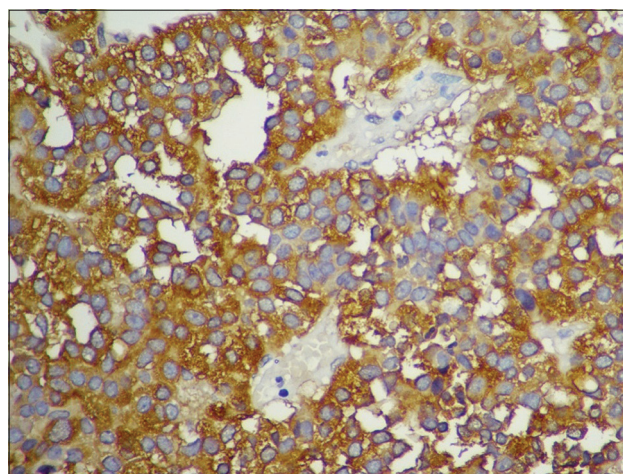


Figure 3: The tumor cells were positive for follicle stimulating hormone immunostaining (High Power Field 40x)

**Table 1: Comparison of pre- and postoperative semen analysis**

	Before operation		3 months after operation		Reference range
	No. 1	No. 2	No. 1	No. 2	
Sexual abstinence (days)	6	6	6	6	2-7
Semen volume (ml)	0.5	0.4	2.8	2.7	≥1.5
pH	7.8	7.7	7.5	7.6	≥7.2
Sperm concentration (10 <sup>6</sup> /ml)	10.6	10	16	16	≥15
Progressive motility (PR%)	9	9	28	30	≥32

**Table 2: Comparison of pre- and postoperative sex hormones**

	Before operation		3 months after operation		Reference range
	No. 1	No. 2	No. 1	No. 2	
Sexual abstinence (days)	6	6	6	6	2-7
Semen volume (ml)	0.5	0.4	2.8	2.7	≥1.5
pH	7.8	7.7	7.5	7.6	≥7.2
Sperm concentration (10 <sup>6</sup> /ml)	10.6	10	16	16	≥15
Progressive motility (PR%)	9	9	28	30	≥32

hormone (ACTH), producing their respective clinical phenotypes of amenorrhea-galactorrhea syndrome, acromegaly or gigantism, secondary hyperthyroidism, and Cushing's disease or Nelson's syndrome, respectively. Tumors that are not associated with a clinical hypersecretory state (gonadotrophic adenomas, null cell adenomas, oncocytomas, and various silent adenomas) are collectively designated as being clinically nonfunctional. Most clinically nonfunctioning pituitary adenomas are gonadotrope-derived, and, in most cases, these adenomas secrete low levels of FSH, LH, or only the biologically inert alpha or beta subunits of these hormones. Therefore, most pituitary adenomas are endocrinologically silent and the patients commonly present with a mass effect such as impaired vision, headache, or hypopituitarism.<sup>[3]</sup>

Our patient had increased blood FSH, normal TSH, GH, LH levels, and a decreased blood testosterone (T) level. Heseltine *et al.*, reported FSH-producing pituitary macroadenomas with testicular enlargement in four patients who improved after surgery and showed decreased testicular volumes after an operation for the pituitary adenoma.<sup>[4]</sup> In contrast, other previously reported male patients harbouring a FSH-secreting pituitary adenoma have been reported to have either a normal or a small testicular size.<sup>[5]</sup>

In a study that included 30 men with gonadotrophic adenomas (13 cases with elevated serum FSH), all patients were reported to be having a normal testicular volume (no detailed data was presented).<sup>[6]</sup> Our patient had a normal

testicular size with loss of libido. He also had an erectile dysfunction accompanied by decreased volume of ejaculation.

Clinically, nonfunctional pituitary adenomas are often derived from gonadotropin producing cells. However, gonadotropinomas causing elevated serum levels of FSH and clinical signs of FSH hypersecretion are very rarely described.<sup>[7]</sup> In this report, the primary symptom was sexual and reproductive dysfunction associated with neurological symptoms and visual field defects. The serum FSH level was elevated in the blood accompanied by a decrease in the testosterone level. Thus, our patient had secondary infertility caused by a raised FSH level, which showed improvement within 3 months of follow up. There is often a discrepancy between the cell lineage of this tumor and its serum hormone level. It may be because the hormone is formed and stored in cells belonging to a particular cell lineage but is not secreted; or, there is the possibility that a subunit of that particular hormone is secreted but is not traceable by our standard tests.

Through this report, we would like to draw attention to the fact that FSH-secreting pituitary adenomas in male patients may present with secondary infertility. Improvement in the clinical status may be expected after surgery in such cases.

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#### Conflicts of interest

There are no conflicts of interest.

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