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Macroorchidism in a Patient with FSH-Secreting Pituitary Macroadenoma

FSH Salgılayan Hipofiz Makroadenomlu Bir Hastada Makroorşidizm

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Abstract

Follicle-stimulating hormone-secreting pituitary macroadenoma (FSHoma) is a very rare and usually asymptomatic entity. FSHoma can clinically present as ovarian hyperstimulation syndrome in female patients, but symptoms and clinical signs are usually not observed in males. An increase in testicular volume has been reported in male patients with FSHoma. In some male patients, the first finding may be macroorchidism. A 20-year-old male patient presented to our clinic due to enlarged testes (testicular volume: 45 cc). Scrotal ultrasonography showed macroorchidism. Tests required to determine the etiology of macroorchidism showed that the patient had an elevated FSH concentration. Macroadenoma was diagnosed based on pituitary magnetic resonance imaging. FSHoma was suspected and transsphenoidal resection was performed. Pathology test results indicated FSHoma. The present case shows that FSHoma is very rare and that it can present in association with macroorchidism in male patients. *Turk Jem 2012; 16: 95-8*

Keywords: Follicle-stimulating hormone-secreting pituitary macroadenoma, macroorchidism

Özet

Folikül-uyarıcı hormon salgılayan hipofiz adenomu (FSHoma) çok nadirdir ve genellikle asemptomatiktir. Kadın hastalarda ovaryan hiperstimülasyon sendromuna benzer tabloya neden olabilmektedir. Fakat, erkek hastalarda genellikle herhangi bir semptom ve klinik belirti görülmez. FSHoma'lı erkeklerde testiküler hacimde artış görülebileceği bildirilmiştir. Hastalarda nadiren ilk bulgu makroorşidizm olabilmektedir. Yirmi yaşında erkek hasta, testislerinde büyüme olması nedeniyle kliniğimize başvurdu. Hastanın testikuler hacmi 45 cc idi. Skrotal ultrasonografide makroorşidizm saptandı. Hastanın makroorşidizm etiyoloji araştırılmak üzere istenen tetkiklerinde FSH konsantrasyonu yüksek olarak bulundu. Hipofiz manyetik rezonans görüntülemesinde makroadenom saptandı. Hastada FSHoma düşünüldü ve transsfenoidal rezeksiyon yapıldı. Patoloji sonucu FSHoma olarak değerlendirildi. Sonuç olarak, FSHoma çok nadir görülmektedir ve erkek hastalarda nadiren makroorşidizm ile karşımıza çıkmaktadır. *Türk Jem 2012; 16: 95-8*

Anahtar kelimeler: Folikül-uyarıcı hormon salgılayan hipofiz makroadenomu, makroorşidizm

Introduction

Pituitary adenomas account for 15% of all intracranial neoplasms. Non-functional pituitary adenomas, of which 80% are gonadotropin-secreting adenomas, were reported to account for between 15% and 45% of all pituitary tumors. Follicle-stimulating hormone-secreting pituitary macroadenoma (FSHoma) is extremely rare (1,2). Gonadotroph tumors usually secrete their products inefficiently and in low concentrations and, thus, very rarely cause any clinical syndrome other than sellar mass effects (3,4). Excessive secretion of FSH has more commonly been reported in men with gonadotropin-secreting adenomas, however, it does not cause any symptoms (5-7). Several cases of FSH-secreting microadenoma with macroorchidism have been reported (8,9). Herein, we report a patient with FSHoma who presented with macroorchidism-a rarely observed clinical symptom.

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Case Report

A 20-year-old male patient presented to our clinic due to enlarged testes (enlargement occurred during the 3 weeks prior to presentation). Scrotal ultrasonography showed macroorchidism. Testicular volume was 45 cc and endocrine evaluation showed the following: luteinizing hormone (LH): 1.49 µIU/mL (normal: 0.8-7.6 µIU/mL); FSH: 93.7 µIU/mL (normal: 0.7-1.1 µIU/mL); thyrotropin: 1.32 µIU/mL (normal: 0.4-4 µIU/mL); free thyroxine: 1.2 ng/dL (normal: 0.8-1.9 ng/dL); estrogen: 38.9 pg/mL (normal: 0-56 pg/mL); prolactin: 27.7 ng/mL (normal: 2.5-17 ng/mL); dehydroepiandrosterone: 216 µg/dL (normal: 80-560 µg/dL); total testosterone: 502 ng/mL (normal: 262-1593 ng/mL); basal morning serum cortisol level: 18 µg/dL (Table 1).

Pituitary magnetic resonance imaging (MRI) was scheduled because the patient's prolactin and FSH concentrations were elevated. Pituitary MRI showed an intrasellar tumor measuring 115x25x25mm, consistent with macroadenoma (Figure 1). There were heterogeneous parenchymal areas and cystic degeneration in the central and the optic chiasm displaced to the cranium. The patient's cortisol level was 1 µg/dL based on the 1-mg dexamethasone suppression test. A 100-g oral glucose tolerance test was administered with a basal growth hormone (GH) level of 0.3 ng/mL in order to diagnose acromegaly; GH levels were measured and suppression was seen as in normal people (GH<1 ng/mL). The insulin-like growth factor-I (IGF-I) level was 228 ng/mL (normal: 150-562 ng/mL), which was within normal limits. The prolactin levels may increase due to the inhibitory effect of dopamine in diseases affecting the pituitary stalk. A visual field test was performed due to the existence of a macroadenoma and the results were normal. There were neither signs nor symptoms of compression to the optic tract. As such, FSHoma was diagnosed and the patient underwent transsphenoidal resection of the pituitary mass. As the patient's basal morning serum cortisol level was 18 µg/dL, the reserve was thought to be sufficient and surgery under steroid therapy conditions was considered to be unnecessary. Immunohistochemical staining of the pituitary adenoma specimen was positive for FSH (Figure 2) and LH, whereas staining was

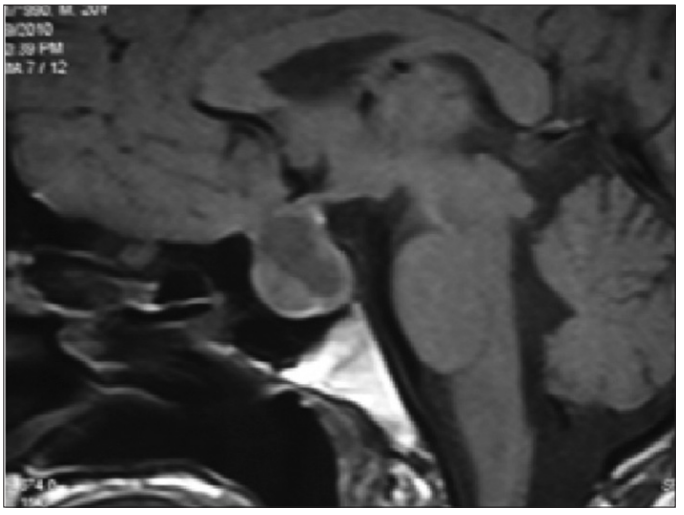

Figure 1. MRI of the pituitary gland shows a 15x25x25 mm intrasellar tumor characteristic of macroadenoma

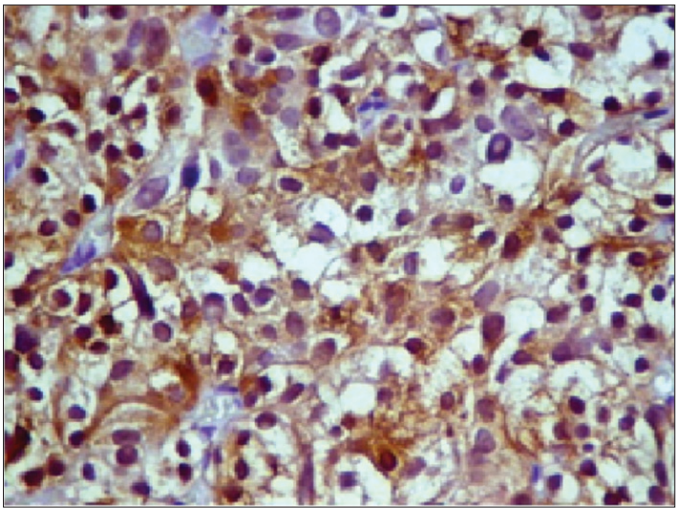

Figure 2. Immunohistochemical staining of the pituitary adenoma specimen was positive for FSH

Table 1. Basal morning serum hormone values

	Before Surgery	3 Months After Surgery	Normal Range
LH (µIU/mL)	1.49	1.5	0.8-7.6
FSH (µIU/mL)	93.7	1	0.7-1.1
TSH (µIU/mL)	1.32	2.3	0.4-4
fT4 (ng/dL)	1.2	1.1	0.8-1.9
Estrogen (pg/mL)	38.9	25	0-56
Prolactin (ng/mL)	27.7	12.3	2.5-17
Total testosterone (ng/mL)	502	568	262-1593
IGF-I (ng/mL)	228	214	150-562
GH (ng/ml)	0.3	0.28	
Serum cortisol level (µg/dL)	18	15	

negative for GH, prolactin, and adrenocorticotropic hormone. At follow-up, 6 weeks after surgery, serum FSH (1 µIU/mL) and prolactin (12.3 ng/mL) levels were normalized. The testicular volume was 22 cc 3 months post surgery. Residue was not observed via postoperative (3 months) MRI. The patient was being followed-up without any additional treatment.

Discussion

Non-functional pituitary adenomas are a type of pituitary tumor. Generally, LH and FSH levels are normal or low, and ineffective in non-functional pituitary macroadenomas. Isolated gonadotropin-secreting pituitary adenoma with an elevated FSH level is a rare condition (1,2). Excessive secretion of FSH is more common in men with gonadotropin-secreting adenomas, however, it does not cause any symptoms (3). The clinical symptoms are generally mild or even nonexistent. Patients with gonadotropin-secreting adenomas may present with symptoms such as visual defects, headache, cranial nerve palsies, and hypopituitarism. Gonadotroph tumors usually secrete their products inefficiently and in low concentrations and, therefore, very rarely cause a clinical syndrome other than sellar masses (4). Kwekkeboom et al. (5) reported that the most frequently observed symptoms of this tumor subtype were headache and secondary hypogonadism.

FSHoma is difficult to diagnose and is usually associated with ovarian hyperstimulation syndrome seen in women in pre-menopausal period (3,6). Full-blown ovarian hyperstimulation syndrome is characterized by massive ovarian enlargement, multiple cysts, and an increase in capillary permeability which may cause ascites or edema. This syndrome is usually associated with an extremely high serum estradiol level following gonadotropin therapy for ovulation induction (7). Testicular volume may increase in male patients with FSHoma (8-10).

In adults, normal testicular volume is between 15 and 25 mL. A testicular volume >95th percentile for age is considered macroorchidism (11). Testicular volume in the presented case at presentation was 45 mL. Some studies have reported that testicular volume positively correlated with height, weight and body mass index. Local tumors, lymphoma, severe primary hypothyroidism, congenital adrenal hyperplasia, and, rarely, FSHoma may associate with macroorchidism (12). FSHoma is specified in the etiology of macroorchidism, however, only a few cases have been reported (8-10). The presented patient aged 20 years and presented with a high FSH level and macroorchidism.

FSH and LH both play a role in the induction of spermatogenesis, and FSH stimulates testis growth (13,14). There is a positive relationship between testicular weight and the number of Sertoli cells, which have FSH receptors. FSH is a primary determinant of Sertoli cells and causes hyperplasia, proliferation and differentiation, however, IGF-I, vascular endothelial growth factor and transforming growth factor may play a role as a main determinant. Macroorchidism may be a consequence of a high number of Sertoli cells and is generally associated with elevated FSH levels. In contrast, Alvarez-Acevedo et al. (12) reported an increased number of Sertoli cells found on biopsy, with normal FSH levels, which might have been due to FSH receptor hyperfunction. LH-secreting adenomas have been found to be associated with high testicular volume and supranormal testosterone levels and 70%-100% of non-functional adenomas secrete free subunits that exhibit no biological activity (15). The presented case had a pituitary macroadenoma and a high FSH level, but a normal testosterone level.

Microscopic examination of pituitary adenoma specimens shows many gonadotropin cells with small secretory granules and, immunohistochemical examination shows pituitary gonadotropic hormone antibody positivity. The primary treatment is surgery. If the adenoma is surgically removed, FSH serum concentration and testicular volume decrease. The gonadotropin level should be measured in order to determine the response to surgery. There are no effective medical therapies for this subtype of adenoma. Additionally, some studies emphasize the effects of bromocriptine, cabergoline, and quinagolide therapies in the treatment of FSHoma (16). Radiation therapy may be required in cases of recurrent tumors. In the presented case, the FSH level was normal 6 weeks following pituitary surgery, at which time MRI showed the absence of pituitary adenoma.

The measurement of testicular volumes for both testes was done by detailed ultrasound scan at 3 and 8 months after the pituitary surgery. This showed a reduction in testicular size at 8 months after the surgery (10). Dahlqvist et al. (9) reported decreased testicular size in a patient with FSHoma-producing pituitary macroadenomas at follow-up, 3 months after surgery. Our case is in line with a report by Dahlqvist et al. that presented a case of FSH-producing pituitary macroadenomas with testicular enlargement and decreased testicular volumes at 3 months after pituitary surgery.

In conclusion, FSHoma is a rare condition and is associated with clinical symptoms that are generally mild, however, FSHoma may present as macroorchidism. Unusual coexistence of elevated serum FSH levels and large testicular size should be kept in mind in the differential diagnosis of FSHoma.

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