INTERNATIONAL JOURNAL OF
INTEGRATIVE AND
MODERN MEDICINE

The Role of Inactive Pituitary Adenoma in the Development of Hypogonadotropic Hypogonadism

Khamraeva Dilafruz Ismatullo kizi
Basic doctoral student at the RSSPMCE named after academician Yo.Kh.Turakulov

Kholova Dilorom Sharifovna
PhD, leading researcher of the scientific department "Neuroendocrinology with pituitary gland surgery"

Khalimova Zamira Yusufovna
MD, professor, deputy director for science at the RSSPMCE named after academician Yo.Kh.Turakulov

Abstract: This article explores the impact of inactive pituitary adenoma on the development of hypogonadotropic hypogonadism in women. A clinical study was conducted on 76 female patients aged 18 to 47 years to assess hormonal changes and clinical manifestations. The study found that hypogonadotropic hypogonadism is the most frequent clinical indication of pituitary insufficiency (67%) in tumors of the chiasmatic-sellar region. Key symptoms include menstrual irregularities, infertility, neurovegetative and urogenital disorders, and underdevelopment of the uterus and ovaries. The symptoms of hypogonadism typically emerge in the early stages of the disease, preceding the onset of visual and neurological impairments. The diagnosis is confirmed by reduced levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), and estradiol.

Keywords: Hypogonadotropic hypogonadism, pituitary adenoma, chiasmatic-sellar region tumors, amenorrhea, infertility, neurovegetative disorders, hormonal imbalance.

Introduction:

Pituitary adenomas occur in 94–77.6 cases per 100,000 individuals. Incidentalomas represent 14.7–22.2% and, in some cases, up to 30–35% of all pituitary adenomas. It is estimated that 80–90% of incidentalomas originate from gonadotrophs, whereas somatotrophs, lactotrophs, and corticotrophs are less common. The clinical "silence" of these adenomas is due to inefficient hormone production. The gender distribution shows a higher prevalence of lactotroph adenomas in women (1:1.28) and FSH/LH-producing adenomas in men (1:0.58 and 1:0, respectively). Despite the high prevalence of gonadotrophic adenomas, their clinical presentation is less understood, making them frequently categorized as "silent" tumors.

Hypogonadotropic Hypogonadism in Women:

Hypogonadism refers to the diminished activity of gonads—testes in men and ovaries in women—resulting in insufficient sex hormone production (testosterone in men, estrogen and progesterone in women) or insensitivity to these hormones. Female hypogonadism leads to ovarian dysfunction, often manifesting as anovulation, menstrual disorders (secondary amenorrhea or oligomenorrhea), and infertility. Secondary hypogonadism in women is characterized by menstrual cycle disturbances, infertility, sexual dysfunction, reduced bone density, and decreased muscle mass. Previously, sex steroids were believed to primarily target reproductive organs; however, modern research has demonstrated their impact on various non-reproductive systems, including the brain, cardiovascular, musculoskeletal, and urinary systems.

Objectives:

This study aims to investigate the role of inactive pituitary adenoma in the development of hypogonadotropic hypogonadism and assess the clinical and hormonal characteristics of affected women.

Materials and Methods:

The study involved 76 women aged 18 to 47 years (median age: 36) diagnosed with inactive pituitary adenoma. Clinical history, laboratory tests, and hormonal evaluations—including thyroid-stimulating hormone (TSH), free T4, adrenocorticotropic hormone (ACTH), cortisol, prolactin (PRL), LH, FSH, and estradiol—were analyzed. Data were processed using Microsoft Excel and Statistica 6.0, with statistical significance determined at $p<0.05$.

Results and Discussion:

Among the 76 patients, sexual dysfunction was the first clinical manifestation in 62% of cases. Menstrual irregularities were present in 62% of women, with primary amenorrhea in 14%, secondary amenorrhea in 41%, and oligomenorrhea in 7%. Infertility was the primary reason for seeking medical attention in 18% of cases. Headaches were the first symptom in 53% of patients, while 32% reported visual impairments. Unexplained weight gain was observed in 15%, weight loss in 4%, and galactorrhea in 3% of women.

Main Symptoms at Disease Onset:

- Sexual dysfunction: 62%
- Headache: 53%
- Visual impairment: 32%
- Increased thirst and polyuria: 11%
- Unexplained weight gain: 15%
- Weight loss: 4%
- Galactorrhea: 4%

The duration from symptom onset to diagnosis ranged from six months to 15 years. In over half of the cases, hypogonadism symptoms were the first clinical signs, emerging before neurological or visual disturbances. Primary clinical indicators were identified in 67% of patients with chiasmatic-sellar region tumors, confirmed through hormonal and ultrasound assessments.

Clinical Features of Hypogonadotropic Hypogonadism in Women with Inactive Pituitary Adenoma:

- Menstrual disorders (71%)
  - ✓ Primary amenorrhea: 31%
  - ✓ Secondary amenorrhea: 66%
  - ✓ Oligomenorrhea: 3%
- Infertility (25%)
  - ✓ Primary infertility: 3%
  - ✓ Secondary infertility: 22%
  - ✓ Neurovegetative symptoms (75%)
  - ✓ Urogenital disorders (63%)
  - ✓ Galactorrhea (9%)

Ultrasound revealed significantly smaller uterine and ovarian sizes in women with primary amenorrhea compared to those with secondary amenorrhea, indicating pronounced infantilism. The time from menstrual irregularity onset to diagnosis was significantly shorter in primary amenorrhea cases.

Hormonal Findings: Patients with clinical hypogonadism exhibited significantly lower levels of LH, FSH, and estradiol ($p<0.001$). Neurovegetative symptoms such as hot flashes, palpitations, and anxiety were observed in 75% of women, with no significant differences between those with shorter and longer amenorrhea durations.

Conclusion:

1. Hypogonadotropic hypogonadism is the most common (67%) clinical manifestation of pituitary insufficiency in chiasmatic-sellar tumors.
2. The primary symptoms include menstrual irregularities (amenorrhea, oligomenorrhea), infertility, neurovegetative (75%) and urogenital (63%) disorders, and uterine and ovarian hypoplasia (100%).
3. Symptoms of hypogonadotropic hypogonadism appear early, often 2.1 ±1.4 years before visual or neurological symptoms.
4. Hormonal analysis confirms significant reductions in LH, FSH, and estradiol levels in 67% of cases.

Clinical Significance: Early diagnosis of hypogonadotropic hypogonadism is crucial to preventing long-term complications and improving patient outcomes. Diagnostic tools include hormone level assessments, imaging studies, and genetic testing. Treatment options vary depending on the underlying cause and may involve hormone replacement therapy, infertility treatments, and, in some cases, surgical interventions.

References:

1. Sullivan KA, Silverman A-J. 1993 The ontogeny of gonadotropin-releasing hormone neurons in the chick. Neuroendocrinology. 58:597-608.
2. Boyar RM, Finkelstein JW, Witkin M, Kapen S, Weitzman E, Hellman L. 1973 Studies of endocrine function in "isolated" GnRH deficiency. Journal of Clinical Endocrinology and Metabolism. 36:64-72.
3. Kallmann FJ, Schoenfeld WA. 1944 The genetic aspects of primary eunuchoidism. American Journal of Mental Deficiency. 158:203-236.
4. Fromantin M, Gineste J, Didier A, Rouvier J. 1973 Les impuberismes et les hypogonadismes a l'incorporation. Probl Actuels Endocrinol Nutr. 16:179-199.
5. Resorlu B, Abdulmajed MI, Kara C, Unsal A, Aydos K. Is intracyto-plasmic sperm injection essential for the treatment of hypogonado-trophic hypogonadism? A comparison between idiopathic and secondary hypogonadotrophic hypogonadism. Hum Fertil (Camb). 2009;12(4):204-8, http://dx.doi.org/10.3109/14647270903331139
6. 22. Bakircioglu ME, Erden HF, Ciray HN, Bayazit N, Bahceci M. Gonadotrophin therapy in combination with ICSI in men with hypogonadotrophic hypogonadism. Reprod Biomed Online. 2007; 15(2):156-60, http://dx.doi.org/10.1016/S1472-6483(10)60703-1
7. 23. Zorn B, Pfeifer M, Virant-Klun I, Meden-Vrtovec H. Intracytoplasmic sperm injection as a complement to gonadotrophin treatment in infertile men with hypogonadotrophic hypogonadism. Int J Androl. 2005; 28(4):202-7.
8. 24. Fahmy I, Kamal A, Shamloul R, Mansour R, Serour G, Aboulghar M. ICSI using testicular sperm in male hypogonadotrophic hypogonadism unresponsive to gonadotrophin therapy. Hum Reprod. 2004;19(7):1558-61, http://dx.doi.org/10.1093/humrep/deh243

9. 25. Vaitukaitis JL, Ross GT, Braunstein GD, Rayford PL. Gonadotropins and their subunits: basic and clinical studies. Recent Prog Horm Res. 1976;32:289-331.

10. 26. Gonadotropin preparations: past, present, and future perspectives. Fertil Steril. 2008;90(5 Suppl):S13-20.

11. 27. Bosch E. Recombinant human follicular stimulating hormone and recombinant human luteinizing hormone in a 2:1 ratio combination. Pharmacological characteristics and clinical applications. Expert Opin Biol Ther.2010;10(6):1001-9, http://dx.doi.org/10.1517/14712598.2010.485607

12. 28. Esteves S, Papanikolaou V. Clinical Efficacy, Safety and Tolerability of Recombinant hCG to Restore Spermatogenesis and Androgenic Status of Hypogonadotropic Hypogonadism Males. Fertil Steril. 2011;96(3):S230, http://dx.doi.org/10.1016/j.fertnstert.2011.07.884

13. Misell LM, Holochwost D, Boban D, Santi N, Shefi S, Hellerstein MK, et al. A stable isotope-mass spectrometric method for measuring human spermatogenesis kinetics in vivo. J Urol. 2006;175(1):242-6; discussion 6.